



MEDICAL UNIVERSITY – PLEVEN
FACULTY OF MEDICINE

**DEPARTMENT OF INFECTIOUS DISEASE, EPIDEMIOLOGY,
PARASITOLOGY AND TROPICAL MEDICINE**

Lecture №4

Influenza **and** **Varicella**

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INFLUENZA (GRIPPE)

DEFINITION

- ✘ Influenza is highly infectious viral illness caused by influenza virus, of which there are 3 types – A, B and C.
- ✘ The disease is characterized by chills, malaise, fever, muscular pains and cough.
- ✘ The disease is spreading epidemic and pandemic.
- ✘ All known pandemics were caused by A strains.

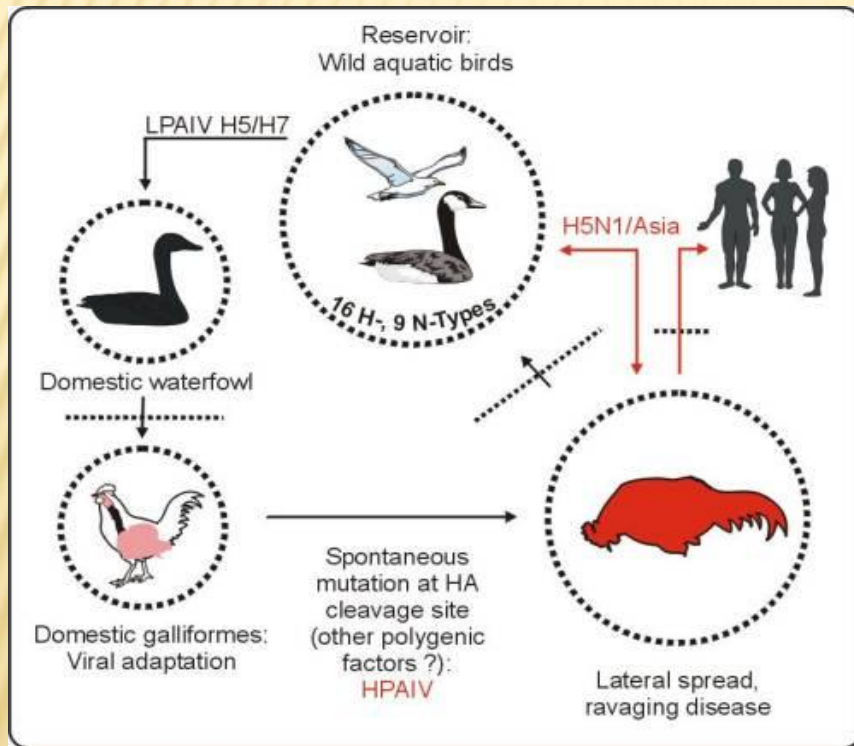
PROBLEM STATEMENT

- ✘ Influenza is a public health problem that affects 5-20% of the world population annually causing high morbidity and mortality especially in risk groups.
- ✘ First pandemic is in 1580. At least 4 pandemics in 19th century.
- ✘ Estimated 21 million deaths worldwide in pandemic of 1918-1919.
- ✘ Last pandemic is in 2009.

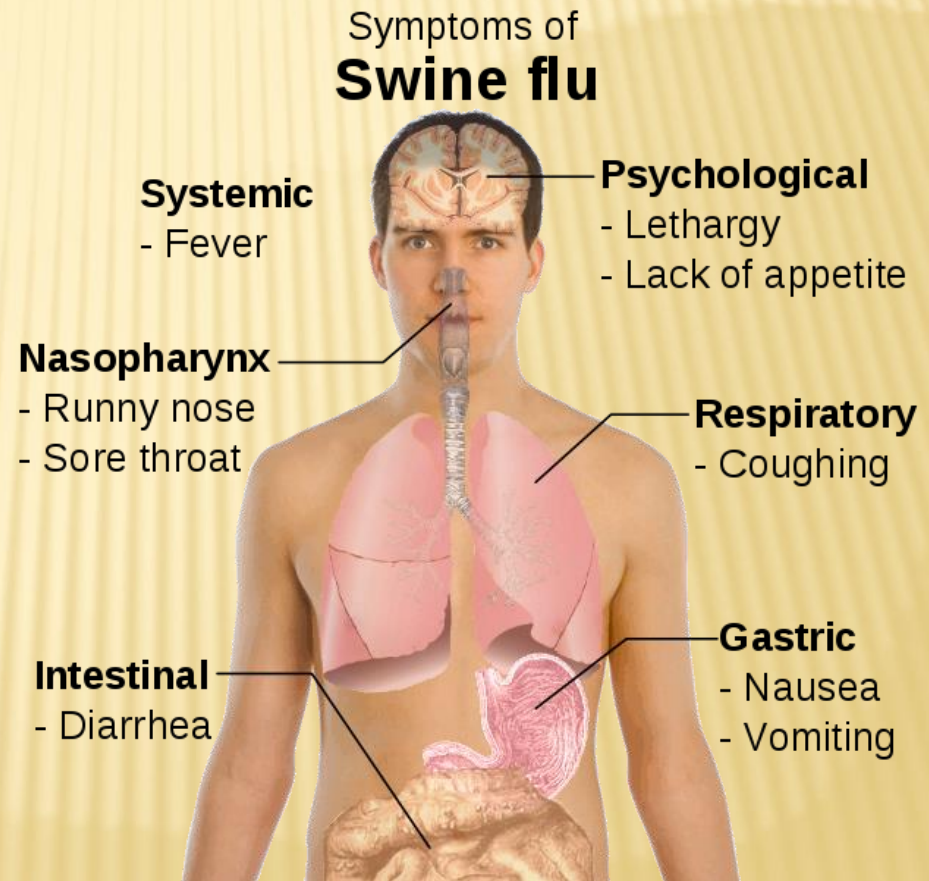
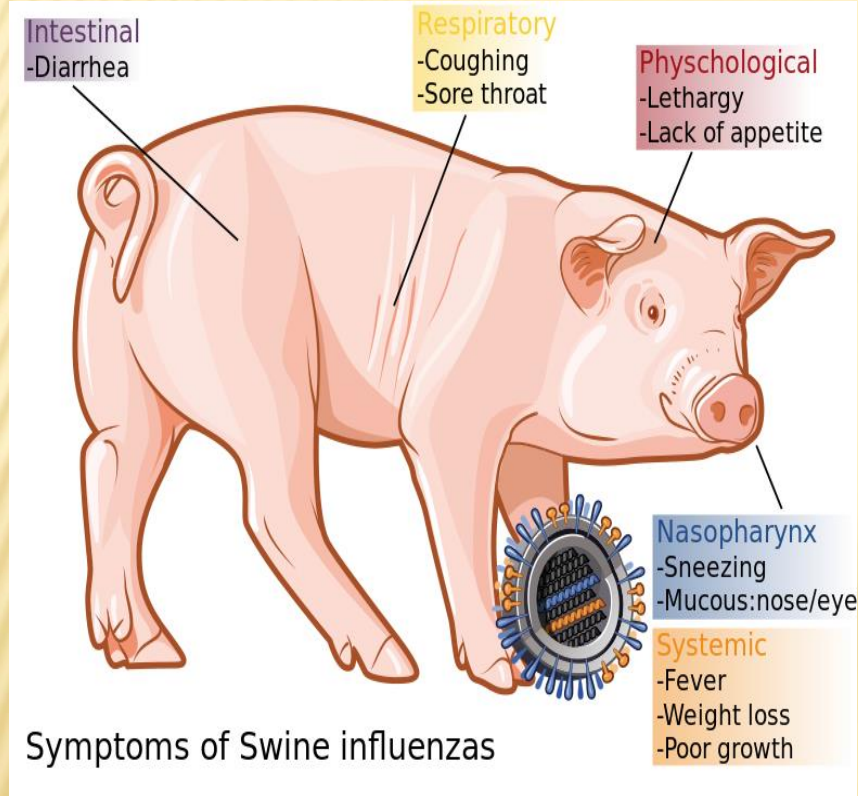
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- ✘ Influenza occurs in all countries and affects millions of people every year.
 - ✘ Influenza spreads around the world in seasonal epidemics, resulting in about three to five million yearly cases of severe illness and about 250,000 to 500,000 yearly deaths, rising to millions in some pandemic years.

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- ✘ In the 20th century three influenza pandemics occurred, each caused by the appearance of a new strain of the virus in humans, and killed tens of millions of people.
 - ✘ Often, new influenza strains appear when an existing flu virus spreads to humans from another animal species, or when an existing human strain picks up new genes from a virus that usually infects birds or pigs.

AN AVIAN STRAIN NAMED **H5N1** RAISED THE CONCERN OF A NEW INFLUENZA PANDEMIC AFTER IT EMERGED IN ASIA IN THE 1990S, BUT IT HAS NOT **EVOLVED** TO A FORM THAT SPREADS EASILY BETWEEN PEOPLE.



IN APRIL 2009 A NOVEL FLU STRAIN EVOLVED THAT COMBINED GENES FROM HUMAN, PIG, AND BIRD FLU. INITIALLY DUBBED "SWINE FLU" AND ALSO KNOWN AS **INFLUENZA A/H1N1**, IT EMERGED IN MEXICO, THE UNITED STATES, AND SEVERAL OTHER NATIONS.



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- ✘ The World Health Organization officially declared the outbreak to be a pandemic on 11 June 2009.
 - ✘ The WHO's declaration of a pandemic level 6 was an indication of spread, not severity, the strain actually having a lower mortality rate than common flu outbreaks.

AGENT

- ✘ In virus classification influenza viruses are RNA viruses, family Orthomyxoviridae.
- ✘ There are three viral sub-type: Influenza virus A, Influenza virus B, Influenza virus C.

INFLUENZA VIRUS A

- ✘ This genus has one species, influenza A virus. Wild aquatic birds are the natural hosts for a large variety of influenza A.
- ✘ Occasionally, viruses are transmitted to other species and may then cause devastating outbreaks in domestic poultry or give rise to human influenza pandemics.

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- ✘ The type A viruses are the most virulent human pathogens among the three influenza types and cause the most severe disease.
 - ✘ The influenza A virus can be subdivided into different serotypes based on the antibody response to these viruses.

THE SEROTYPES THAT HAVE BEEN CONFIRMED IN HUMANS, ORDERED BY THE NUMBER OF KNOWN HUMAN PANDEMIC DEATHS, ARE:

- × H1N1, which caused Spanish Flu in 1918, and Swine Flu in 2009
- × H2N2, which caused Asian Flu in 1957
- × H3N2, which caused Hong Kong Flu in 1968
- × H5N1, which caused Bird Flu in 2004
- × H7N7, which has unusual zoonotic potential
- × H1N2, endemic in humans, pigs and birds
- × H9N2
- × H7N2
- × H7N3
- × H10N7

INFLUENZA VIRUS B

- ✘ This genus has one species, influenza B virus. Influenza B almost exclusively infects humans and is less common than influenza A.
- ✘ The only other animals known to be susceptible to influenza B infection are the seal and the ferret.
- ✘ This type of influenza mutates at a rate 2–3 times slower than type A and consequently is less genetically diverse, with only one influenza B serotype.

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- ✘ As a result of this lack of antigenic diversity, a degree of immunity to influenza B is usually acquired at an early age.
 - ✘ However, influenza B mutates enough that lasting immunity is not possible.
 - ✘ This reduced rate of antigenic change, combined with its limited host range (inhibiting cross species antigenic shift), ensures that pandemics of influenza B do not occur.

INFLUENZA VIRUS C

- ✘ This genus has one species, influenza C virus, which infects humans, dogs and pigs, sometimes causing both severe illness and local epidemics.
- ✘ However, influenza C is less common than the other types and usually only causes mild disease in children.

- ✘ Influenza viruses A, B and C are very similar in overall structure.
- ✘ The virus particle is 80–120 nm in diameter and usually roughly spherical, although filamentous forms can occur.

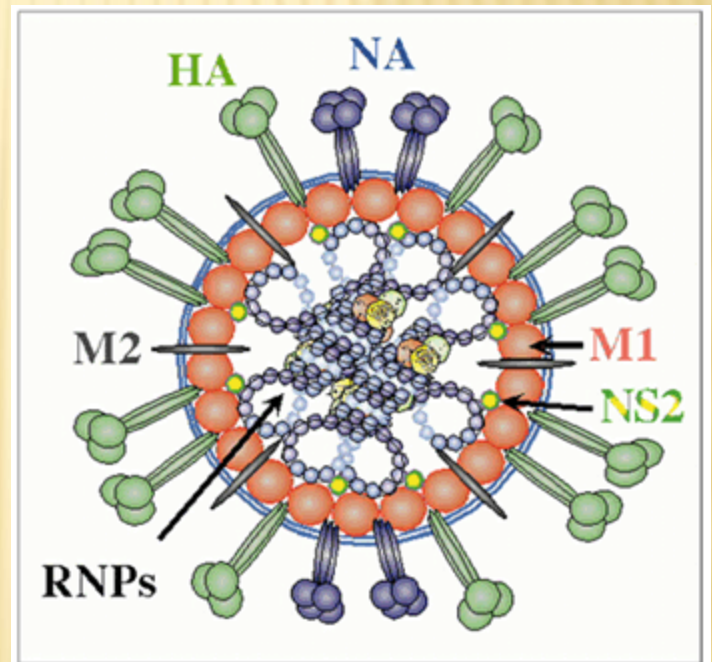


Diagram kindly provided by Paul Digard, University of Cambridge

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- ✘ These filamentous forms are more common in influenza C, which can form cordlike structures up to 500 μm long on the surfaces of infected cells.
 - ✘ However, despite these varied shapes, the viral particles of all influenza viruses are similar in composition.

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- ✘ These are made of a viral envelope containing two main types of glycoproteins, wrapped around a central core.
 - ✘ The central core contains the viral RNA genome and other viral proteins that package and protect this RNA.
 - ✘ RNA tends to be single stranded but in special cases it is double.

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- ✘ Unusually for a virus, its genome is not a single piece of nucleic acid; instead, it contains seven or eight pieces of segmented negative-sense RNA, each piece of RNA containing either one or two genes, which code for a gene product (protein).

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- ✘ Hemagglutinin (HA) and neuraminidase (NA) are the two large glycoproteins on the outside of the viral particles.
 - ✘ HA is a lectin that mediates binding of the virus to target cells and entry of the viral genome into the target cell, while NA is involved in the release of progeny virus from infected cells, by cleaving sugars that bind the mature viral particles.
 - ✘ Thus, these proteins are targets for antiviral drugs.

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- ✘ The influenza A virus is unique among the viruses because it is frequently subject to antigenic variation, both major and minor.
 - ✘ When there is a sudden complete or major change, it is called a **shift**, and when the antigenic change is gradual over a period of time, it is called a **drift**.

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- ✘ Antigenic shift appears to result from genetic recombination of human with animal or avian virus, providing a major antigenic change.
 - ✘ This can cause a major epidemic or pandemic involving most or all age groups.

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- ✘ Antigenic drift involves “point mutation” in the gene owing to selection pressure by immunity in the host population.
 - ✘ Antigenic changes occur to a lesser degree in the B group influenza viruses.
 - ✘ Influenza C appears to be antigenically stable.

RESERVOIR OF INFECTION

- ✘ It has become increasingly evident that a major reservoir of influenza virus exist in animals and birds.
- ✘ Many influenza viruses have been isolated from a wide variety of animals and birds (swine, horses, dogs, cats, domestic poultry, wild birds, etc.).

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- ✘ Some of these include the major H and N antigens related to human strains.
 - ✘ There is increasing evidence that the animal reservoirs provide new strains of influenza virus by recombination between the influenza viruses of man, animal and birds.

SOURCE OF INFECTION

- ✘ Usually a case or subclinical case.
- ✘ During epidemics, a large number of mild and asymptomatic infections occur, which play an important role in the spread of infection.
- ✘ The secretions of the respiratory tract are infective.

- ✘ **Period of infectivity**

- ✘ Virus is present in the nasopharynx from 1 to 2 days before and 1 to 2 days after onset of symptoms.

HOST FACTORS

- ✘ **Age and sex:**
- ✘ Influenza affects all ages and both sexes.
- ✘ In general, the attack rate is lower among adults.
- ✘ Children constitute an important link in the transmission chain.

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- ✘ The highest mortality rate during an epidemic occurs among certain high-risk groups in the population such as old people (generally over 65 years of age), children under 18 months, and persons with diabetes or chronic heart disease, kidney and respiratory tract.

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- ✘ **Human mobility:** This is an important factor in spread of infection.
 - ✘ **Immunity:** Antibodies are important in immunity against influenza. Antibody to **H** neutralizes the virus, antibody to **N** modifies the infection.
 - ✘ **Secretory antibodies** develop in the respiratory tract after infection and consist predominantly of IgG.

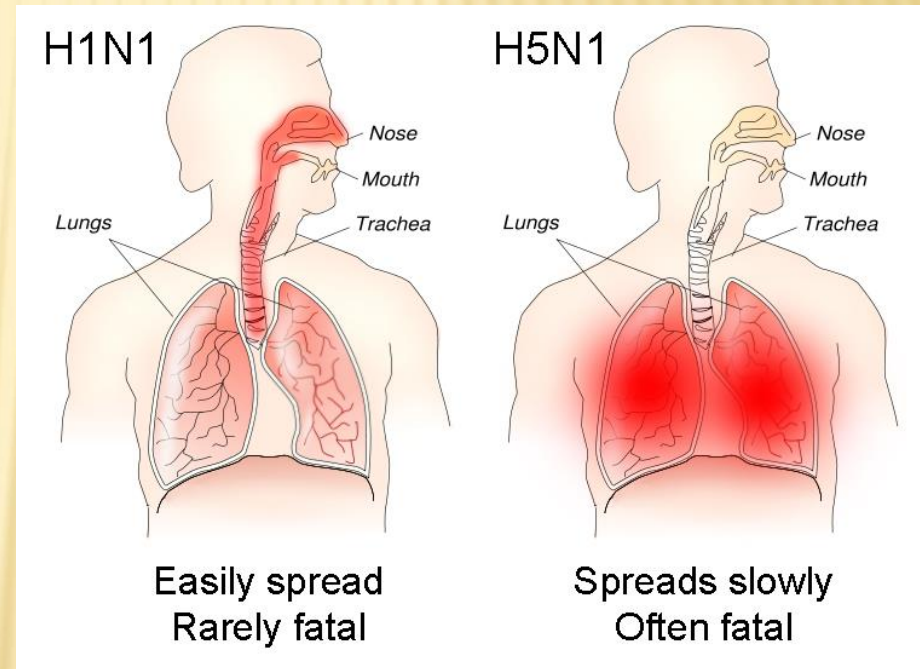
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- ✘ Antibodies must be present in sufficient concentration at the superficial cells (site of virus invasion) of the respiratory tract.
 - ✘ This is possible only if the antibody titer is high in the blood or if the antibody is secreted locally.
 - ✘ Antibodies appear in about 7 days after an attack and reach a maximum level in about 2 weeks.
 - ✘ After 8 to 12 months, the antibody level drops to pre-infection levels.

ENVIRONMENTAL FACTORS

- ✘ **Season:** The seasonal incidence is striking, epidemics usually occurring in winter months in the Northern Hemisphere and the winter or rainy season in the Southern Hemisphere. In India, epidemics have often occurred in summer.
- ✘ **Overcrowding:** The attack rates are high in close population groups (schools, institutions, etc.)

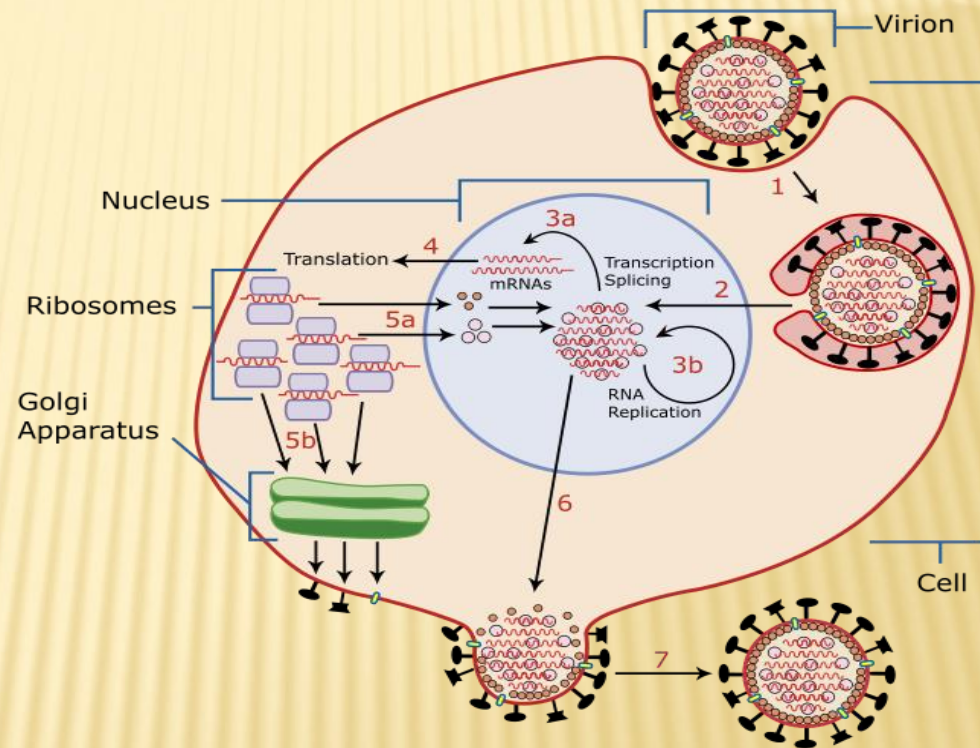
MODE OF TRANSMISSION

- ✘ Influenza is spread mainly from person to person by droplet infection or droplet nuclei created by sneezing, coughing or talking.
- ✘ The portal of entry of the virus is the respiratory tract.



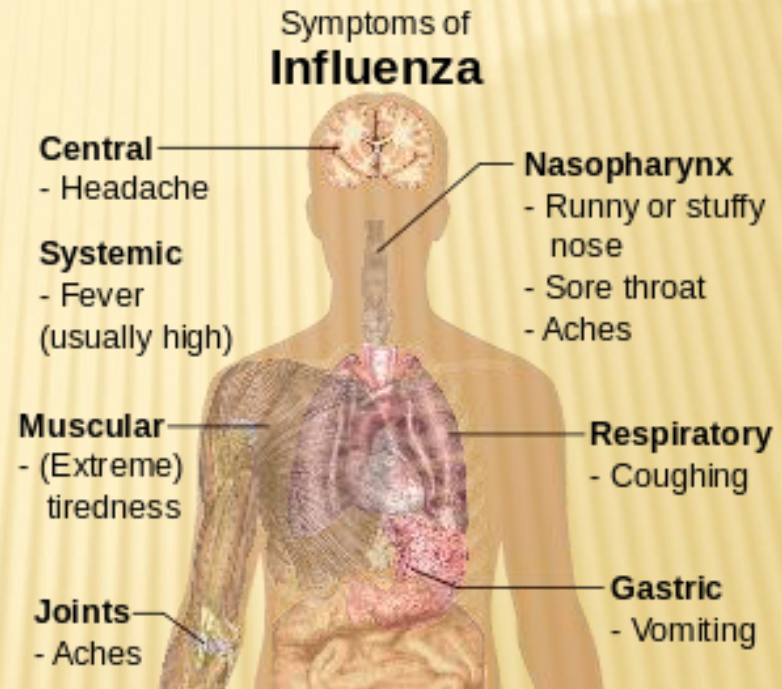
✘ Incubation period:
18 to 72 hours

✘ Replication
(on the figure)



CLINICAL FEATURES

- × fever (usually 39-40° C in adults and often even higher in children),
- × chills,
- × respiratory symptoms such as cough (more often in adults), sore throat (more often in adults), runny or stuffy nose (especially in children),
- × headache,
- × muscle aches,
- × fatigue, sometimes extreme.



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- ✘ Although nausea, vomiting, and diarrhea can sometimes accompany influenza infection, especially in children, gastrointestinal symptoms are rarely prominent.
 - ✘ Most people who get the flu will have mild illness, will not need medical care or antiviral drugs, and will recover in less than two weeks.

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- ✘ Some people, however, are more likely to get flu complications that result in being hospitalized and occasionally result in death.
 - ✘ Pneumonia, bronchitis, sinus infections and ear infections are examples of flu-related complications.
 - ✘ The flu also can make chronic health problems worse.

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- × People at high risk for developing flu-related complications: children younger than 5, but especially children younger than 2 years old;
 - × adults 65 years of age and older;
 - × pregnant women.

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- ✘ **People who have medical conditions including:** asthma; neurological and neurodevelopment conditions: including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy (seizure disorders), stroke, intellectual disability (mental retardation), moderate to severe developmental delay, muscular dystrophy, or spinal cord injury;

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- ✘ chronic lung disease such as chronic obstructive pulmonary disease (COPD) and cystic fibrosis; heart disease such as congenital heart disease, congestive heart failure and coronary artery disease; blood disorders such as sickle cell disease; endocrine disorders such as diabetes mellitus; kidney disorders; liver disorders; metabolic disorders such as inherited metabolic disorders and mitochondrial disorders;

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- ✘ weakened immune system due to disease or medication (such as people with HIV or AIDS, or cancer, or those on chronic steroids); people younger than 19 years of age who are receiving long-term aspirin therapy; people who are morbidly obese (Body Mass Index, or BMI, of 40 or greater).

LABORATORY DIAGNOSIS

- ✘ Rapid influenza diagnostic test (RIDT)
- ✘ Direct fluorescent antibody stain (DFA)
- ✘ Viral culture
- ✘ Real-time polymerase chain reaction (RT-PCR)
- ✘ Influenza A or B antibody tests

PREVENTION OF INFLUENZA

- ✘ **Vaccination recommendations:**
- ✘ Various public health organizations, including the World Health Organization, have recommended that yearly influenza vaccination be routinely offered to patients at risk of complications of influenza and those individuals who live with or care for high-risk individuals, including:

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- ✘ the elderly (UK recommendation is those aged 65 or above)
 - ✘ patients with chronic lung diseases (asthma, etc.)
 - ✘ patients with chronic heart diseases (congenital heart disease, chronic heart failure, ischaemic heart disease)
 - ✘ patients with chronic liver diseases (including cirrhosis)
 - ✘ patients with chronic renal diseases (such as the nephrotic syndrome)
 - ✘ patients who are immunosuppressed (those with HIV or who are receiving drugs to suppress the immune system such as chemotherapy and long-term steroids) and their household contacts

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- ✘ people who live together in large numbers in an environment where influenza can spread rapidly, such as prisons, nursing homes, schools, and dormitories.
 - ✘ people who plan to attend or participate in a high profile important event with large amounts of people from various places (such as the Olympic Games, FIFA World Cup, and the World's Fair).
 - ✘ people who are in the armed forces.
 - ✘ healthcare workers (both to prevent sickness and to prevent spread to patients)

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- ✘ pregnant women. However, a 2009 review concluded that there was insufficient evidence to recommend routine use of trivalent influenza vaccine during the first trimester of pregnancy. Influenza vaccination during flu season is part of recommendations for influenza vaccination of pregnant women in the United States.
 - ✘ children from ages six months to two years

VACCINES

- ✘ **Global Action Plan for Influenza Vaccines (GAP)** is a comprehensive strategy to reduce the present global shortage of influenza vaccines for seasonal epidemics and pandemic influenza in all countries of the world through three major approaches:
 - ✘ Increase in seasonal vaccine use;
 - ✘ Increase in vaccine production capacity;
 - ✘ Research and development.

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- ✘ The **influenza vaccination**, also known as a **flu shot**, is an annual vaccination using a vaccine specific for a given year to protect against the highly variable influenza virus. Each seasonal influenza vaccine contains three influenza viruses: one influenza type A subtype H3N2 virus strain, one influenza type A subtype H1N1 (seasonal) virus strain, and one influenza type B virus strain.

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- ✘ A quadrivalent flu vaccine administered by nasal mist was approved by the U.S. Food and Drug Administration (FDA) in March 2012. Fluarix Quadrivalent was approved by the FDA in December 2012.

TYPES OF VACCINES

- ✘ **Live attenuated vaccines (LAIV)** – intranasal, trivalent, duration of immunity at least 1 year
- ✘ **Inactivated**
 - ✘ a/ **Whole – virus vaccines** – in the past
 - ✘ b/ **Split – virus vaccines**, intramuscular/deep subcutaneous (**Vaxigrip-Sanofi Pasteur**; **Fluarix-GSK**) or intradermal (**IDflu-Sanofi Pasteur**), trivalent, duration of immunity 1 year or less
 - ✘ c/ **Sub-unit /influenza virus surface antigens** (HA and NA)- intramuscular/deep subcutaneous (**Influvac-Abbott**), trivalent, duration of immunity 1 year or less

NAME OF VACCINE CONSIST

Virus type	Geographic origin	Strain number	Year of isolation	Virus subtype
A /	California /	7 /	2009	(H1N1)

COMPOSITION OF THE 2018/2019 YEAR

Influvac

A/Michigan/45/2015 (H1N1)pdm09

A/Singapore/INFIMH/16-0019/2016 (H3N2)

B/Colorado/06/2017

B /Phuket/3073/2013

Vaxigrip Tetra

A/Michigan/45/2015 (H1N1)pdm09

A/Singapore/INFIMH/16-0019/2016 (H3N2)

B/Colorado/06/2017

B /Phuket/3073/2013

✘ Duration of protection

- ✘ According to work published in 1973, 1983, and 2004, after vaccination against seasonal flu, antibody titers peak after typically two to four weeks.
- ✘ They decrease by about 50% over the next six months (the decrease is less for older adults), then remain stable for two to three years; protection without revaccination persists for at least three years for children and young adults.

EPIDEMIOLOGICAL SURVEILLANCE FOR INFLUENZA

- ✘ The Global Influenza Programme (GIP) provides Member States with strategic guidance, technical support and coordination of activities essential to make their health systems better prepared against seasonal, zoonotic and pandemic influenza threats to populations and individuals.

CHICKENPOX (VARICELLA)

DEFINITION

- ✘ Chickenpox or varicella is a highly contagious illness caused by primary infection with **varicella zoster virus** (VZV). It generally begins with a vesicular skin rash appearing in two or three waves, mainly on the body and head rather than the hands and becoming itchy raw pockmarks, small open sores which heal mostly without scarring.

PROBLEM STATEMENT

- ✘ Primary varicella is a disease that is endemic to all countries worldwide.
- ✘ Varicella has a prevalence that is stable from generation to generation.
- ✘ In temperate countries, chickenpox is primarily a disease of children, with most cases occurring during the winter and spring, most likely due to school contact.

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- ✘ It is one of the classic diseases of childhood, with the highest prevalence in the 4–10 year old age group.
 - ✘ Varicella is highly communicable, with an infection rate of 90% in close contacts.
 - ✘ In temperate countries, most people become infected before adulthood but 10% of young adults remain susceptible.

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- ✘ In the tropics, chickenpox often occurs in older people and may cause more serious disease.
 - ✘ In adults the pock marks are darker and the scars more prominent than in children.
 - ✘ Pregnant women and those with a suppressed immune system are at highest risk of serious complications.

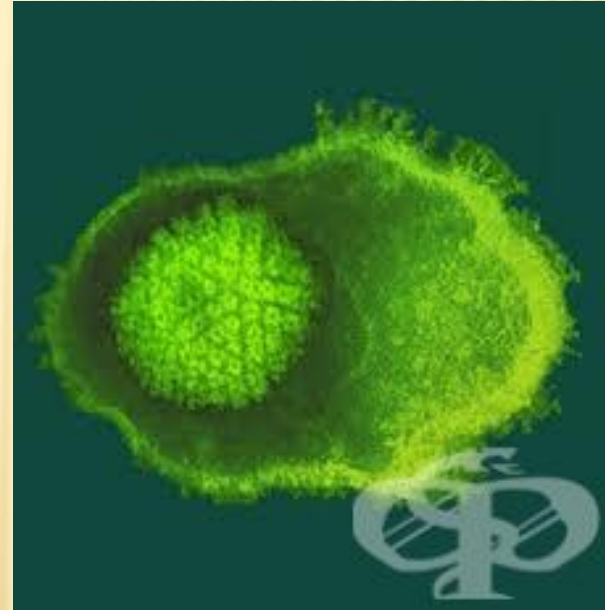
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- ✘ The most common late complication of chickenpox is shingles, caused by reactivation of the varicella zoster virus decades after the initial episode of chickenpox.

AGENT

- ✘ **Varicella zoster virus (VZV)** or chickenpox virus, varicella virus, zoster virus, and human herpes virus type 3 (HHV-3)

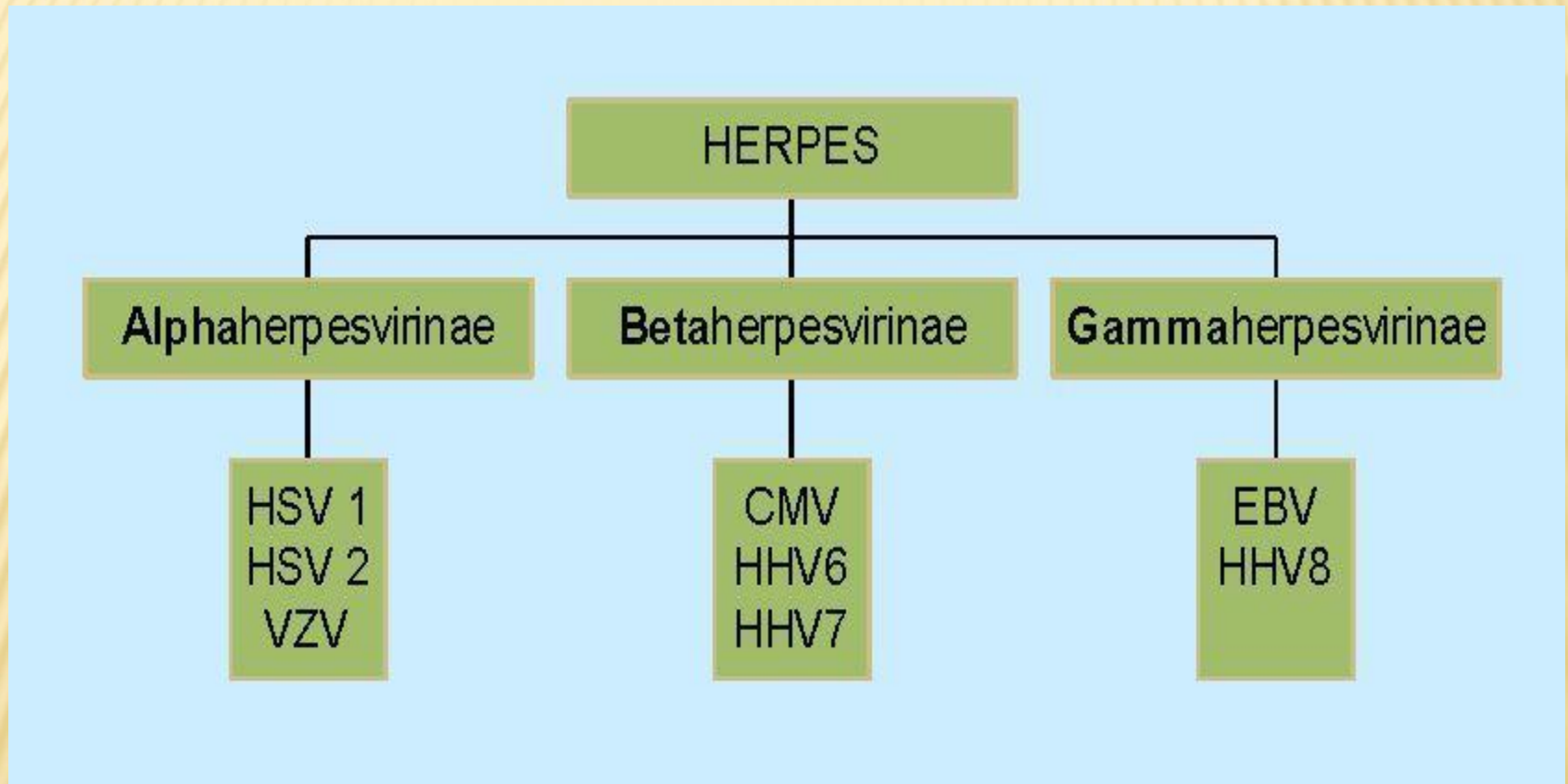
Family: *Herpesviridae*

Subfamily: *Alphaherpesvirinae*

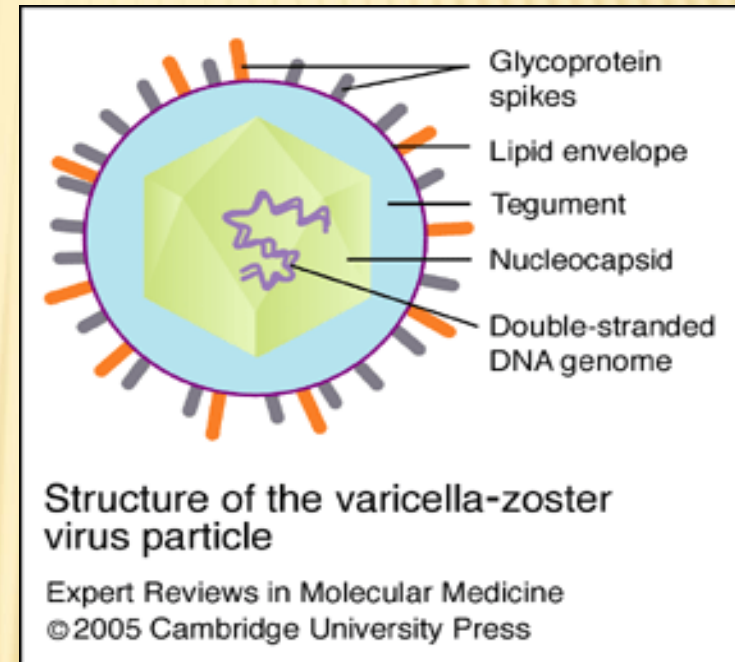


AGENT FACTORS

FAMILY: *HERPESVIRIDAE*



- ✘ VZV virions are spherical and 180–200 nm in diameter.
- ✘ Their lipid envelope encloses the 100 nm nucleocapsid of 162 hexameric and pentameric capsomeres arranged in an icosahedral form.
- ✘ Its DNA is a single, linear, double-stranded molecule



GENOME

- ✘ The genome is a linear duplex DNA molecule, a laboratory strain has 124,884 base pairs.
- ✘ The genome has 2 predominant isomers, depending on the orientation of the S segment, P (prototype) and I_S (inverted S) which are present with equal frequency for a total frequency of 90-95%.

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- ✘ The L segment can also be inverted resulting in a total of four linear isomers (I_L and I_{LS}).
 - ✘ This is distinct from HSV's equiprobable distribution, and the discriminatory mechanism is not known.
 - ✘ A small percentage of isolated molecules are circular genomes, about which little is known. (It is known that HSV circularizes on infection.)
 - ✘ There are at least 70 open reading frames in the genome.

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- ✘ There are at least five clades of this virus. Clades 1 and 3 include European/North American strains;
 - ✘ clade 2 are Asian strains, especially from Japan;
 - ✘ and clade 5 appears to be based in India.
 - ✘ Clade 4 includes some strains from Europe but its geographic origins need further clarification.

- ✘ **Reservoir**
- ✘ Varicella is a human disease.
- ✘ No animal or insect source or vector is known to exist.



SOURCE OF INFECTION

- 1./ Usually a case of chickenpox. The virus occurs in the oropharyngeal secretions and lesions of skin and mucosa.
- 2./ Rarely the source of infection may be a patient with herpes zoster. The virus can be readily isolated from the vesicular fluids\ during the first days of illness.
- 3./ Varicella infection in pregnant women could lead to viral transmission via the placenta and infection of the fetus.

PERIOD OF INFECTIVITY

- ✘ The period of infectivity of patients with varicella is estimated to range from 1 to 2 days before the appearance of rash, and 4 to 5 days thereafter.
- ✘ The virus tends to die before the pustular stage.
- ✘ The patient ceases to be infectious once the lesions have crusted.

- ✘ **Secondary attack rate:** Chickenpox is highly communicable.
- ✘ The SAR in household contacts approaches 90%.



HOST FACTORS

- ✘ **Age and sex:** Chickenpox affects both sexes. Disease occurs primarily among children under 10 years of age. In general, the attack rate is lower among adults. The disease can be severe in normal adults.
- ✘ **Human mobility:** This is an important factor in spread of infection.

IMMUNITY

- ✘ One attack gives durable immunity; second attacks are rare.
- ✘ The acquisition of maternal antibody protects the infant during the first few months of life.
- ✘ No age, however, is exempt in the absence of immunity.

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- ✘ The IgG antibodies persist for life and their presence is correlated with protection against varicella.
 - ✘ The cell-mediated immunity appears to be important in recovery from V-Z infections and in protection against the reactivation of latent V-Z virus.

PREGNANCY

- ✘ Infection during pregnancy presents a risk for the fetus and neonate.
- ✘ For pregnant women, antibodies produced as a result of immunization or previous infection are transferred via the placenta to the fetus.

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- ✘ Women who are immune to chickenpox cannot become infected and do not need to be concerned about it for themselves or their infant during pregnancy.

ENVIRONMENTAL FACTORS

✘ Season:

- ✘ The disease shows a seasonal trend in winter months in the Northern Hemisphere. In India and other countries, the disease occurring mostly during the first six months of the year. In temperate areas, varicella has a distinct seasonal fluctuation, with the highest incidence occurring in winter and early spring.

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- ✘ In the United States, incidence is highest between March and May and lowest between September and November.
 - ✘ Herpes zoster has no seasonal variation and occurs throughout the year.

× **Overcrowding:**

- × The attack rates are high in close population groups (kindergartens, crèches, schools, institutions, etc.)

MODE OF TRANSMISSION

- ✘ Chickenpox is spread mainly from person to person **by droplet infection** or **droplet nuclei** created by sneezing, coughing or talking or through direct contact with secretions from the rash.
- ✘ The **portal of entry** of the virus is the **respiratory tract**.

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- × **Contact infection** undoubtedly plays a role when an individual with herpes zoster is an index case.
 - × The virus can cross the **placental barrier** and infect the fetus.

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- ✘ **Incubation period:** Chickenpox has a 10-21 day incubation period, usually 14-16 days.
 - ✘ **Clinical features:**
 - ✘ The clinical spectrum of chickenpox may vary from **a mild illness** with only a few scattered lesions to **a severe febrile illness** with widespread rash.

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- ✘ Inapparent infection is estimated to occur in no more than 5 per cent of susceptible children.
 - ✘ In the majority of cases, the disease tends to be mild and typical.

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- ✘ The clinical course of chickenpox may be divided into two stages:
 - ✘ **Pre-eruptive stage:** Onset is sudden with mild or moderate fever, pain in the back, shivering and malaise.
 - ✘ This stage is very brief, lasting about 24 hours. In adults, the prodromal illness is usually more severe and may last for 2-3 days before the rash comes out.

- ✘ Eruptive stage:
- ✘ In children the rash is often the first sign.
- ✘ It comes on the day the fever starts.



THE DISTINCTIVE FEATURES OF THE RASH ARE:

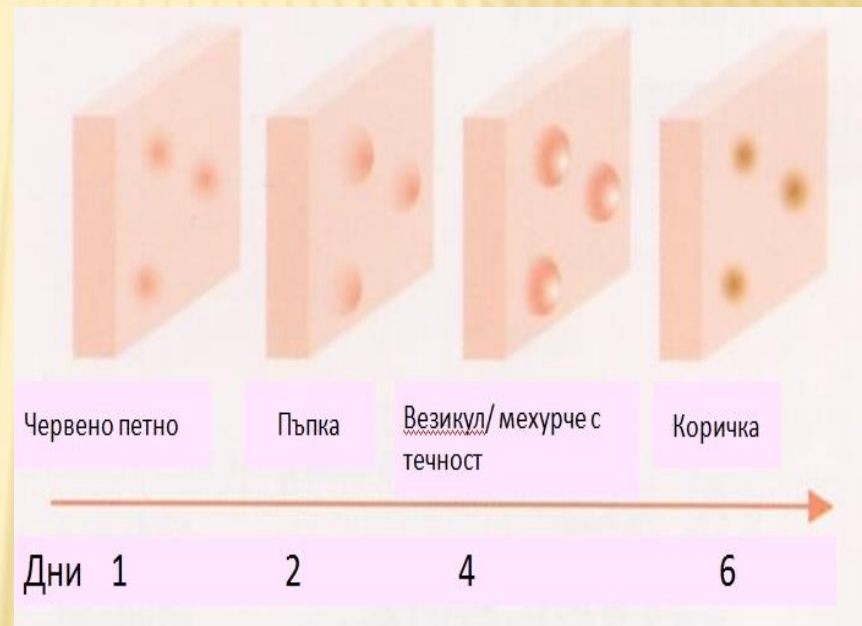
- ✘ Centripetal distribution:
- ✘ The rash is symmetrical.
- ✘ It first appears on the trunk where it is abundant, and then comes on the face, arms and legs where it is less abundant.



- ✘ Mucosal surfaces (buccal, pharyngeal) are generally involved.
- ✘ Axilla may be affected, **but palms and soles are not usually affected.**
- ✘ The density of the eruption diminishes centrifugally.



- ✘ **Rapid evolution:**
- ✘ The rash advances quickly through the stages of macule, papule, vesicle and scab.
- ✘ In fact, the first to attract attention are often the vesicles filled with clear fluid and looking like “dew-drops” on the skin.



- ✘ They are superficial in site, with easily ruptured walls and surrounded by an area of inflammation.
- ✘ Usually they are not umbilicated.
- ✘ The vesicles may form crusts without going through the pustular stage.
- ✘ Many of the lesions may abort.
- ✘ Scabbing begins 4 to 7 days after the rash appears.



- ✘ **Pleomorphism:**

- ✘ A characteristic feature of the rash in chickenpox is its pleomorphism, that is, all stages of the rash (papules, vesicles and crusts) may be seen simultaneously at one time, in the same area.
- ✘ This is due to the rash appearing in successive crops for 4 to 5 days in the same area.

COMPLICATIONS

- ✘ Secondary bacterial infections of skin lesions with Staphylococcus or Streptococcus.
- ✘ Pneumonia following varicella is usually viral but may be bacterial.
- ✘ Central nervous system manifestations of varicella range from aseptic meningitis to encephalitis.
- ✘ Involvement of the cerebellum, with resulting cerebellar ataxia, is the most common and generally has a good outcome.

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- ✘ Reye syndrome is an unusual complication of varicella and influenza and occurs almost exclusively in children who take aspirin during the acute illness.
 - ✘ Rare complications of varicella include aseptic meningitis, transverse myelitis, Guillain-Barré syndrome, thrombocytopenia, hemorrhagic varicella, purpura fulminans, glomerulonephritis, myocarditis, arthritis, orchitis, uveitis, iritis, and hepatitis.

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- ✘ The risk of complications from varicella varies with age.
 - ✘ Complications are infrequent among healthy children.
 - ✘ They occur much more frequently in persons older than 15 years of age and infants younger than 1 year of age.
 - ✘ Immunocompromised persons have a high risk of disseminated disease (up to 36% in one report).

INFECTION IN PREGNANCY AND NEONATES

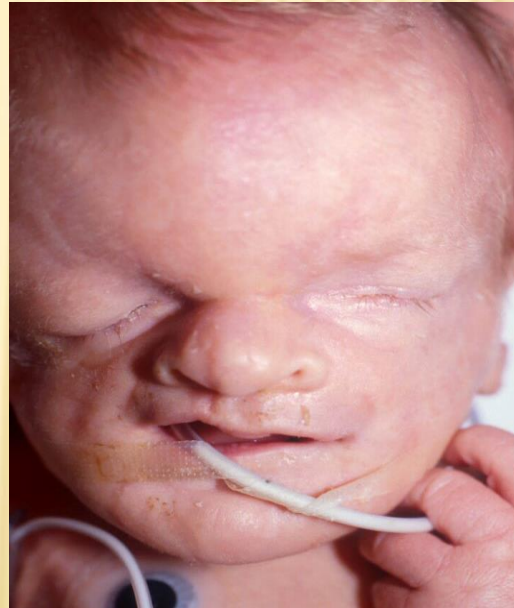
- ✘ Varicella infection in pregnant women can lead to viral transmission via the placenta and infection of the fetus. If infection occurs during the first 28 weeks of gestation, this can lead to fetal varicella syndrome (also known as congenital varicella syndrome).

POSSIBLE PROBLEMS INCLUDE:

- × **Damage to brain:**
encephalitis,
microcephaly,
hydrocephaly, aplasia of
brain



- × **Damage to the eye:**
(optic stalk, optic cap,
and lens vesicles),
microphthalmia,
cataracts,
chorioretinitis, optic
atrophy.



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- × **Other neurological disorder:** damage to cervical and lumbosacral spinal cords, motor/sensory deficits, absent deep tendon reflexes, anisocoria/Horner's syndrome.
 - × **Damage to body:** hypoplasia of upper/lower extremities, anal and bladder sphincter dysfunction

- ✘ Skin disorders:
- ✘ (cicatrical) skin lesions,
- ✘ hypopigmentation



RECURRENT DISEASE (HERPES ZOSTER)

- ✘ Herpes zoster, or shingles, occurs when latent VZV reactivates and causes recurrent disease.
- ✘ The immunologic mechanism that controls latency of VZV is not well understood.
- ✘ However, factors associated with recurrent disease include aging, immunosuppression, intrauterine exposure to VZV, and having had varicella at a young age (younger than 18 months).
- ✘ In immunocompromised persons, zoster may disseminate, causing generalized skin lesions and central nervous system, pulmonary, and hepatic involvement.

LABORATORY DIAGNOSIS

- ✘ Polymerase chain reaction (PCR) is the method of choice for diagnosis of varicella.
- ✘ Real-time PCR methods are widely available and are the most sensitive and specific method of the available tests.
- ✘ If real-time PCR is unavailable, the direct fluorescent antibody (DFA) method can be used.
- ✘ Serologic tests for varicella antibody are available commercially including a latex agglutination assay (LA) and a number of enzyme-linked immunosorbent assays (ELISA).

VACCINES CONTAINING VARICELLA VIRUS

- ✘ varicella vaccine (Varivax)
- ✘ combination measles-mumps-rubella-varicella (MMRV) vaccine (ProQuad)
- ✘ and herpes zoster vaccine (Zostavax)

VARICELLA ZOSTER IMMUNE GLOBULIN

- ✘ Varicella zoster immune globulin (VZIG) can be used for patients who have been exposed to varicella and who are at increased risk for severe disease and complications.