

Five (5) viruses:

- A. Hepatitis A virus (HAV)
- B. Hepatitis B virus (HBV)
- C. Hepatitis C virus (HCV)
- D. Hepatitis D virus (HDV): Defective virus and can cause infection only if HBV is present. It is also called the delta agent.
- E. Hepatitis E virus (HEV)

All these viruses infect the hepatocytes causing liver inflammation (hepatitis).

Structure of hepatitis viruses:

- A. Hepatitis A virus (HAV): positive-sense single stranded RNA non-enveloped
- B. Hepatitis B virus (HBV): double stranded DNA enveloped
- C. Hepatitis C virus (HCV): positive-sense single stranded RNA enveloped
- D. Hepatitis D virus (HDV): negative-sense single stranded RNA enveloped
- E. Hepatitis E virus (HEV): positive-sense single stranded RNA non-enveloped

Based on structure, transmission of hepatitis viruses occurs mainly through:

- A. Hepatitis A virus (HAV): fecal-oral route (water or food contaminated by fecal material)
- B. Hepatitis B virus (HBV): blood (transfusion, injection drug use, needlestick injuries), mother-to-child, sexual, organ transplant patients, hemodialysis patients.
- C. Hepatitis C virus (HCV): blood (transfusion, injection drug use, needlestick injuries), organ transplant patients, hemodialysis patients. Mother-to-child, and sexual can occur but less compared to HBV.
- D. Hepatitis D virus (HDV): same as HBV except for sexual transmission.
- E. Hepatitis E virus (HEV): fecal-oral route (water or food contaminated by fecal material).

Clinical features:

- The incubation period is few weeks for HAV and HEV.
- The incubation period is few months for HBV, HCV and HDV.
- All 5 viruses cause acute hepatitis: Jaundice (يرقان، صفار), nausea, vomiting, anorexia (فقدان في الشهية), and fever with high levels of liver enzymes (ALT and AST).

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- Asymptomatic acute infection can occur.
- All 5 viruses can cause fulminant hepatitis (acute liver failure) in a minority of patients (less than 1% on average).
- HBV, HCV and HDV cause chronic infection (continue to be present in the body for more than 6 months). Chronic infection progress to cirrhosis (تشمع الكبد) and subsequently to hepatocellular carcinoma. So, HBV and HCV can be considered as **oncoviruses**.

Diagnosis:

- A. Hepatitis A virus (HAV): Serology. HAV IgM (acute infection). HAV IgG (past infection or vaccination).
- B. Hepatitis B virus (HBV): Serology, molecular detection.
- C. Hepatitis C virus (HCV): Serology, molecular detection.
- D. Hepatitis D virus (HDV): First, HBV must be present. Serology, molecular detection.
- E. Hepatitis E virus (HEV): Serology. HEV IgM (acute infection).

Treatment:

- Acute infection: Supportive care
- Chronic HBV: Antiviral medications (nucleoside analogs), interferon.
- Chronic HCV: Antiviral medications (**direct-acting antivirals DAAs**), interferon.
- Chronic HDV: Interferon. HBV control. Newer drugs are evaluated.

Prevention:

- HAV: Inactivated vaccine (very effective). Two doses
- HBV: Subunit vaccine. Three doses. HBV vaccination prevents HDV infection.

A final note (Not for the exam)

“WHO estimates that 296 million people were living with chronic hepatitis B infection in 2019, with 1.5 million new infections each year.”

“Globally, an estimated 58 million people have chronic hepatitis C virus infection, with about 1.5 million new infections occurring per year.”

Sources:

<https://www.who.int/news-room/fact-sheets/detail/hepatitis-c>; <https://www.who.int/news-room/fact-sheets/detail/hepatitis-b>;

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Two groups of single stranded positive sense non-enveloped RNA viruses:

A. Rhinoviruses

B. Enteroviruses

Rhinoviruses:

More than 150 types classified into 3 groups (A, B and C).

Cellular receptors: intercellular adhesion molecule-1 (ICAM-1) and low-density lipoprotein receptor (LDLR).

Acid labile (complete inactivation occurs at a pH of 3.0).

Disease: Upper respiratory tract infection (also called: common cold, coryza, rhinosinusitis).

The symptoms include: Chilliness is an early symptom of the common cold. Other symptoms include runny nose, sore throat, coughing, sneezing, nasal congestion, headache, low-grade fever and fatigue. Asymptomatic infection can occur.

Acute asthma exacerbations.

Short incubation period: 2-4 days. The illness usually lasts 7 days.

The disease is common in fall, winter and spring.

Transmission: hand-to-hand, hand-to-eye, or hand-to-object- (e.g., doorknob) to-hand contamination. Rhinoviruses can survive for hours on contaminated environmental surfaces.

Diagnosis: real-time PCR.

Treatment: symptomatic. Prevention: hand washing.

Enteroviruses:

1. Poliovirus (الفيروس المسبب لشلل الأطفال)

Three antigenic types of polioviruses.

Transmission: The mouth is the portal of entry of the virus, and primary multiplication takes place in the oropharynx or intestine. Poor hygiene and sanitation is linked to virus spread.

After 1–2 weeks incubation disease may appear, which can be:

1. Asymptomatic infection in 90–99% of the cases (sub-clinical disease)
2. Acute febrile illness: the most common form of symptomatic disease. Includes: fever, headache, nausea, vomiting, constipation, and sore throat.
3. Nonparalytic poliomyelitis (aseptic meningitis – التهاب السحايا): stiffness and pain in the back and neck. Recovery is rapid and complete.
4. In less than 1/1000: Paralytic poliomyelitis (شلل): flaccid paralysis resulting from lower motor neuron damage and subsequent muscle atrophy. Fatality in 5–10 % of the cases (due to respiratory failure caused by depression of the respiratory centers).

Poliovirus can spread along axons of peripheral nerves to the CNS, where it continues to progress along the fibers of the lower motor neurons to increasingly involve the spinal cord or the brain.

Diagnosis: virus culture, PCR.

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Immunity is permanent following infection by each antigenic type. Cross-protection is observed between types.

Prevention: Both live-virus (oral polio vaccine OPV, also called Sabin vaccine) and killed-virus (inactivated polio vaccine IPV, also called Salk vaccine) vaccines are available.

2. Coxsackieviruses A and B

Diseases:

- A. Aseptic meningitis: full recovery in most patients.
- B. Herpangina: fever and sore throat with discrete vesicles on the posterior half of the palate, pharynx, tonsils, or tongue. The illness is self-limited and most frequent in small children. Caused by group A coxsackieviruses.
- C. Acute febrile illness with or without skin rash especially during summer.
- D. Common cold.
- E. Hand-foot-and-mouth disease: caused by coxsackievirus A16 and enterovirus 71. Oral and pharyngeal ulcerations and a vesicular rash of the palms and soles that may spread to the arms and legs. Self-limited.
- F. Pleurodynia (epidemic myalgia): Caused by group B coxsackieviruses. Fever and stabbing chest pain. Self-limited.
- G. Myocarditis: acute inflammation of the heart or its covering membranes (pericarditis). Can be fatal.

3. Echoviruses:

4. Enteroviruses:

5. Parechoviruses:

Diseases: Aseptic meningitis, encephalitis, febrile illnesses with or without rash, common cold, and acute hemorrhagic conjunctivitis (enterovirus 70).

No vaccines or antiviral drugs are currently available for prevention or treatment of these diseases.

Diagnosis: real-time PCR.

The virus family *Herpesviridae* has 8 members that can cause human disease:

1. Human herpes virus 1 (herpes simplex virus type 1) **حمو فيروس في الغم غالباً في الفم**
2. Human herpes virus 2 (herpes simplex virus type 2) **حمو تناسلي**
3. Human herpes virus 3 (varicella zoster virus) **جدري الماء والحزام الناري وباللهجة الكويتية العقنقز**
4. Human herpes virus 4 (Epstein Barr virus) **الحمى الغدية وبعض السرطانات الليمفاوية**
5. Human herpes virus 5 (cytomegalovirus) **الحمى الغدية وأمراض عند ذوي المناعة الخلوية الضعيفة**
6. Human herpes virus 6 **الطفح الوردي في الأطفال**
7. Human herpes virus 7 **الطفح الوردي في الأطفال**
8. Human herpes virus 8 (Kaposi's sarcoma-associated herpesvirus) **ورم خبيث في الأوعية الدموية**

THE MOST IMPORTANT FEATURE: ALL herpesviruses establish lifelong persistent latent infection in the body, with periodic reactivation that can be asymptomatic or symptomatic especially if cellular immunity is suppressed.

عند دخول جميع الفيروسات المنتمة لعائلة الهيريس إلى الجسم فإنها تبقى إلى الأبد في الجسم ولن تخرج منه أبداً. ستبقى في غالب الأحيان كامنة بدون أعراض ولكنها قد تنشط في بعض الأحيان خاصة إذا ما حدث نقص في المناعة الخلوية

Structure

Enveloped with double-stranded DNA genome.

Classification

HHV-1, HHV-2 and HHV-3 are alphaherpesvirinae viruses

HHV-5, HHV-6 and HHV-7 are betaherpesvirinae viruses

HHV-4 and HHV-8 are gammaherpesvirinae viruses

Human herpes viruses 1 and 2 (herpes simplex virus types 1 and 2) HSV-1 and HSV-2:

Transmission: Direct contact, saliva, sexual, vertical.

Pathogenesis and clinical features: After contact, the virus infects the skin and mucous membranes causing the skin lesions (macules which are small flat lesions, that will evolve into papules which are small raised lesions that will develop into vesicles which are small raised lesions filled with clear fluid **التي يُطلق عليها حويصلات** followed by opening of the vesicles to form ulcers **والتي يُطلق عليها تقرحات** followed by crusting). The skin lesions last about 1–2 weeks, followed by complete recovery. The lesions can be extremely painful.

During this primary infection, the virus enters the sensory nerve endings and is transported by retrograde axonal transport into the dorsal (posterior) root ganglia (nuclei of sensory neurons) and the virus will establish latency there for life. During latency, **NO** active replication of the virus occurs. So, there is no production of virus proteins and the immune system cannot see the virus. Certain triggers can



cause activation of the latent virus to cause reactivation. These triggers include stress, fever, and suppressed cellular immunity. On reactivation, the virus will move by anterograde axonal transport into the skin and mucous membranes to cause lesions similar to primary infection. A majority of primary and reactivation cases are **asymptomatic**.

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Common sites of latency are the trigeminal nerve ganglia for HSV-1 and the sacral ganglia for HSV-2.

Diseases:

Gingivostomatitis.

Pharyngitis, tonsillitis.

Conjunctivitis (التهاب الطبقة الخارجية للعين والسطح الداخلي للجفن)

Keratitis (التهاب قرنية العين وهو التهاب خطير قد يؤدي للعمى)

Cold sores (fever blisters, herpes labialis)

Cutaneous herpes.

Herpetic whitlow (in the fingers).

Eczema herpeticum (in patients with allergic dermatitis).

Genital herpes.

Herpes encephalitis (infection of the brain tissue)

Herpes meningitis (infection affecting the meninges)

Neonatal herpes: Severe form with mortality of about 60%.

Disseminated severe disease in immunosuppressed patients (e.g., in AIDS patients).

Diagnosis:

Clinical.

PCR.

Antibodies: IgM in primary infection and IgG indicates past infection.

Nuclear inclusions in cells (technique called Tzanck smear).

Treatment:

Antivirals: acyclovir, valacyclovir, and vidarabine, all of which are inhibitors of viral DNA synthesis.

Prevention: Vaccines have not been approved for prevention so far.

Epidemiology: In young adults, more than 90% have already been infected by HSV-1. Much lower prevalence of HSV-2 has been reported due to its sexual spread.

Human herpes virus 3 (varicella zoster virus) VZV

Transmission: Direct contact, aerosols.

Pathogenesis and clinical features: For primary infection (chickenpox, varicella, جدري الماء), after access into the upper respiratory tract, local replication occurs, followed by spread into the blood (primary viremia), followed by replication in the liver and spleen, followed by spread from the blood (secondary viremia) into the skin to give rise to chickenpox skin rash which is highly pruritic, itchy (تتسبب بحكة شديدة). Similar to HSV-1 and HSV-2, VZV establish latency in dorsal root ganglia.



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Herpesviruses

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Upon reactivation, VZV cause lesions in one or a few skin segments innervated by the dorsal root ganglia. These lesions are called zoster or shingles (الحزام الناري).

Reactivation occurs in older individuals and in case of immune suppression. The lesions are extremely painful. Even after the lesions disappear, pain may continue for several months (called post-herpetic neuralgia).



VZV is highly infectious. After an incubation period of 2–3 weeks, the patient is very infectious. The patient is also infectious by the end of the incubation period. Infection gives immunity from chickenpox. But if the patient was not infected before, and gets exposed to shingles, the individual will get chickenpox which is the primary infection. So, the source of primary infection (chickenpox) is from outside the body, while the source of shingles is internal (latent VZV).

Complications of chickenpox can occur including pneumonia and meningitis. However, mortality is very low (1/100,000, and slightly higher among adults). Neonatal VZV is severe with mortality of about 30%.

Diagnosis:

Clinical.

PCR.

Antibodies: IgM in primary infection and IgG indicates past infection.

Nuclear inclusions in cells (technique called Tzanck smear).

Treatment:

Chickenpox: symptomatic. Zoster: acyclovir, valacyclovir, and famciclovir can reduce the length and severity shingles. For postherpetic neuralgia: tricyclic antidepressants, gabapentin and pregabalin, opioids, tramadol, etc. بتأخوذها إن شاء الله في علم الأدوية.

Prevention:

Live attenuated vaccine is available to prevent chickenpox.

Therapeutic vaccines are available to reduce the occurrence of zoster (both recombinant subunit and live attenuated vaccines).

Epidemiology:

In countries where vaccination is not offered (due to cost), a majority of children get infected. Zoster likelihood increase with age.

Epstein Barr virus (EBV)

Transmission: saliva. So, the primary infection by EBV is called “kissing disease”.

Tropism: Epithelial cells and B lymphocytes. **Site of latency:** B lymphocytes.

Receptor: CD21 (complement receptor 2)

Clinical features: The majority of primary infections is asymptomatic especially in children. In adults, primary infection is called “infectious mononucleosis”.

Infectious mononucleosis = Fever + pharyngitis + cervical lymphadenopathy (تضخم العقد الليمفاوية في العنق)

Other features of infectious mononucleosis: fatigue, headache, splenomegaly.

Since EBV is an oncovirus, it has been linked the following cancers:

- A. Burkitt lymphoma
- B. Nasopharyngeal carcinoma
- C. Hodgkin and non-Hodgkin lymphomas
- D. Gastric carcinoma

Other disease linked to EBV infection in AIDS patients: **oral hairy leukoplakia**, which is a BENIGN wart-like growth that on the tongue. ورم حميد على لسان مرضى الإيدز.

Diagnosis:

- A. Clinical.
- B. Blood film showing atypical lymphocytes (large reactive T cells).
- C. PCR.
- D. Serology: IgM to viral capsid antigen (VCA) in primary infection and IgG to EBV nuclear antigen (EBNA) indicates past infection.

Treatment:

EBV primary infection is a self-limited disease. Treatment is supportive.

Prevention: Vaccines have not been approved for prevention so far.

Epidemiology: In young adults, more than 90% have already been infected by EBV. In developing countries infection occurs in early childhood. In developed countries, infection occurs later in life at the beginning of sexual activities, kissing.

Cytomegalovirus (CMV)

Transmission: saliva, direct contact, mother-to-child

Tropism: many many many cells. **Site of latency:** many many many cells. **Receptor:** many many many receptors.

Clinical features: The majority of primary infections is asymptomatic especially in children. In adults, primary infection is called “infectious mononucleosis-like syndrome”.

Infectious mononucleosis = Fever + pharyngitis + cervical lymphadenopathy (تضخم العقد الليمفاوية في العنق)

Other causes of infectious mononucleosis-like syndrome: EBV, herpes simplex viruses.

Other Diseases:

- A. The importance of CMV reactivation is among **immunosuppressed patients** (for example in AIDS patients). It can cause: Pneumonia, gastroenteritis, retinitis (التهاب شبكية العين)
- B. Congenital infection: CMV is the most common cause of **congenital infection**. Congenital CMV infection can result in deafness, blindness, mental retardation (تخلف عقلي)

Diagnosis:

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Lecture 9: 18 December 2022

Herpesviruses (EBV, CMV, roseola viruses, and Kaposi sarcoma herpesvirus). Malik Sallam, MD, PhD

- A. Clinical (primary infection is mostly asymptomatic)
- B. Blood film showing atypical lymphocytes (large reactive T cells).
- C. PCR.
- D. Serology: IgM in primary infection and IgG to indicates past infection.

Treatment:

CMV primary infection is a self-limited disease. Treatment is supportive.

In immunocompromised patients and in congenital infection: Ganciclovir (antiviral drug) is used.

Prevention: Vaccines have not been approved for prevention so far.

Epidemiology: In young adults, more than 90% have already been infected by CMV.

Roseola viruses (HHV-6 and HHV-7)

Transmission: saliva.

Clinical features: infection is usually acquired in the first year of life (in infants). The disease is called roseola infantum (exanthema subitum or sixth disease). The disease is characterized by **high fever and skin rash**. Importance of latency and reactivation is not known 😊

Diagnosis:

- A. Clinical
- B. PCR

Treatment:

Supportive. Antipyretics خافض حرارة

Prevention: Vaccines have not been approved for prevention so far.

Epidemiology: In children, more than 90% have already been infected.

Kaposi sarcoma herpesvirus (HHV-8)

Transmission: saliva, sexual especially among male homosexuals, mother-to-child transmission.

Clinical features: Primary infection is asymptomatic. In AIDS patients, or in the elderly Kaposi sarcoma can occur (cancer of the blood and lymph vessels). It appears on the skin or mucous membranes.

Diagnosis:

- A. Histopathology
- B. PCR

Prevention: Vaccines have not been approved for prevention so far.

Epidemiology: The prevalence is low in the general population. The prevalence is high among male homosexuals.

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Poxviridae

Double-stranded DNA, enveloped viruses that are large in size and replicate in the cytoplasm

Variola virus (the cause of smallpox الجذري الذي تم القضاء عليه من خلال حملة تطعيم عالمية وانتهى في العالم منذ السبعينات)

Monkeypox virus (جدري القردة وهو المرض المستجد المنتشر في العالم حالياً)

Molluscum contagiosum virus (مرض جلدي يُشفى تلقائياً شوف تأخذونه بالتفصيل الفصل القادم بإذن الله تعالى)

IMPORTANT: Why eradication of smallpox was successful? لماذا نجحت حملة القضاء على الجدري؟؟؟

1. Variola virus is a DNA virus that is stable antigenically.
2. The live-attenuated vaccine was effective and gave long-term immunity.
3. The disease affected humans only with animal reservoir.
4. All cases were symptomatic with no subclinical infections or carrier states.
5. The disease had high mortality rate and for those who survived infection, permanent scars remained causing emotional damage. So, people collaborated in the vaccination efforts.

Parvoviridae

Single-stranded DNA, non-enveloped viruses that are very small in size and replicate in the nucleus

Parvovirus B19 and bocaviruses

Transmission: respiratory secretions, mother-to-child

Tropism: erythroid progenitors for B19 virus. Why not in mature RBCs? Because they lack nuclei. Respiratory cells for bocaviruses.

Clinical features: For bocavirus: upper and lower respiratory tract infections.

For parvovirus B19: In children, it causes fever and rash which is called erythema infectiosum (fifth disease or slapped cheek syndrome). In adults, primary infection can cause arthritis (التهاب المفاصل)

Other parvovirus B19 disease in special groups of patients:

- A. Immunosuppressed patients: Pure red cell aplasia (chronic anemia)
- B. Underlying chronic anemia: Transient aplastic crisis (severe acute anemia)
- C. Congenital infection: Hydrops fetalis (anemia that could be fatal)

Diagnosis:

- A. Clinical
- B. PCR.
- C. Serology: IgM in primary infection and IgG to indicates past infection.

Treatment: Supportive.

Prevention: Vaccines have not been approved for prevention so far.

Epidemiology: Common infection. No latent state.

Adenoviridae

Double-stranded DNA, non-enveloped viruses that replicate in the nucleus. The virus has many serotypes.

Transmission: respiratory secretions, fecal-oral, direct contact

Tropism: epithelial cells of the respiratory tract, eyes, gastrointestinal tract and urinary tract.

Clinical features:

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- A. Upper and lower respiratory tract infections (adenoviruses are the most common causes of pharyngitis).
- B. Gastroenteritis.
- C. Conjunctivitis.
- D. Cystitis (urinary bladder infection التهاب المثانة البولية)

Diagnosis:

Antigen detection.

PCR.

Treatment: Supportive.

Prevention: Live attenuated vaccine is available for a few serotypes that can cause pneumonia.

Epidemiology: Infection can occur year around without seasonality (ليس موسمياً).

Papillomaviridae (Human papillomaviruses (HPV))

Double-stranded DNA, non-enveloped viruses that replicate in the nucleus. The virus has many types.

Transmission: direct contact, sexual

Tropism: epithelial cells of the skin and mucous membranes.

Important features:

1. HPV is the most common cause of sexually transmitted infections worldwide.
2. Most HPV infections resolve spontaneously within 2-3 years.
3. Many infections are totally asymptomatic, so the patient can have HPV without knowing
4. Some HPV types are benign, some have low-risk of causing cancer and some are high-risk types that can cause the following cancers: cervical, penile, anal, oropharyngeal, and vulvar cancers.
5. High-risk HPV types have transforming proteins that are related to cancer development.

Clinical features:

- A. Common warts (الثآليل)
- B. Condyloma acuminata (genital warts الثآليل التناسلية) caused mainly by HPV-6 and HPV-11
- C. Laryngeal papilloma.
- D. Cervical cancer (سرطان عنق الرحم في الإناث) caused mainly by HPV-16 and HPV-18
- E. Other cancers: penile, anal, oropharyngeal, and vulvar cancers. Caused by high-risk HPV types (e.g., HPV-16 and HPV-18)

Diagnosis:

- A. Clinical.
- B. Pap smear (Papanicolaou smear is a cytology method of cervical screening to look for precancerous lesions in the cervix).
- C. PCR.

Treatment: Most do not require treatment. Other methods: surgical excision, laser therapy, chemical agents (e.g., podophyllotoxin and podophyllin, imiquimod).

Prevention: Subunit vaccines:

1. Cervarix (bivalent vaccine for HPV-16 and 18).
2. Gardasil (quadrivalent vaccine for HPV-6, HPV-11, HPV-16, and HPV-18).
3. Nonavalent vaccine (for the following types: 6, 11, 16, 18, 31, 33, 45, 52, 58).

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Epidemiology: The global HPV prevalence is about 10%.

Polyomaviridae

Double-stranded DNA, non-enveloped viruses that replicate in the nucleus

JC virus, BK virus and Merkel cell polyomavirus

The vast majority of these infection remain latent in the body without symptoms.

Transmission: not established 😊

Clinical features:

- A. BK virus: cystitis in bone marrow transplant patients
- B. JC virus: progressive multifocal leukoencephalopathy (PML) in AIDS patients.
- C. Merkel cell polyomavirus: Merkel cell carcinoma (rare skin cancer). So, Merkel cell polyomavirus is an oncovirus

Diagnosis:

- A. PCR
- B. Radiology
- C. Histopathologic examination

Treatment: No specific treatment.

Prevention: Vaccines have not been approved for prevention so far.

Epidemiology: Widely spread. A majority of humans have the infection by BK and JC viruses.

Orthomyxoviridae (Influenza viruses) الإنفلونزا

Negative sense, single-stranded RNA, enveloped viruses with a SEGMENTED GENOME that replicate in the NUCLEUS. جينوم الإنفلونزا عبارة عن عدة قطع، كل قطعة بتعطي بروتين مختلف

Based on the differences in the nucleoprotein, influenza viruses are classified into types:

Type A, Type B and Type C.

Based on the differences in the hemagglutinin protein (H) and neuraminidase protein (N), only Type A is classified into subtypes (e.g., subtype H1N1 الإنفلونزا الإسبانية, إنفلونزا الخنازير, subtype H5N1 إنفلونزا الطيور, subtype H3N2).

Type A can cause pandemics if exchange of influenza gene segments occurs between human and animal/bird strains (the result is antigenic shift (تحويل مفاجئ)). Type A and type B can cause outbreaks (epidemics), through mutations (antigenic drift (انحراف طفيف)).

Type C causes common cold.

Transmission: respiratory secretions, aerosols.

Tropism: epithelial cells of the respiratory tract.

Clinical features:

- A. High fever and chills.
- B. Frontal headache.
- C. Generalized weakness.
- D. Myalgia, arthralgia (أوجاع في العضلات والمفاصل).
- E. Sore throat.
- F. Dry cough.
- G. Pneumonia (children, elderly, those with chronic disease). Secondary bacterial pneumonia can also occur (*Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, Gram-negative bacilli).

Diagnosis:

Rapid antigen detection.

PCR.

Treatment: Supportive, antivirals (oseltamivir (Tamiflu), zanamivir (Relenza)).

Prevention: Live attenuated, inactivated and recombinant vaccines are available. Trivalent (2 A strains and 1 B strain) or quadrivalent (2 A strains and 2 B strains) are available.

Epidemiology: Seasonal outbreaks occur in winter as a result of declining immunity and antigenic drift with types A and B as the causative agents. Pandemics occur only with type A as a result of antigenic shift.

Coronaviridae

Positive sense, single-stranded RNA, enveloped viruses with a large genome that replicate in the cytoplasm.

Four types cause common cold: 229E, OC43, HKU1 and NL63

Two types caused severe acute respiratory distress syndrome: SARS-CoV-1 and MERS-CoV (Middle East respiratory distress syndrome coronavirus).

Mortality of SARS: about 10%

Mortality of MERS: 36%

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Diagnosis:

PCR.

Treatment: Supportive.

Vaccination: Not available so far.

SARS-CoV-2 and COVID-19 are not required for the exam.

Paramyxoviridae

Negative sense, single-stranded RNA, enveloped viruses that replicate in the cytoplasm.

1. Parainfluenza viruses 1, 2, 3 and 4 (PIV)
2. Respiratory syncytial virus (RSV): the major pediatric respiratory tract pathogen
3. Metapneumovirus
4. Measles فيروس الحصبة
5. Mumps فيروس النكاف أبو دغيم

Transmission: respiratory secretions, aerosols.

Tropism: epithelial cells of the respiratory tract.

Clinical features:

- A. Common cold: PIV, RSV and metapneumovirus
- B. Laryngitis: PIV (with hoarseness of voice, barking cough)
- C. Croup (inflammation of the upper airway, larynx and trachea): PIV, RSV
- D. Bronchiolitis: RSV (the most common cause in infants)
- E. Pneumonia: RSV
- F. Otitis media (التهاب الأذن الوسطى): PIV

Diagnosis:

Rapid antigen detection.

PCR.

Treatment: Supportive, ribavirin (antiviral) can be used for RSV lower respiratory tract infection.

Prevention: Vaccines have not been available so far. Maybe soon for RSV.

Epidemiology: For RSV, about 70% of infants are infected by age 1 and almost all by age 2 years. PIV is also an important pediatric pathogen. Reinfections are common.

Measles:

Highly infectious virus. The disease is characterized by fever, respiratory symptoms, and a maculopapular rash. Complications are common.

Transmission: respiratory secretions.

Viremia occurs transferring the virus into the skin and eye. Central nervous system involvement is common (encephalitis, postinfectious encephalomyelitis, and subacute sclerosing panencephalitis).

The most common complication of measles is otitis media. Pneumonia caused by secondary bacterial infection is the most common life-threatening complication of measles.

Koplik spots (blue/white raised spots on red base on the buccal mucosa opposite the first molar) are pathognomonic/diagnostic of measles (these spots appear one day before the onset of rash. Measles infection causes immune suppression that is transient.

There is only one antigenic type of measles virus. Infection results in life-long immunity.

Diagnosis: serology IgM antibodies.

Treatment: Supportive. Vitamin A treatment in developing countries has decreased mortality and morbidity.

Prevention: Live-attenuated vaccine MMR (measles mumps rubella vaccine).

This is the only material required for the exam. No other source is needed

For any questions you can contact me through the following email: malik.sallam@ju.edu.jo

Mumps:

Highly infectious virus. Enlargement of one or both salivary glands. The disease is mild in children. Complications occur in adults. At least one-third of all mumps infections are subclinical. Central nervous system involvement is common (aseptic meningitis). Testicular inflammation (orchitis) is extremely painful and can lead to sterility. Ovarian inflammation can occur (oophoritis). Pancreatitis is reported as well.

There is only one antigenic type of measles virus. Infection results in life-long immunity.

Transmission: respiratory secretions.

Diagnosis: serology IgM antibodies, PCR.

Treatment: Supportive. Vitamin A treatment in developing countries has decreased mortality and morbidity.

Prevention: Live-attenuated vaccine MMR (measles mumps rubella vaccine).

Togaviridae

Positive sense, single-stranded RNA, enveloped viruses that replicate in the cytoplasm.

Rubella virus: the causative agent of German measles (rubella الحصبة الألمانية)

The mildest form of viral infections that cause skin rash.

Rubella is a three-day rash (morbilliform rash) with low-grade fever.

Risk of congenital infection. The classic triad of congenital rubella consists of cataracts, cardiac abnormalities, and deafness.

Transmission: respiratory secretions, mother-to-child

Diagnosis: serology IgM antibodies, PCR.

Treatment: Supportive.

Vaccination: Live-attenuated vaccine MMR (measles mumps rubella vaccine).

Viruses that cause gastroenteritis:

Transmission is fecal-oral, diagnosis is by antigen detection, PCR or electron microscopy

1. Rotavirus: double-stranded enveloped RNA virus with a segmented genome. The most common cause of gastroenteritis in infants. Live-attenuated vaccine is available.
2. Norovirus: single-stranded positive sense RNA non-enveloped virus. The most common cause of gastroenteritis in adults.
3. Astrovirus: single-stranded positive sense RNA non-enveloped virus.
4. Sapovirus: single-stranded positive sense RNA non-enveloped virus.

Filoviridae

Negative sense, single-stranded RNA, enveloped viruses that replicate in the cytoplasm. Filamentous in shape

Ebola virus: causes severe hemorrhagic fever mainly in Africa. Mortality rate is high. Transmitted by respiratory droplets and direct contact. Vaccines are available. Diagnosis by PCR.

Rhabdoviridae

Negative sense, single-stranded RNA, enveloped viruses that replicate in the cytoplasm. Bullet-shaped (تُشبه الرصاصة)

Rabies virus (الفيروس المسبب للسعار أو داء الكلب)

After bite of a rabid animal (حيوان مسعور مثل الكلاب أو الخفافيش أو الثعالب أو الذئب أو الراكون أو الجرذان), rabies virus multiplies in muscle or connective tissue at the site of inoculation and then enters peripheral nerves at neuromuscular junctions and spreads up the nerves to the central nervous system causing progressive encephalitis.

Once in the central nervous system, rabies virus is fatal (death rate = 100%).

Management: passive immunization to neutralize the virus with vaccination.

Arboviruses Arthropod-borne viruses (الفيروسات التي تنتقل عبر الحشرات)

Flaviviridae

Positive sense, single-stranded RNA, enveloped viruses that replicate in the cytoplasm.

1. Dengue virus: Dengue (breakbone fever) is a mosquito-borne infection characterized by fever, severe headache, muscle and joint pain, nausea and vomiting, eye pain, and rash. It is the most common arbovirus infection worldwide.
2. Yellow fever: causes hepatitis and is transmitted by mosquitoes.
3. West Nile fever: can cause meningitis. A majority of infections are asymptomatic. It is transmitted by mosquitoes.
4. Zika fever: can cause microcephaly if transmitted from the mother to the child. The virus is transmitted by mosquitoes.

Prion disease (الأشهر هو جنون البقر) ليس مطلوباً للامتحان

The proposed cause is a proteinaceous material that does not have nucleic acid. The disease in relation of consumption of infected cows: variant Creutzfeldt Jakob disease (vCJD).

آخِرُ دَعْوَاهُمْ أَنِ الْحَمْدُ لِلَّهِ رَبِّ الْعَالَمِينَ