PSMU
DEPARTMENT OF MICROBIOLOGY, VIROLOGY AND IMMUNOLOGY

RNA VIRUSES.

GENERAL CHARACTERISTICS.

ORTHOMYXOVIRUSES.
PARAMYXOVIRUSES.
PICORNAVIRUSES.

For two-way communication

between the lecturer and students during the lecture,
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ORTHOMYXOVIRUSES

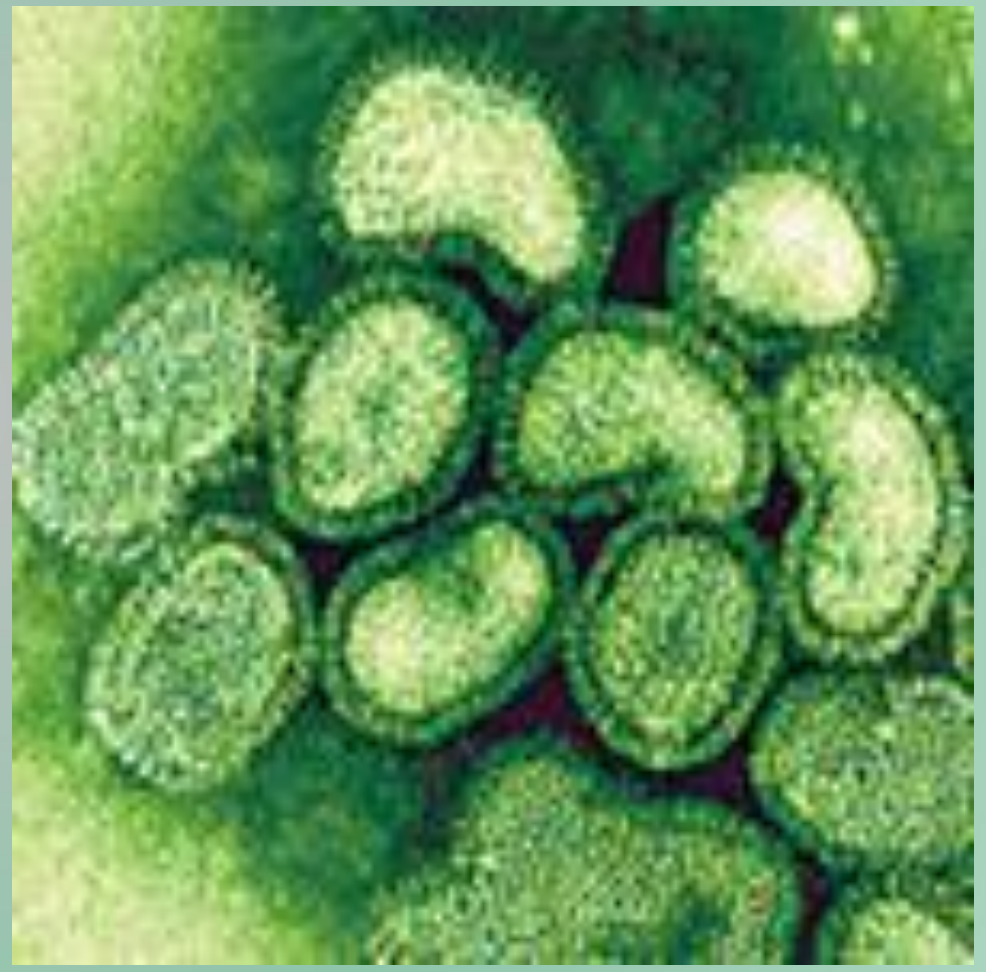
"SPANISH" IS A VIRUS THAT BROKE OUT AND DIED DURING THE FIRST WORLD WAR.

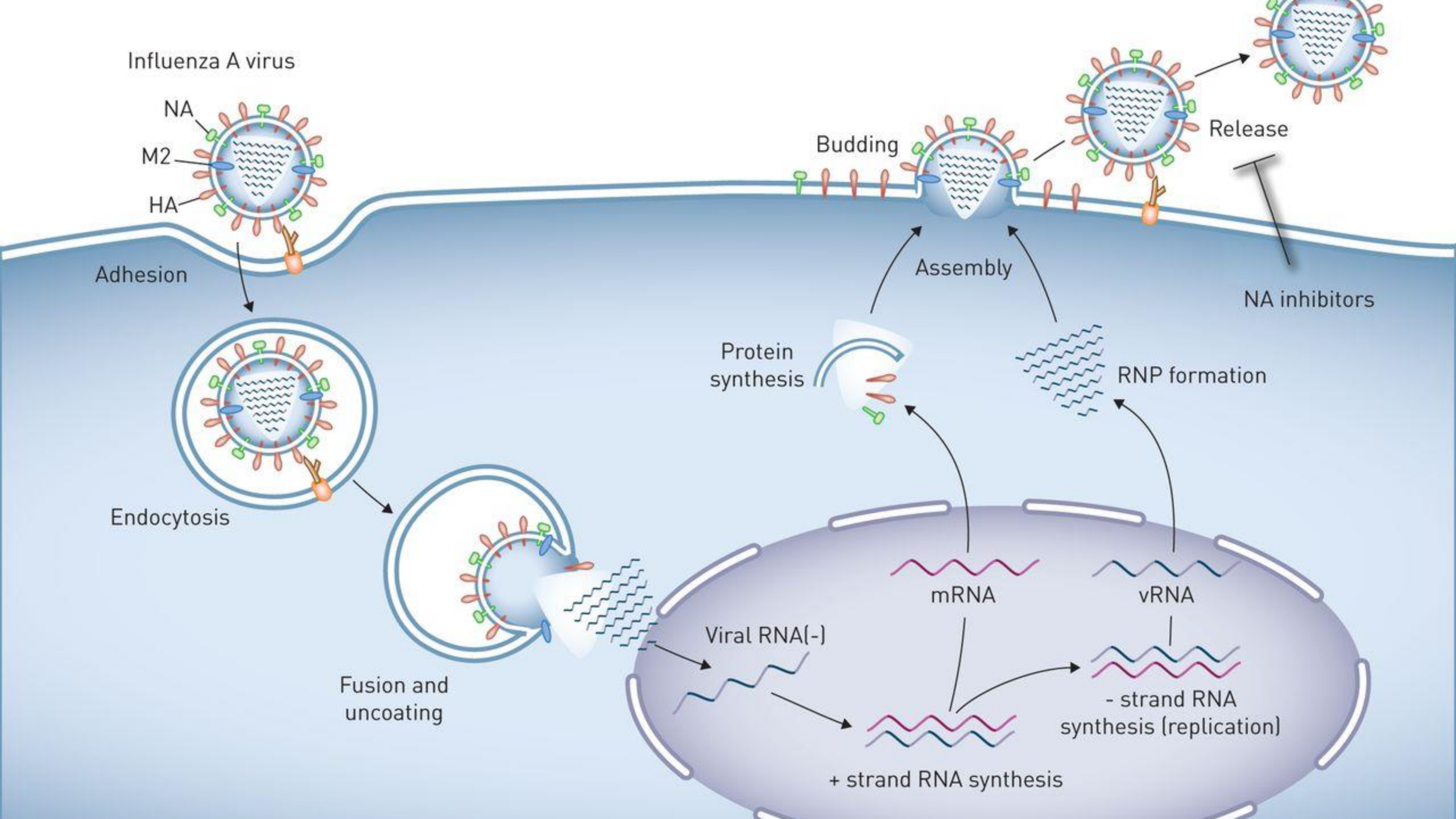
IN 1918, THE DISEASE CAUSED THE LARGEST MORTALITY OF THE INFLUENZA PANDEMIC IN HUMAN HISTORY.

IN THE YEARS 1918-1919 (18 MONTHS) AROUND 50-100 MILLION PEOPLE, OR 2.6-5.2% OF THE EARTH'S POPULATION, DIED WORLDWIDE FROM SPANISH. ABOUT 400 MILLION PEOPLE, OR MORE THAN 20% OF THE WORLD'S POPULATION, WERE INFECTED. THE PANDEMIC BEGAN IN THE LAST MONTHS OF WORLD WAR I AND QUICKLY ECLIPSED THIS LARGEST BLOODSHED BY THE SCALE OF THE VICTIMS.

MORPHOLOGY AND STRUCTURE OF INFLUENZA VIRUS

- **Family Orthomyxoviridae**
- **The influenza virus has a spherical shape, diameter 80 - 120 nanometers.**
- **There filamentous form several micrometers in length.**
- **The influenza virus - referred to as complex virion.**
- **Negative sense single-stranded RNA genome segmented in 8 pieces.**




Influenza A virus
NA
M2
HA
Adhesion
Endocytosis
Fusion and uncoating
Viral RNA(-)
mRNA
vRNA
+ strand RNA synthesis
- strand RNA synthesis (replication)
Protein synthesis
RNP formation
Assembly
Budding
Release
NA inhibitors

GENERA ORTHOMYXOVIRUS

Influenza virus is divided into three serotypes by ribonucleoprotein and matrix protein antigens:

- **- Influenza virus type A, affects Human and some animal species (Avian and Swine).**
- **- Influenza virus type B, affecting only a man.**
- **- Influenza virus type C, affects only a man.**

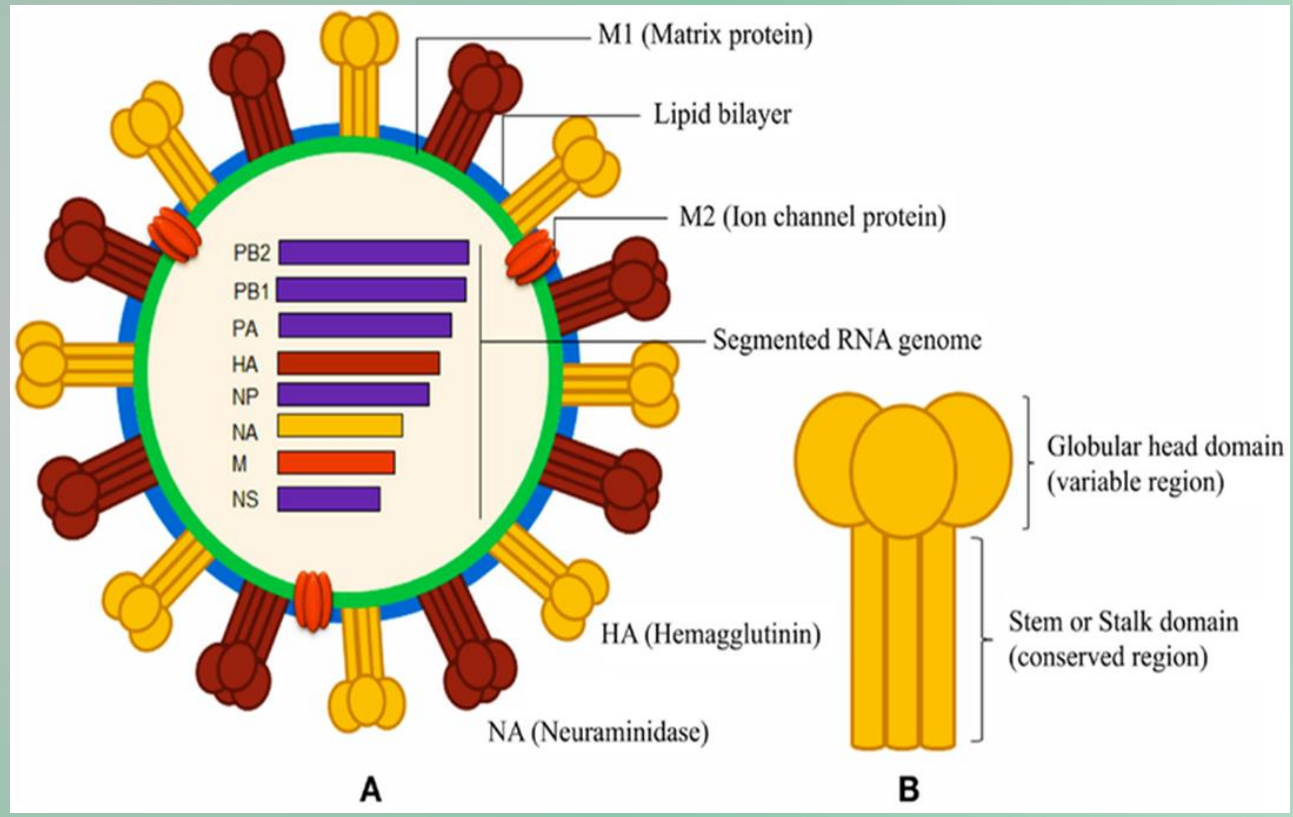
INFLUENZA VIRUS
SUBTYPES OF SEROTYPE A

- **Has two types of spikes (peplomers):**
- **Hemagglutinin (H).**

4 subtypes have been found in human isolates (H 1-3, 5 from 15).

- **Neuraminidase (N).**

2 subtypes have been found in human isolates (N 1, 2 from 19).



HEMAGGLUTININ (H)

-The main strain specific viral antigen with a high degree of uncontrolled variability.

-It is the most immunogenic protein that causes the formation of protective antibodies.

-Hemagglutinin acts as a cellular receptor recognition, virus attachment to cells, followed by penetration.

NEURAMINIDASE (NA)

- An enzyme the virus, which catalyzes the destruction of neuraminic (sialic) acid, it leads to separation of the virus from a cell.

-NA also has antigenic properties. Antibodies formed against NA have protective properties, but does not neutralize infectious activity of the virus.

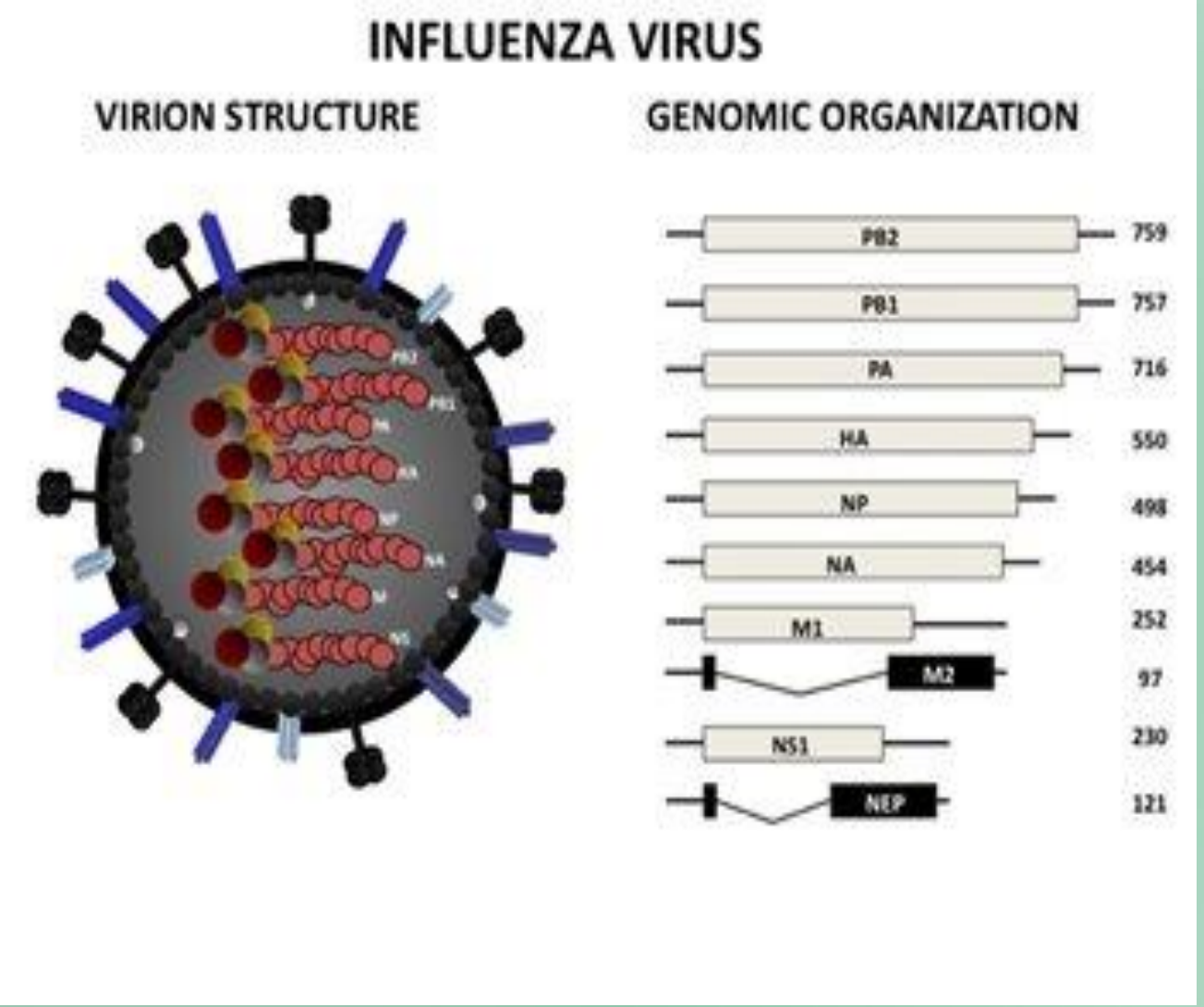
ANTIGENIC VARIATION OF INFLUENZA VIRUS

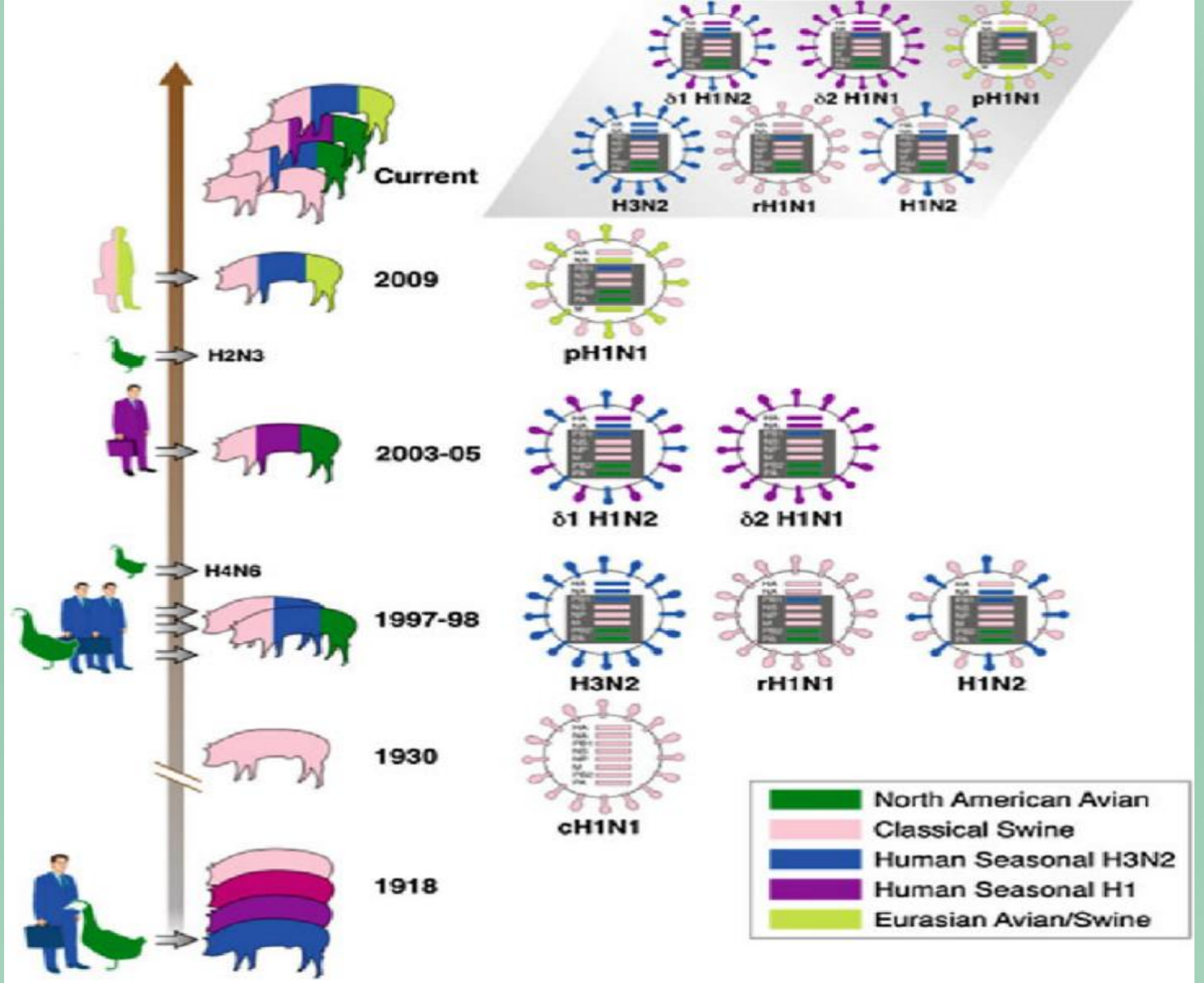
Antigenic drift - These are small changes in the genes of influenza viruses that happen continually over time as the virus replicates. This makes change antigenic properties of hemagglutinins and neuraminidase.

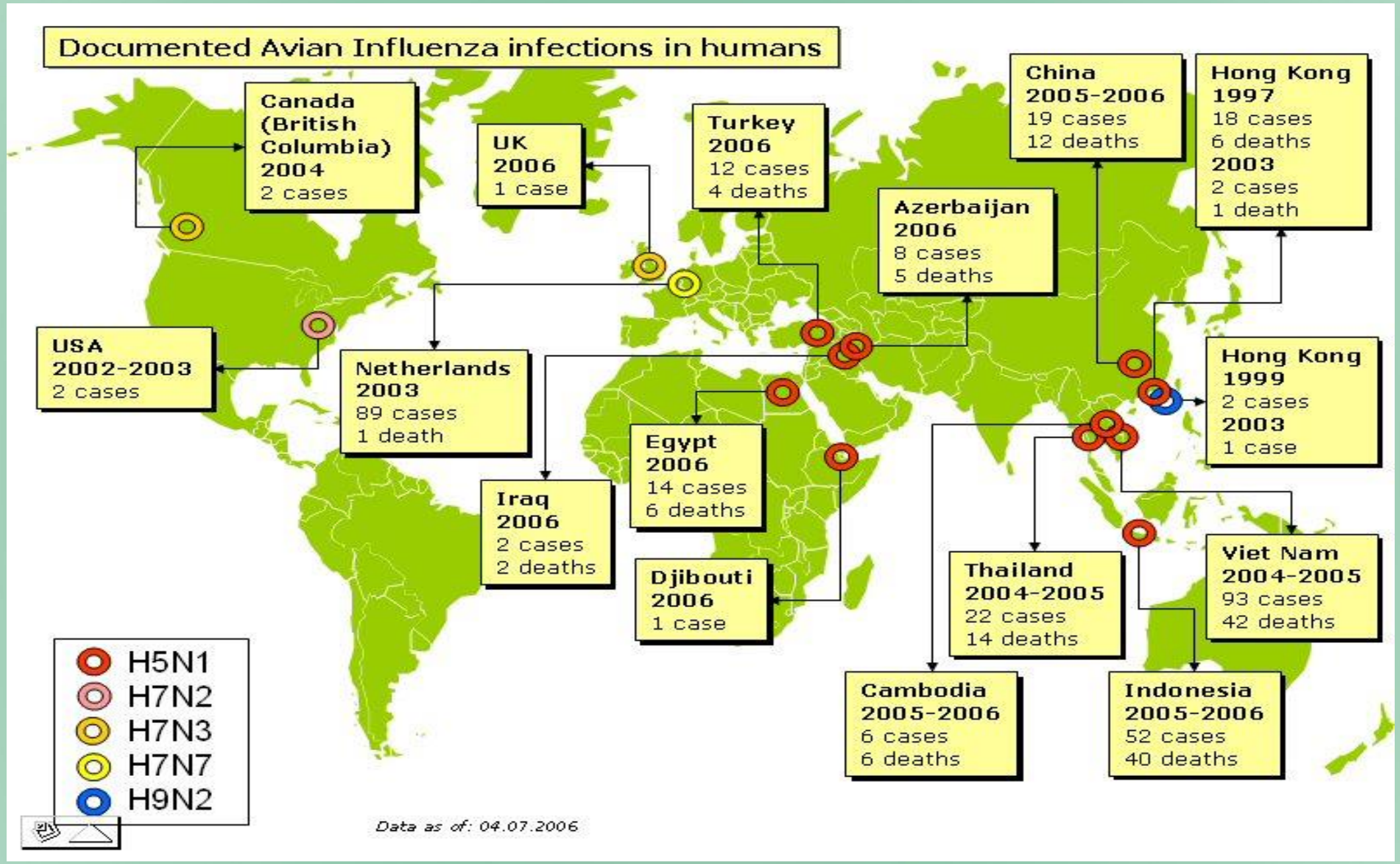
Antigenic shift - complete replacement of the gene leads to qualitative changes in hemagglutinins and neuraminidase subtype and the emergence of new principal antigenic variants virus.

INFLUENZA VIRUS

RNA “-” genome segmented in 8 pieces




Current
2009
H2N3
2003-05
H4N6
1997-98
1930
1918
δ1 H1N2
δ2 H1N1
pH1N1
H3N2
rH1N1
H1N2
pH1N1
δ1 H1N2
δ2 H1N1
H3N2
rH1N1
H1N2
cH1N1
North American Avian
Classical Swine
Human Seasonal H3N2
Human Seasonal H1
Eurasian Avian/Swine


Documented Avian Influenza infections in humans
Canada (British Columbia) 2004
2 cases
UK 2006
1 case
Turkey 2006
12 cases
4 deaths
China 2005-2006
19 cases
12 deaths
Hong Kong 1997
18 cases
6 deaths
2003
2 cases
1 death
Azerbaijan 2006
8 cases
5 deaths
USA 2002-2003
2 cases
Netherlands 2003
89 cases
1 death
Hong Kong 1999
2 cases
2003
1 case
Egypt 2006
14 cases
6 deaths
Iraq 2006
2 cases
2 deaths
Djibouti 2006
1 case
Thailand 2004-2005
22 cases
14 deaths
Viet Nam 2004-2005
93 cases
42 deaths
Cambodia 2005-2006
6 cases
6 deaths
Indonesia 2005-2006
52 cases
40 deaths
H5N1
H7N2
H7N3
H7N7
H9N2
Data as of: 04.07.2006

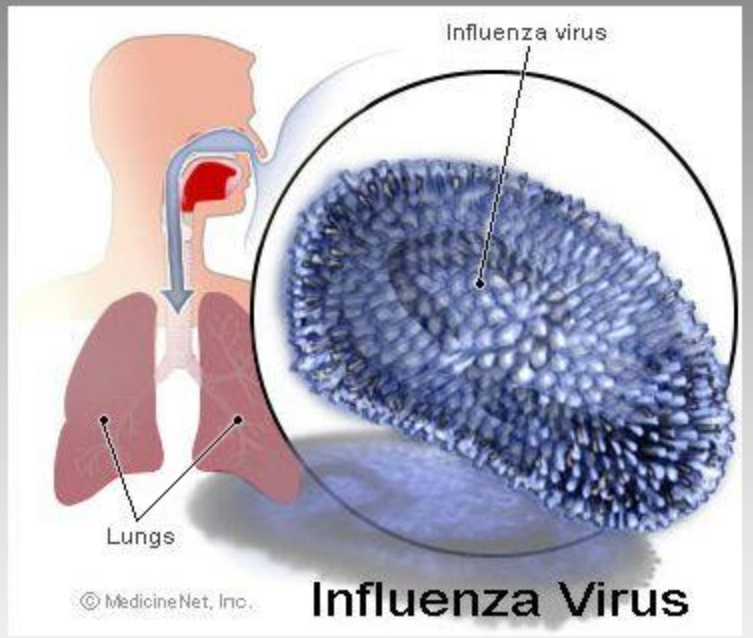
EPIDEMIOLOGY OF INFLUENZA.

- **The source of the pathogen is a sick person or carrier.**
- **The mechanism of pathogen transmission - airborne or aerosol.**
- **Susceptible organism - man.**
- **Groups of health risk: people aged over 65, persons with chronic respiratory disorders and cardiovascular system, pregnant (2nd, 3rd trimester).**

Influenza: Pathogenesis Entry Route

Influenza is often classified as a respiratory disease, entering through the respiratory tract.

The virus is passed from person to person via aerosolized droplets exhaled from the infected host. The new host inhales the aerosol and the viruses are deposited along the respiratory tract.



Pathophysiology

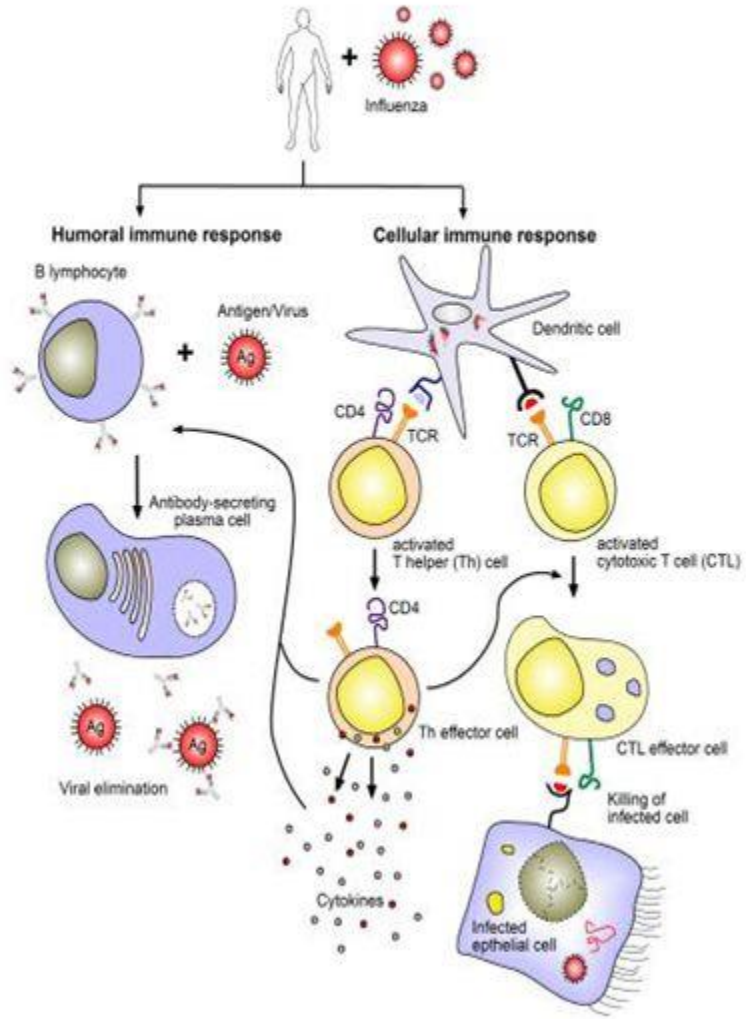
- Influenza virus can infect both upper and lower respiratory tracts. Sialic acid on epithelial cells are the receptors.
- The typical incubation period of influenza is 24 hours to 4 days with average: 2 days.
- Children's are more readily affected than adults.

Easily spread
Rarely fatal

Spreads slowly
Often fatal

Pathogenesis

- The initial event in influenza is infection of the respiratory epithelium
- The cells eventually become necrotic and desquamate
- The degree of viral replication is an important factor in pathogenesis
- Despite systemic signs and symptoms such as fever, myalgias, influenza virus has only rarely been detected in extrapulmonary sites
- Pathogenesis of systemic symptoms in influenza is related to inflammatory mediators(cytokines)



LABORATORY DIAGNOSIS

- 1. **Express Diagnostics – PCR, ELISA, IF.**

- **2. Virological research.**

- **3. Serological examination. For serological studies using paired sera**

(hemagglutination inhibition, complement fixation tests)

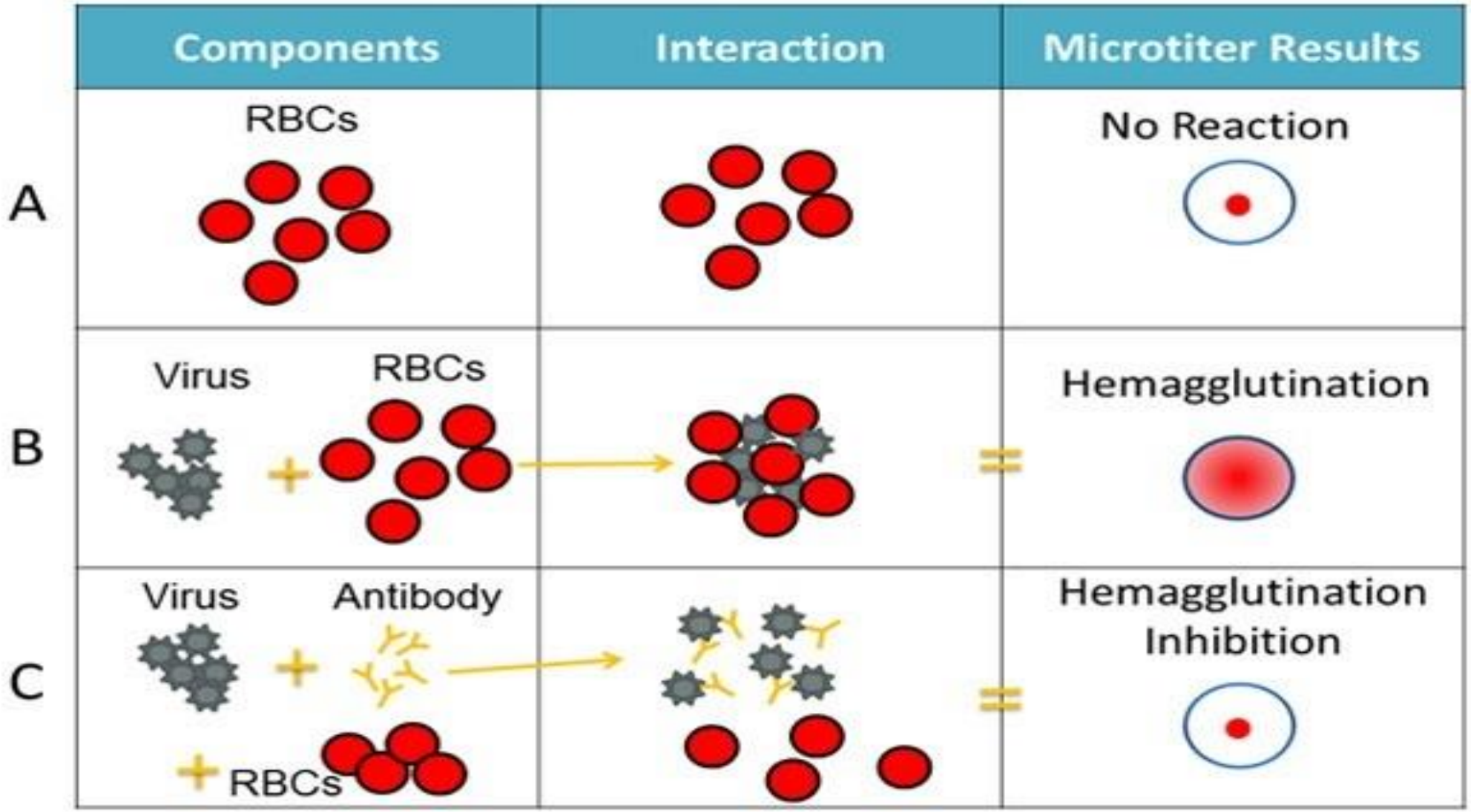
CULTIVATION OF INFLUENZA VIRUS

Influenza viruses are cultivated in chicken embryos and cell cultures.

They show their cytopathogenic action in cell culture of human and monkey kidneys.

Cytoplasmic inclusions are the nonstructural proteins.

DETECTION AND IDENTIFICATION OF VIRUS



IMMUNOPROPHYLAXIS

Vaccines:

- Inactivated
- Subunite
- Recombinant
- Live attenuated

CHEMICAL DRUGS

- **Chemoprophylaxis**:

-Amantadine

-Rimantadine

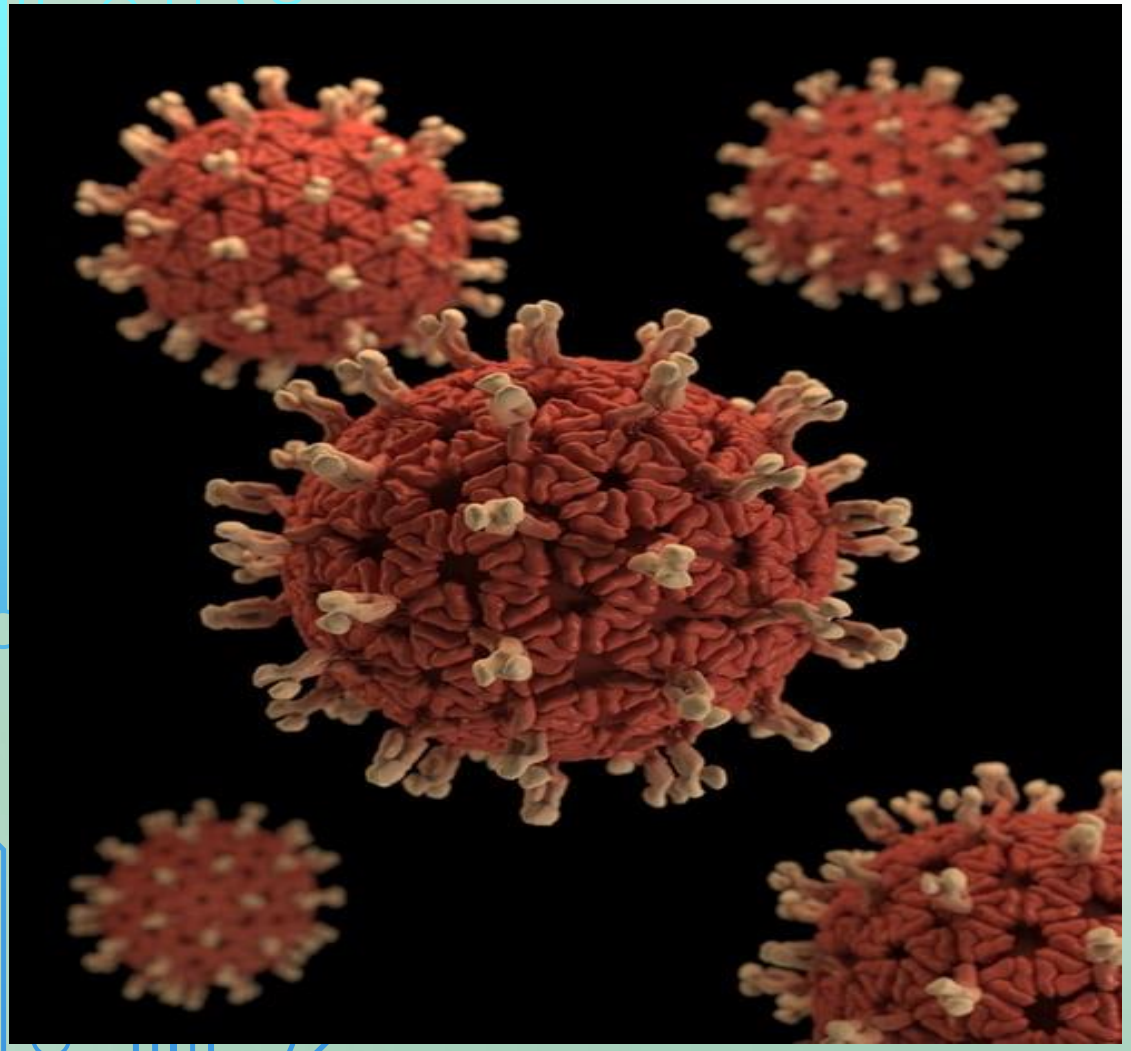
- **Treatment:**

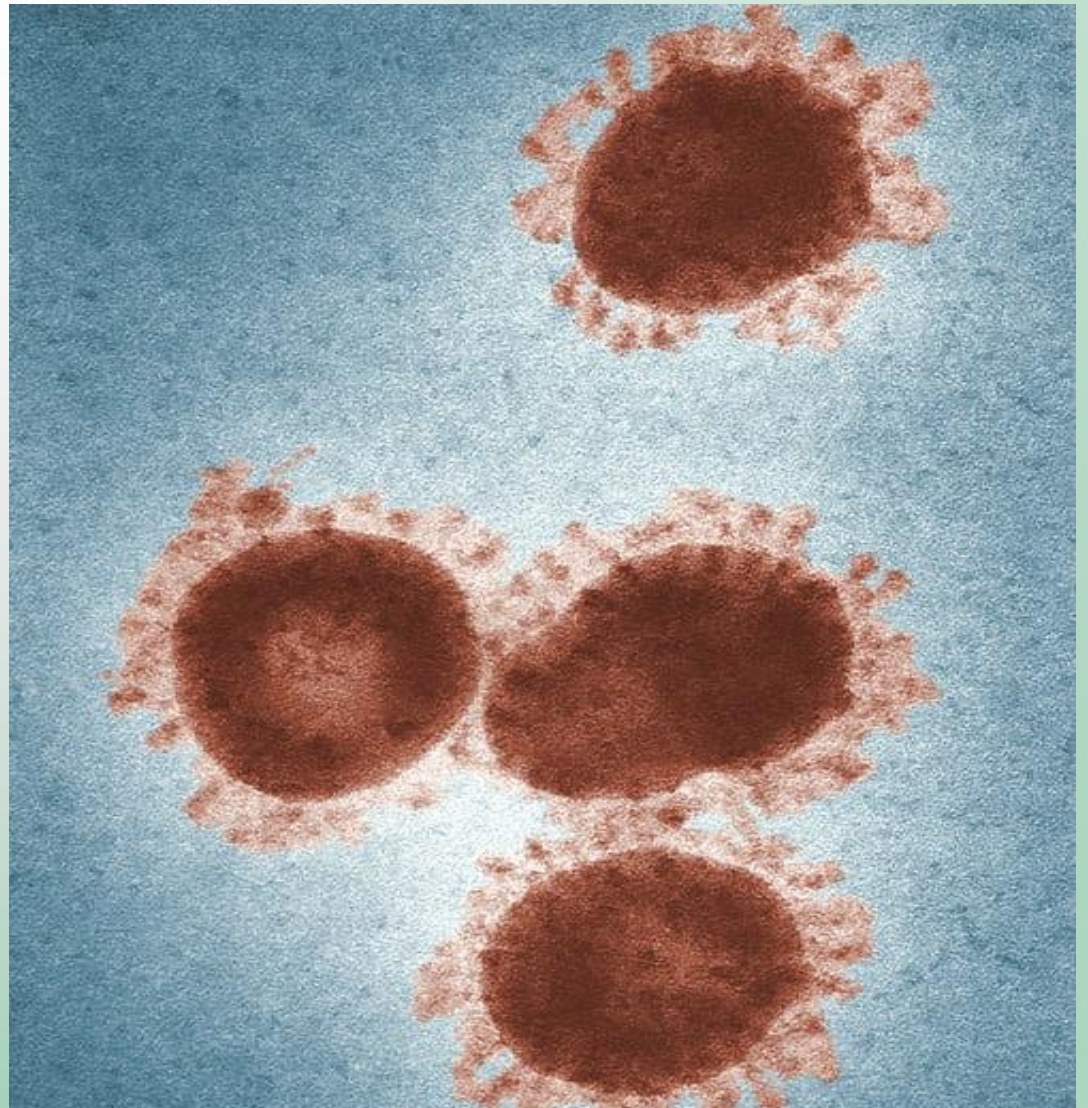
-Amantadine

-Rimantadine

- Zanamivir

CORONAVIRUSES, SARS-COV-2 COVID-2019





EPIDEMIOLOGY

CORONAVIRUSES ARE DISTRIBUTED WORLDWIDE.

IT CAUSE 15-30% OF ALL COLDS.

CORONAVIRUSES ARE COMMONLY ASSOCIATED WITH ACUTE RESPIRATORY DISEASE IN THE ELDERY.

CORONAVIRUSES ARE TRANSMITTED BY CONTACT WITH RESPIRATORY DROPLETS, CONTAMINATED SURFACES, END FOMITES.

ANOTHER CORONAVIRUS DISEASES

Name	Year	Region	Cases	Deaths	Fatality rate
SARS Severe acute respiratory syndrome	2002	Southern China	Over 8000	Over 800	9,6%
MERS Middle East respiratory syndrome	2012	Saudi Arabia	2506	912	36,4%

- Coronavirus disease (COVID-19) represents global public health concern and WHO declares public health emergency.
- The phylogenetic analysis revealed that COVID-19 is potentially a zoonotic virus.
- Special attention is necessary to protect or reduce transmission in susceptible populations.
- COVID-19 develops intestinal symptoms like diarrhea, while low percentage of MERS-CoV or SARS-CoV patients had diarrhea.
- Identification of novel chemotherapeutic drugs for treating COVID-19 infections is urgently warranted.

CORONAVIRUSES, SARS-COV-2 COVID-2019

VIROLOGISTS BELIEVE THAT COMPLETELY DEFEAT THE CORONAVIRUS

COVID-2019 WILL NOT WORK, IT WILL BE FIXED IN THE HUMAN POPULATION AND WILL MANIFEST SEASONALLY, LIKE THE FLU.

THE STRAIN CAN BECOME ENTRENCHED AMONG THOSE PEOPLE WHO HAVE BEEN ASYMPTOMATIC FOR A LONG TIME BY RELEASING THE VIRUS INTO THE ENVIRONMENT.

COVID-19 WILL BE AFFECTED BY EPIDEMIC WAVES THE MOST SUSCEPTIBLE PART OF THE POPULATION ANNUALLY: THE ELDERLY, CHRONIC PATIENTS AND THOSE WHO HAVE IMMUNODEFICIENCY.

WANG CHEN, VICE-PRESIDENT OF THE ACADEMY OF SCIENCES OF CHINA, REPORTED THAT ATYPICAL PNEUMONIA (SARS, MERS) HAD HIGH SPREAD AND MORTALITY PROPERTIES, BUT SUCH COMBINATION DID NOT ALLOW THEM TO REMAIN IN THE HUMAN POPULATION FOR LONG TIME.

PARAMYXOVIRUSES

FAMILY PARAMYXOVIRIDAE

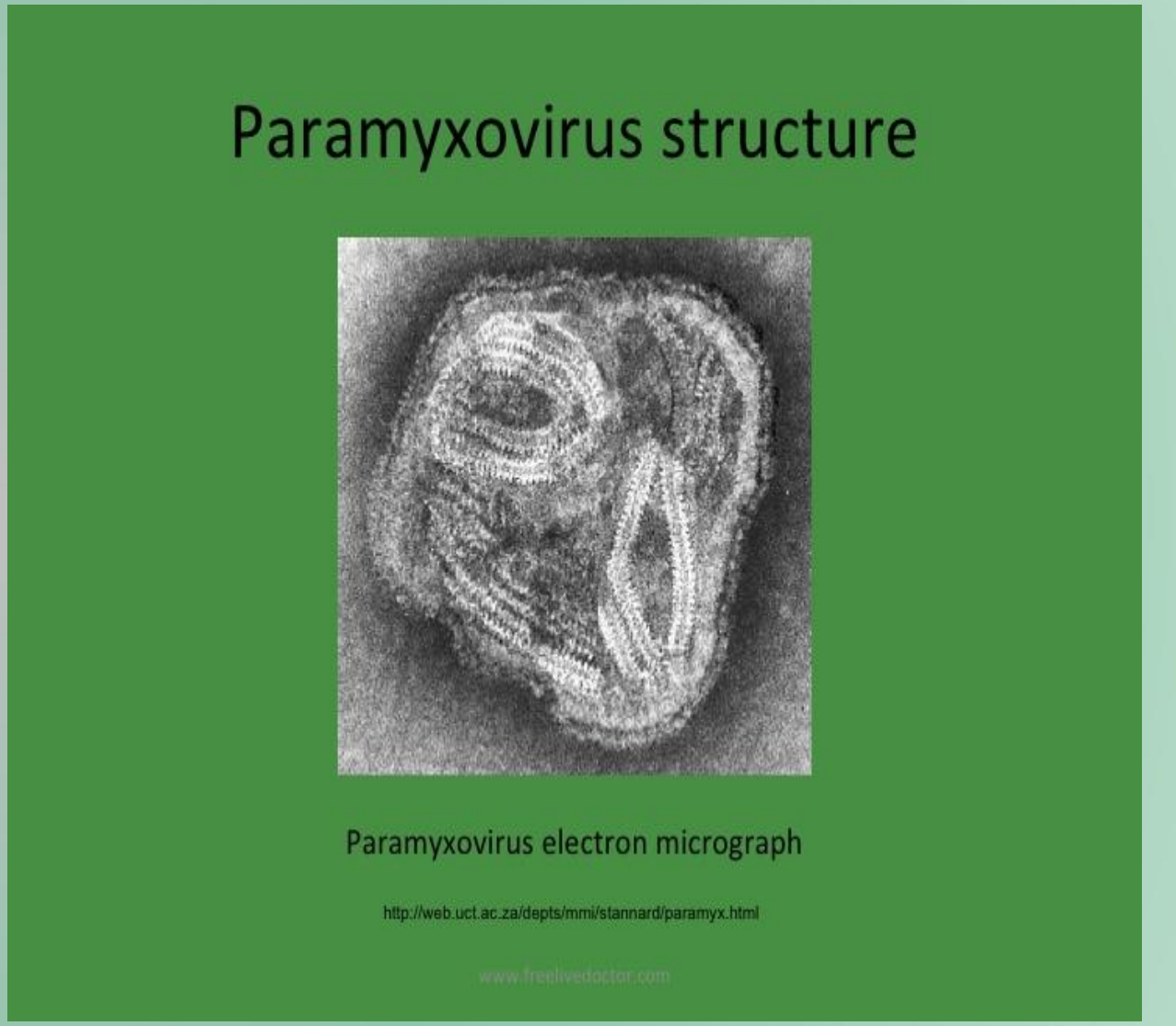
1. Genera Rubulavirus (**Mumps virus**)
2. Genera Parainfluenzavirus (types 1-4)
3. Genera Pneumovirus (respiratory syncytial virus)
4. Genera Morbillivirus (**Measles virus**)

New: Viruses Hendra, Nipah, Metapneumovirus

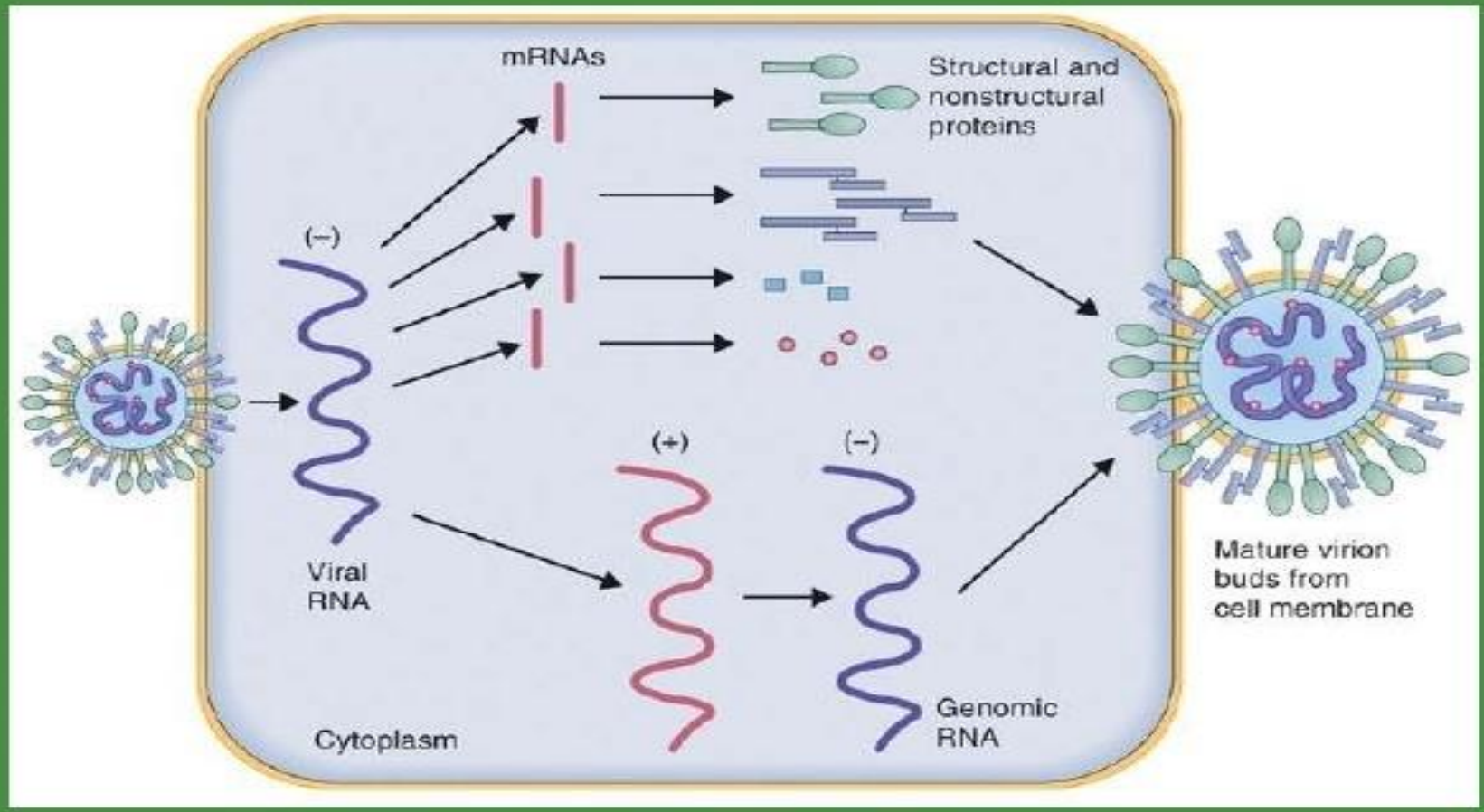
FAMILY PARAMYXOVIRIDAE

Morphology and structure

- Complex virion.
- Viruses have a spherical shape, have hemagglutinin and neuraminidase.
- Negative sense single-stranded RNA genome, no genetic recombination or antigenic variation.



Mononegavirales replication



From Schaechter's Mechanisms of Microbial Disease; 4th ed.; Engleberg, DiRita & Dermody; Lippincott, Williams & Wilkins; 2007; Fig. 34-2

PARAINFLUENZA VIRUS

- Epidemiology:

  The source of the pathogen is a sick person or carrier.

- The mechanism of pathogen transmission:

  airborne or aerosol.

- Susceptible organism - man.

  The most vulnerable are children. Seasonality is typical for parainfluenza.

PARAINFLUENZA

- **Pathogenesis**:

- Virus reproduces in epithelial cells of the upper respiratory tract and enters to the blood, causing virusemia.

Can be:

- - Larynhotraheobronhit
- - Bronchitis and pneumonia
- - Subclinical catar of the upper respiratory tract

LABORATORY DIAGNOSIS

- Paraflue infection can be distinguished only by laboratory diagnostic methods.

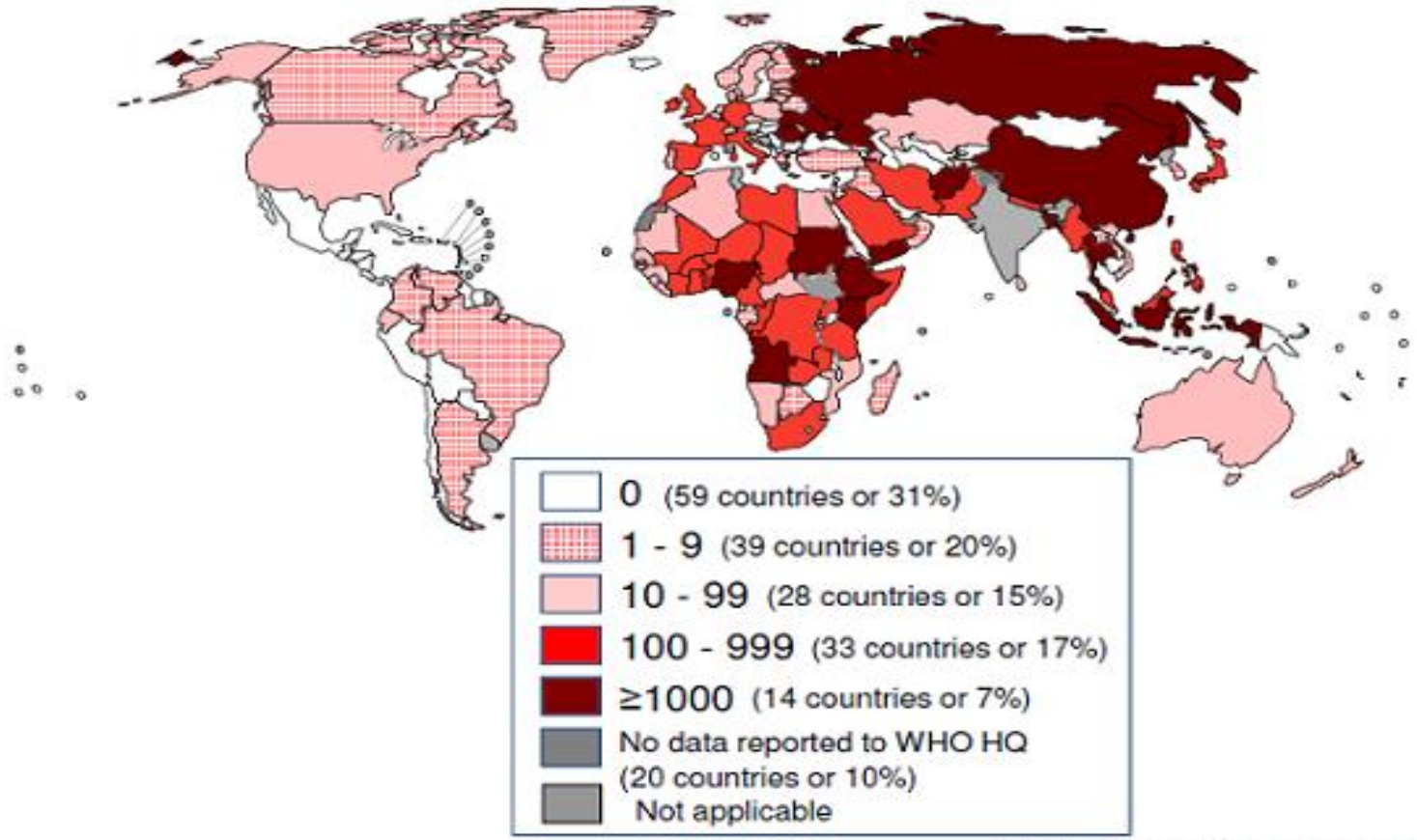
- 1. Virological research.

- 2. Serological examination.

- 3. Express methods: PCR, IF, ELISA

MIASLES VIRUS

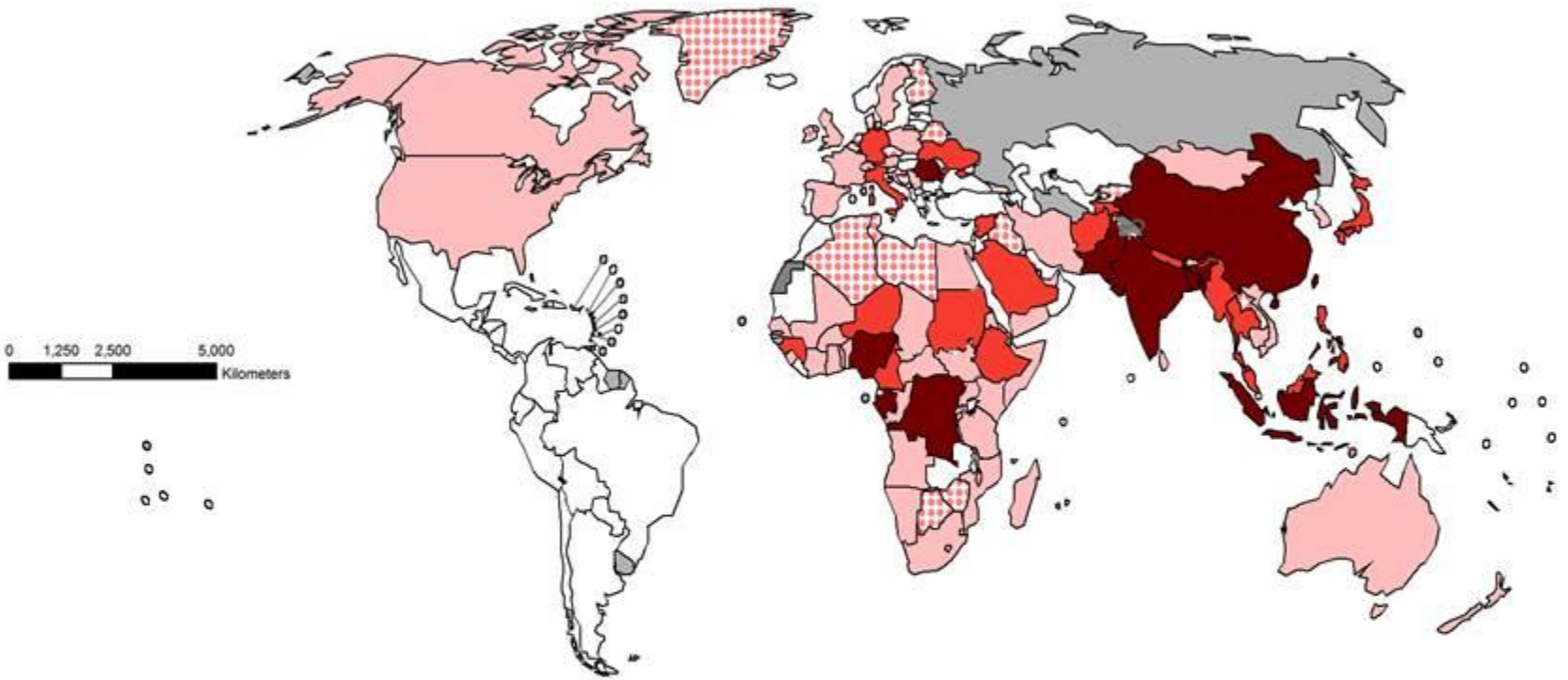
Number of Reported Measles Cases with onset date from Jan 2012 to Jul 2012



Data source: surveillance DEF file
Data in HQ as of 8 August 2012

WHO

Number of Reported Measles Cases with onset date from Sep 2016 to Feb 2017 (6M period)



Data source: surveillance DEF file
Data in HQ as of 11 April 2017

WHO

Epidemiology

- Occurs throughout the world
- Interruption of indigenous transmission of measles achieved in the USA and some parts of Western Hemisphere
- **Host** – man, no animal reservoir, no asymptomatic carrier state
- **Agent** – Measles virus (MV)
- **Transmission** – respiratory airborne
- **Temporal pattern** – late winter and spring
- **Communicability** – 4 days before to 4 days after rash onset, highly communicable, > 90% secondary attack rates

Measles-Pathogenesis

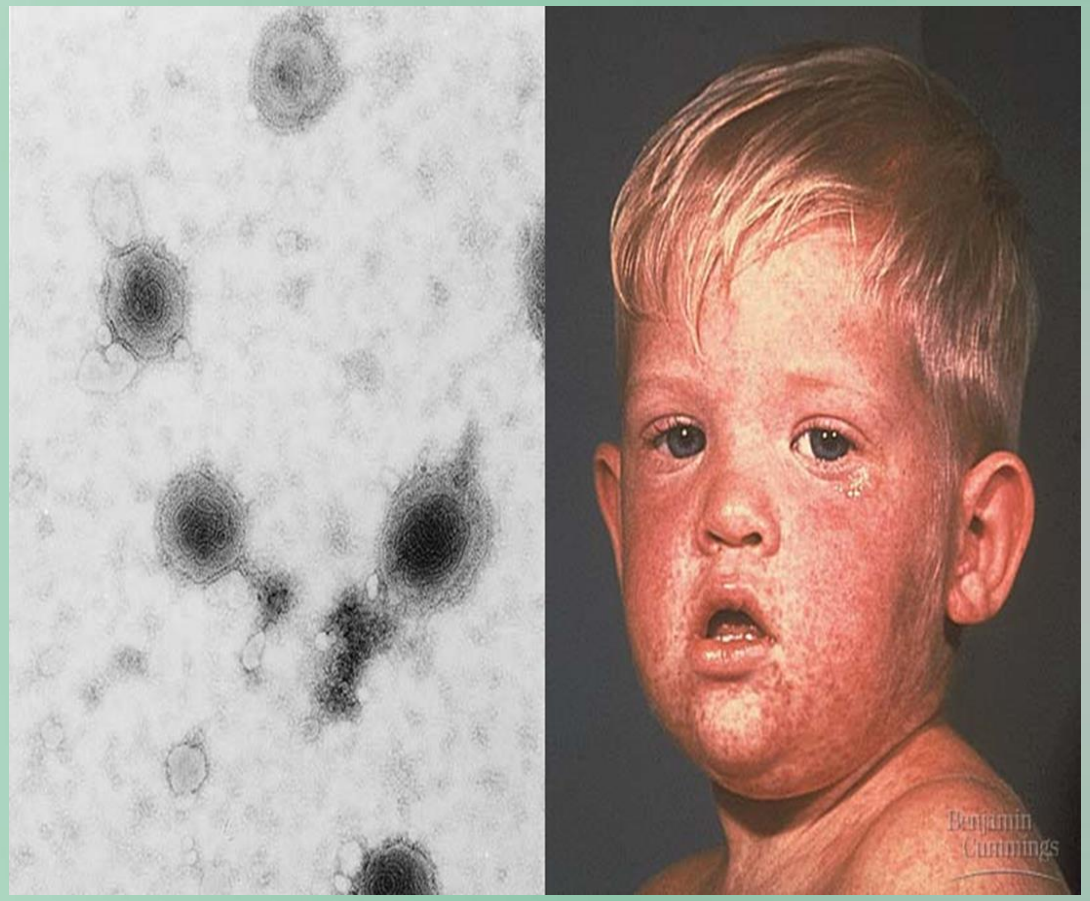
Incubation period: measles virus migrates to regional lymph nodes → primary viremia- disseminates the virus to the reticuloendothelial system → secondary viremia spreads virus to body surfaces

The **prodromal illness** begins after the secondary viremia; associated with epithelial necrosis, giant cell formation & virus shedding

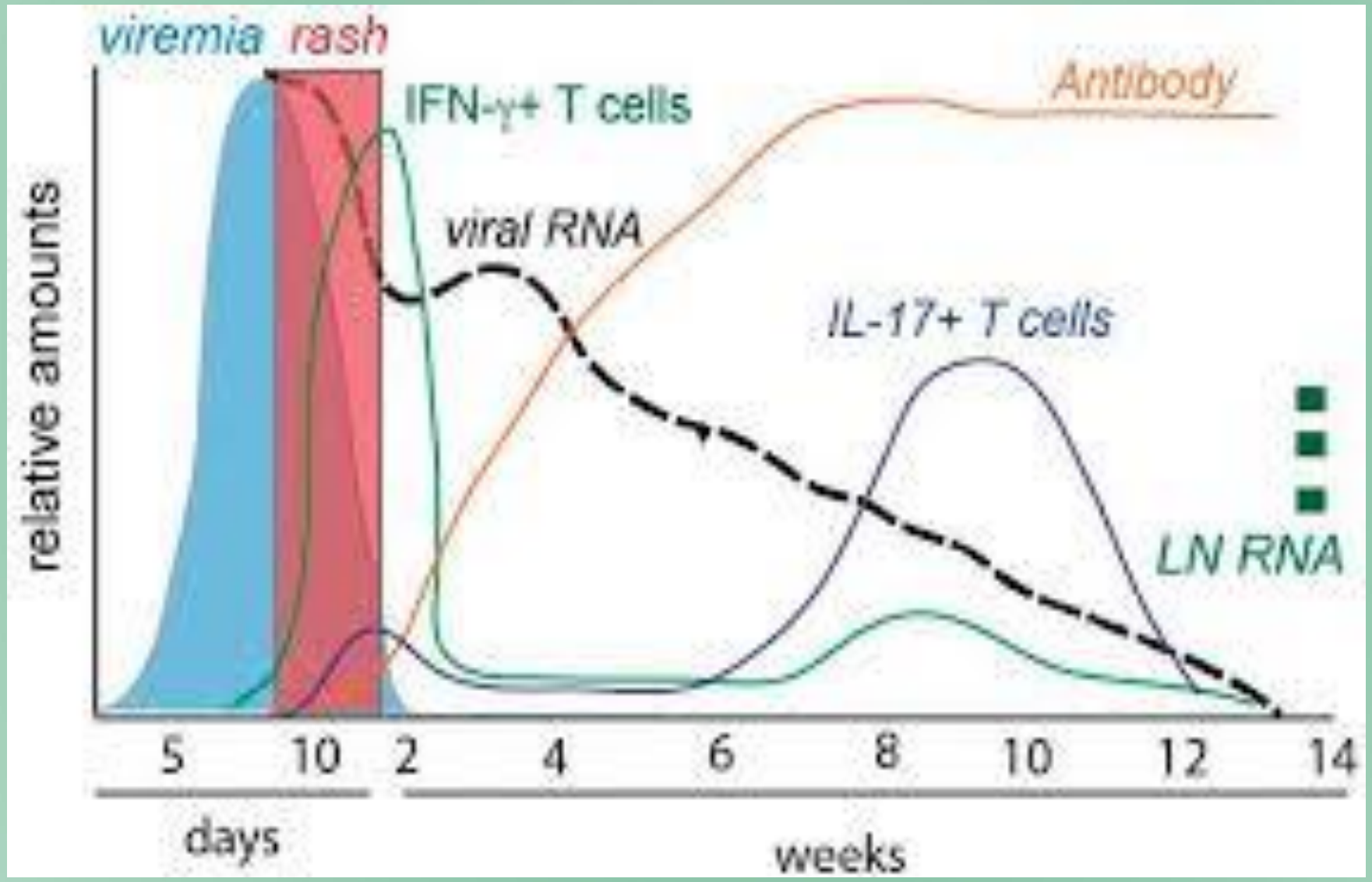
With onset of the **rash**, antibody production begins & viral replication & symptoms begin to subside

KOPLIKS' SPOTS

MEASLES



IMMUNITY


viremia
rash
IFN-γ+ T cells
Antibody
viral RNA
IL-17+ T cells
LN RNA
relative amounts
5
10
2
4
6
8
10
12
14
days
weeks

Measles complications

Corneal scarring causing blindness

Vitamin A deficiency

(Common)

Encephalitis

Older children, adults

≈ 0.1% of cases

Chronic disability

desquamation

Pneumonia & Diarrhea (Common)

Diarrhea common in developing countries

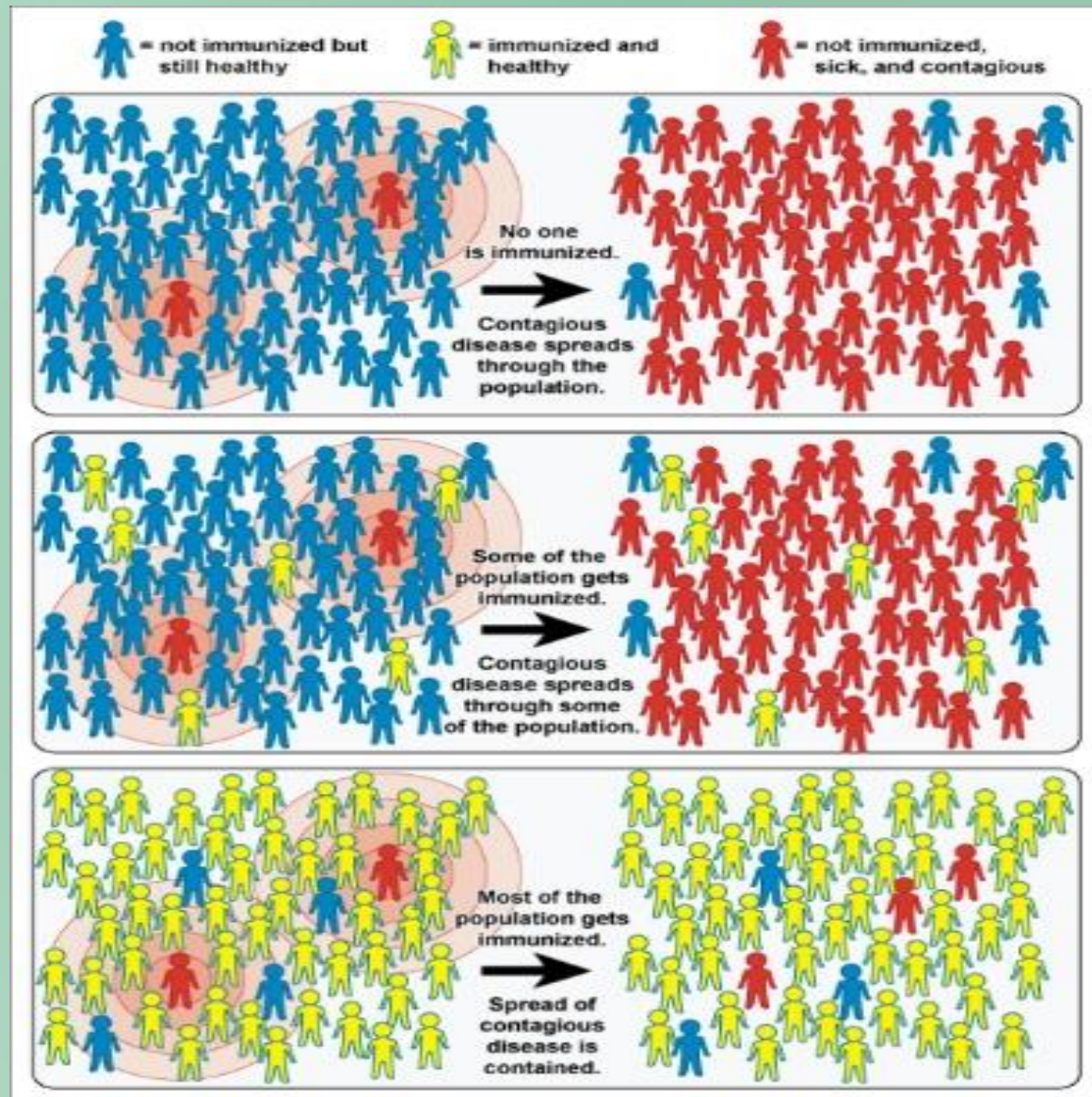
Pneumonia ~ 5-10% of cases, usually bacterial

Diagnosis (cont.)

- Isolation of measles virus from clinical samples is also useful in identifying the genotype of the strain to track transmission patterns.
- All suspected measles cases should be reported immediately to local or health departments.
- During the prodromal stage multinucleated giant cells can be demonstrated in smears of the nasal mucosa.

Measles Vaccine

- Composition — Live virus
- Efficacy — 95% (range, 90%-98%)
- Duration of Immunity — Lifelong
- Schedule — 2 doses
- Should be administered with mumps and rubella as MMR

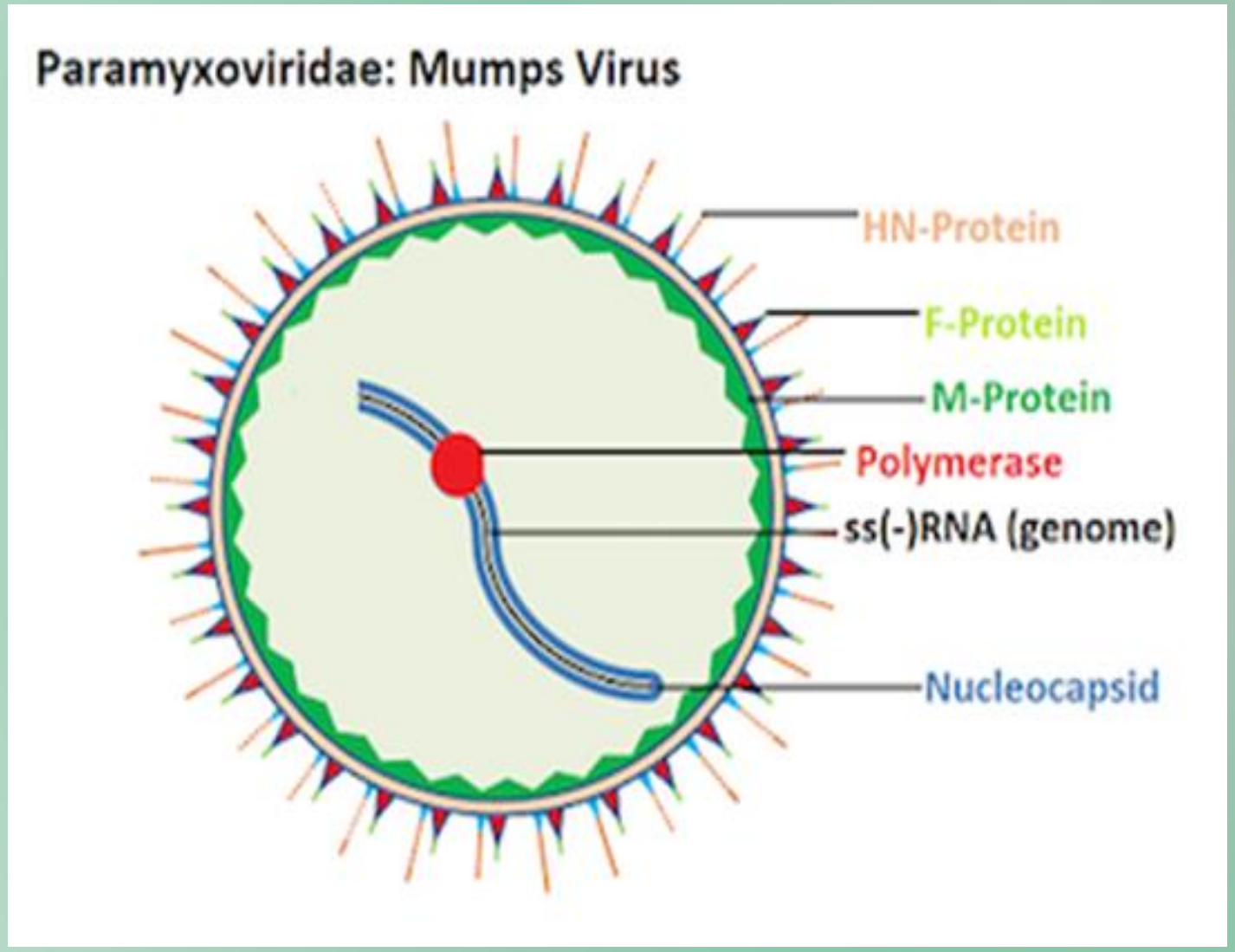


MEASLES & HERD IMMUNITY

thepaltrysapien.com

Monday, February 27, 2012

VIRUS OF EPIDEMIC PAROTITIS (MUMPS)



Mumps Epidemiology

Reservoir	Human
Transmission	Respiratory droplet infection
Communicability	7 days before to 9 days after onset of active disease

- Worldwide distribution
- Many (30%) infections are sub-clinical
- No 'carrier state'.

Mumps pathogenesis

Virus enters respiratory tract

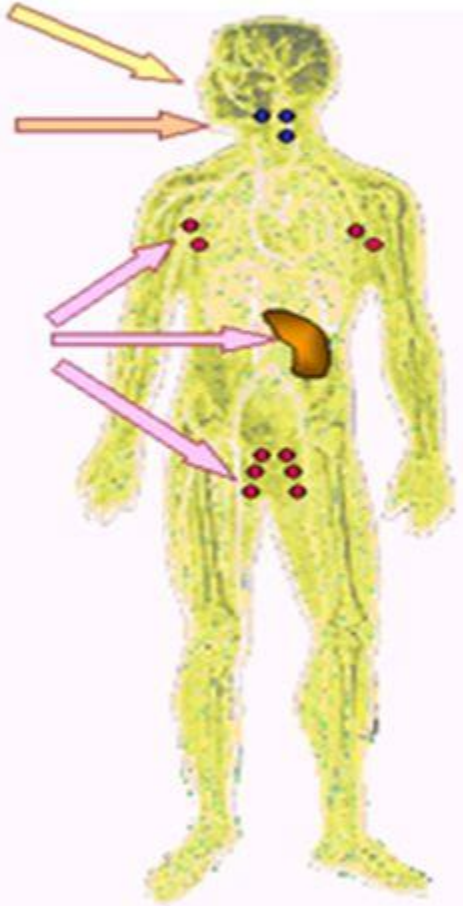
Virus grows in salivary glands and local lymphoid tissue

Virus spreads to spleen and distant lymphoid tissue

Viremia

Virus spreads throughout body to testes, ovary, pancreas, thyroid, salivary glands

DISEASE



7-10 days

Approx 15 days

18 days and after

Mumps Complications

CNS involvement	15% of clinical cases
Orchitis	20%-50% in post-pubertal males
Pancreatitis	2%-5%
Deafness	1/20,000
Death	Average 1 per year (1980 – 1999)

Mumps Laboratory Diagnosis

- Isolation of mumps virus
- Detection of mumps antigen by PCR
- Serologic testing
  - positive IgM antibody
  - significant increase in IgG antibody between acute and convalescent specimens

PROPHYLAXIS

- Attenuated

live virus vaccine

FAMILY PICORNAVIRIDAE

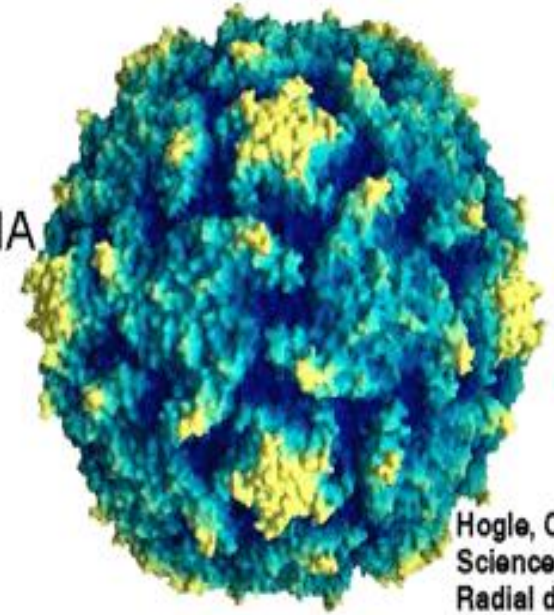
- .

Group IV: (+)sense RNA Viruses			
Family	**Genus**	**Type Species**	**Hosts**
Picornaviridae	*Enterovirus*	*Poliovirus*	Vertebrates
	Rhinovirus	*Human rhinovirus A*	Vertebrates
	Hepatovirus	*Hepatitis A virus*	Vertebrates
	Cardiovirus	*Encephalomyocarditis virus*	Vertebrates
	Aphthovirus	*Foot-and-mouth disease virus O*	Vertebrates
	Parechovirus Parechoviruses:	*Human parechovirus*	Vertebrates

POSITIVE-STRANDED RNA

PICORNAVIRUSES

- SMALL
- ICOSAHEDRAL
- POSITIVE SENSE RNA
- NON-ENVELOPED
- INCLUDE: poliovirus, hepatitis A virus, rhinoviruses, enteroviruses.

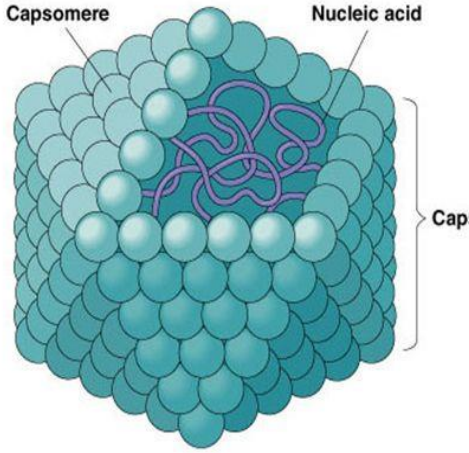


Poliovirus type 1

Hogle, Chow and Filman
Science 229:1358
Radial depth cue rendering
J.Y.Sgro

Morphology of viruses

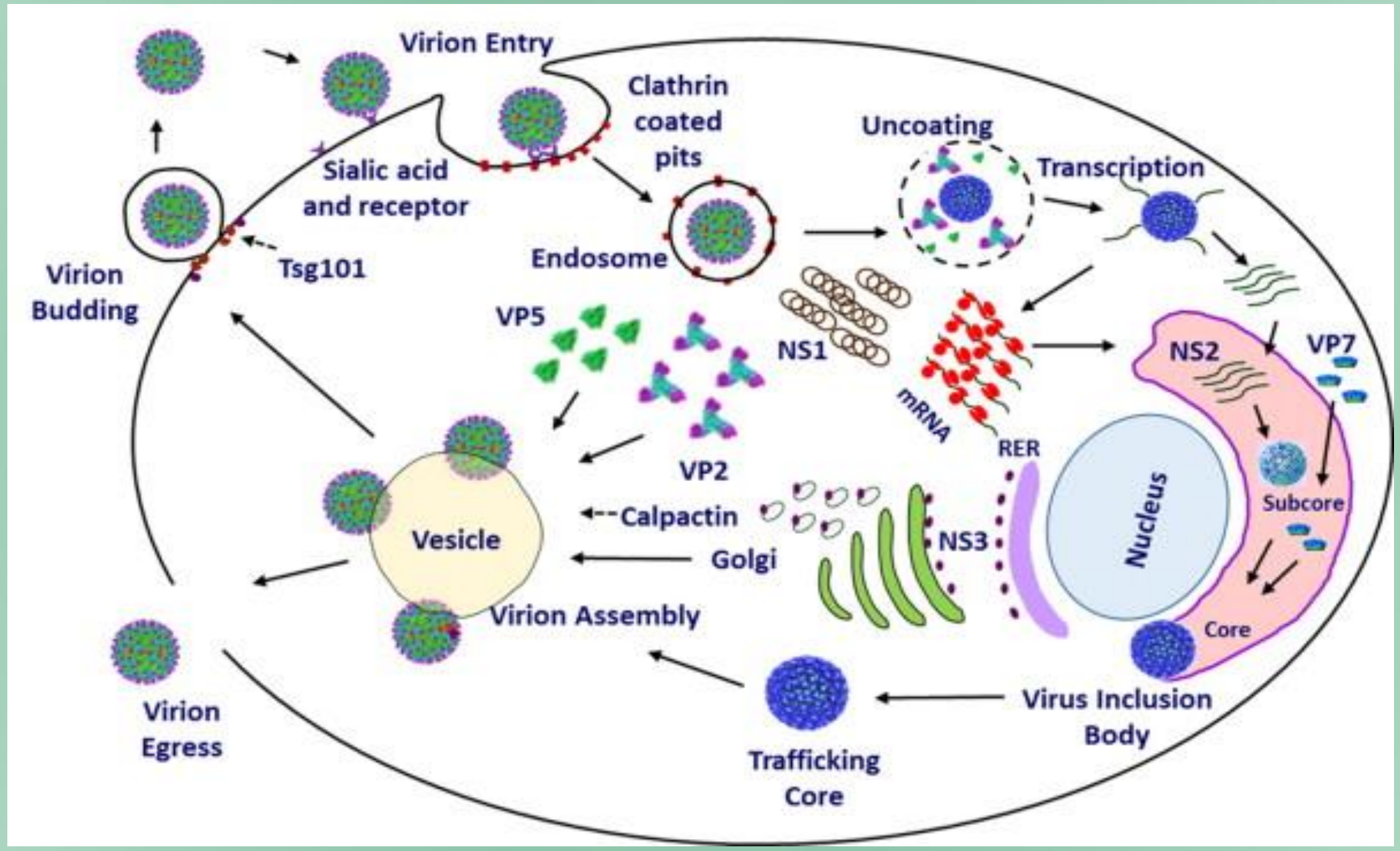
- Polyhedral viruses
  - Icosahedron
    - 20 triangular faces
    - 12 corners
  - Polio virus



(a) A polyhedral virus

Antigenic types

- **Type 1** is the most common and causes epidemic
- **Type 2** usually causes endemic infections
- **Type 3** strains have caused epidemic.


Virion Entry
Clathrin coated pits
Uncoating
Transcription
Sialic acid and receptor
Endosome
Tsg101
Virion Budding
VP5
NS1
mRNA
RER
NS2
VP7
VP2
Calpactin
Vesicle
Golgi
NS3
Nucleus
Subcore
Core
Virion Assembly
Virion Egress
Trafficking Core
Virus Inclusion Body

- Polio virus can survive for long periods in the external environment.

- In a cold environment, it can live in water for 4 months and in faeces for 6 months.

THE SPREAD OF POLIO IN THE WORLD

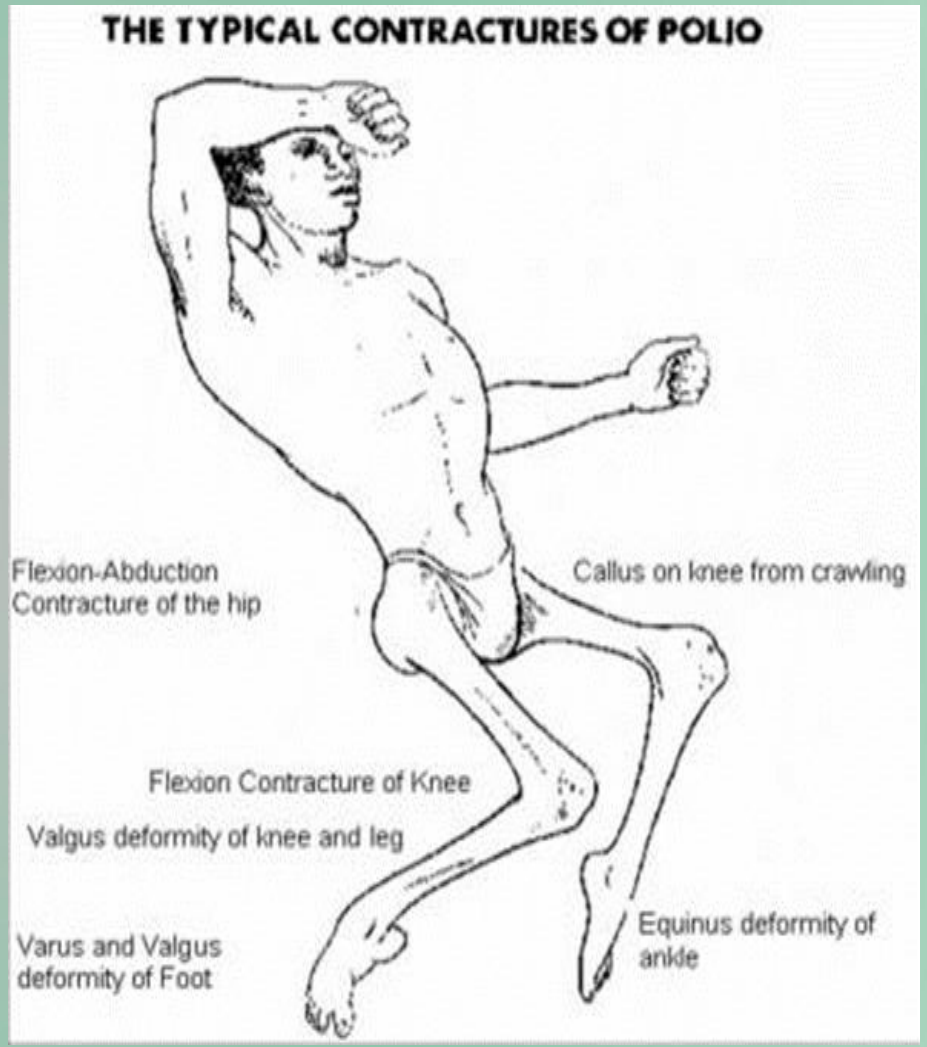
1988

- 350,000 cases
- 125 endemic countries
- World Health Assembly voted to eradicate polio

2016

- 34 cases reported*
- 3 endemic countries

Рис. 1. Барельеф, изображающий поражение ноги после перенесенного полиомиелита



PATHOGENESIS

- Virus multiplies in the lymph pharyngeal ring (tonsils), intestine, regional lymph nodes.
- Then enters the blood, and in some cases in the central nervous system, causing its destruction (especially anterior horn cells of the spinal cord and nucleuses cranial-brain nerves).

Attaching to the cells:

- Human nerve cells have a protruding protein structure on their surface
- The polio virus comes in contact with the nerve cells, the protruding proteins act as receptors and attach to the cell
- The virus injects its genetic material (RNA) into the cell, causing the cell to become an assembly line for manufacturing new viruses. (see slide on how viruses work)
- The polio virus usually enters the lytic cycle

CLASSIFICATION OF POLIOMYELITIS CLINICAL FORMS

- **Inapparent infection** – with seroconversion

- **Minor illness –** primary viremia only

- **Non-paralitic poliomyelitis** (meningeal).

Meningeal form is manifested in the form of serous meningitis.

- **Paralytic poliomyelitis or major illness** (spinal, bulbar)

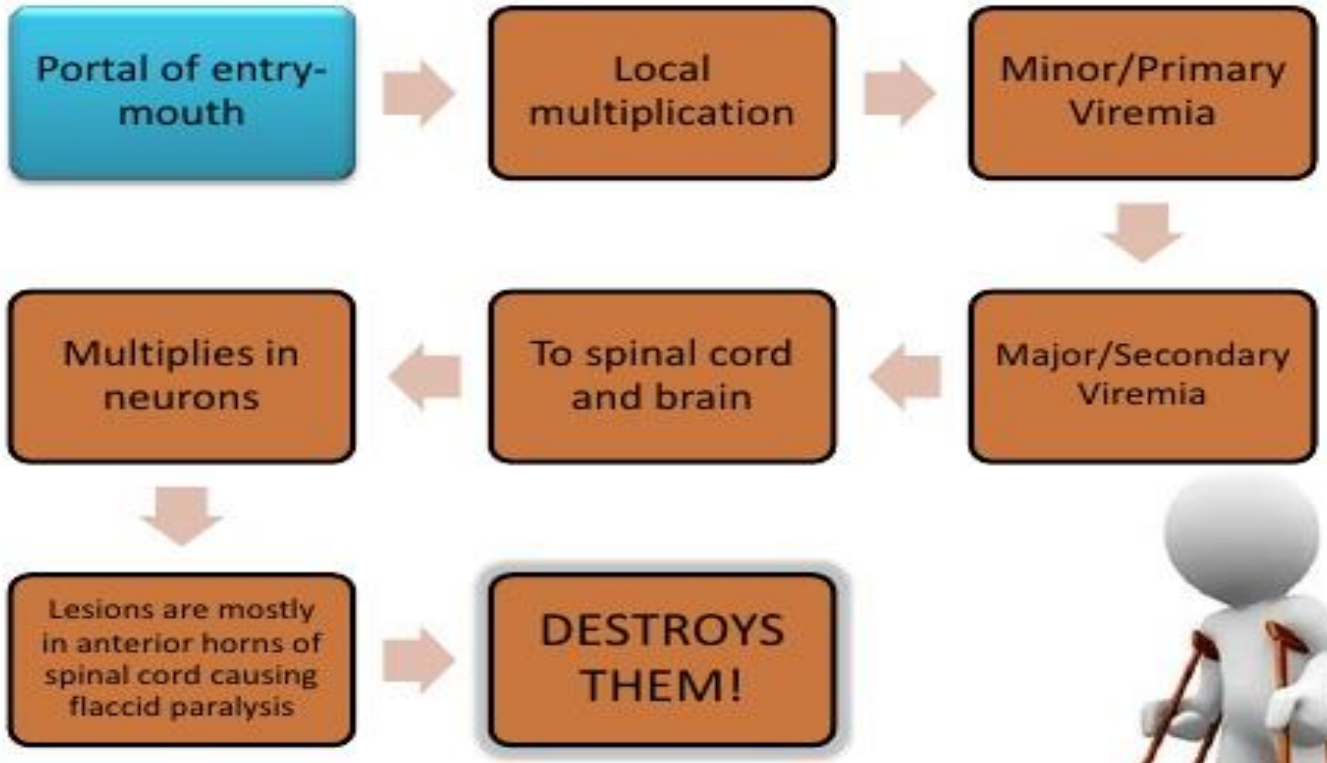
Pathogenesis

Incubation period: 7-10 days (4- 35 days)

- Feco-oral
- Inhalational

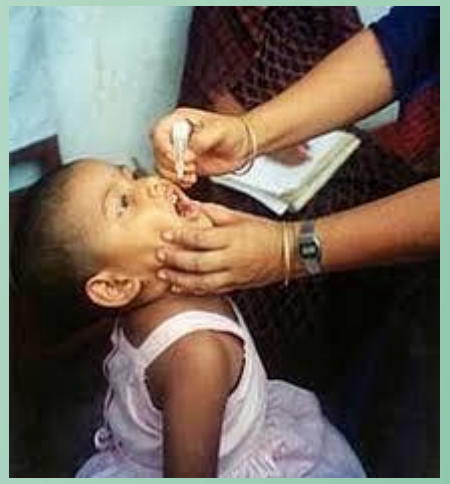
- infects the pharynx and intestinal mucosa.

- Gains entry by binding to an immunoglobulin-like receptor, known as the poliovirus receptor or CD155, on the cell membrane



Poliovirus

- Diagnostic & Management strategy of Case scenarion:
- **Throat swab, Stool, CSF** sent to Diagnostic Microbiology Dept. for viral studies
- Throat swab and stool specimen tested positive for **Cytopathic effect (CPE) in tissue culture.**
- Virus was confirmed as Poliovirus type 1 by **Neutralization test**
- **Reverse Transcriptase PCR** was positive for Poliovirus in CSF
- Patient improved on supportive treatment.

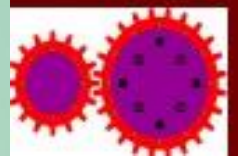


Differences between salk and sabin vaccine?

Jonas Salk developed salk vaccine.	Albert Sabin developed sabin vaccine.
An inoculation dead polio virus.	An inoculation of attenuated live polio viruses.
It is administered as an injection.	It is administrated in oral route.
Complete dose includes a satisfactory immune response.	1or2 doses of oral vaccine gives 90 to 100% result.
Systemic antibody response.	Local immunity in gut.

Passive immunization against mumps

- Immune globulin ineffective for post exposure prophylaxis
  - does not prevent disease or reduce complications
- Transplacental maternal antibody appears to protect infants for first year of life



THANKS
FOR ATTENTION