Virology

Lec (9)
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Teaching Objectives:
1. Know general characteristic of Togaviridae and Coronavirus.
2. Distinguish Characteristic of strains.
3. Recognize the mechanism of entry and replication.
4. Understand methods of diagnosis.
5. Know treatment and prevention.

Togaviridae family

Rubella virus a member of Togaviridae family, alphavirus genus consist of about 30 viruses, most viruses transmit through mosquitoes or other blood -feeding arthropods except rubella is classified in a separate genus in the Togaviridae family, has no arthropod vector and is not an arbovirus , but is acquired via the respiratory route. Rubella (means 'little red') Enveloped (toga=cloak), also known as German measles, is a mild disease in children and adults, but can cause devastating problems if it infects the fetus, especially if the infection is in the first few weeks of pregnancy.

Important properties

- Those possess a single stranded, positive-sense RNA, and therefore has no virion polymerase. Measuring about 70 nm in diameter.
- Nucleocapsid has icosahedral symmetry.
- The envelope surrounded by particle contains two glycoprotein (Surface spikes contain hemagglutinin).
- All alpha viruses are antigenically related. Only one major antigenic type
- Viruses are inactivating by acid, pH, heat, lipid solvents, detergents, bleach, phenol, 70% alcohol and formaldehyde.
- Replicates in the cytoplasm.

Mode of Transmission:

- The virus is transmitted via droplets.
- Infected mother to fetus transplacentally.

Pathogenesis and Immunity:

- Initial replication of the virus occurs in the nasopharynx and cervical lymph nodes. From there it spreads via blood to the internal organs and skin.
- The origin of the rash is unclear; it may be due to Ag-Ab-mediated vasculitis. Infection leads to lifelong immunity. Second cases of rubella do not occur; similar rashes are caused by other viruses, such as coxsackievirus and echovirus, Ab cross the placenta and protects the newborn.
- The disease occurs worldwide. For several years, cytomegalovirus rather than rubella virus has been the leading viral cause of congenital abnormalities.

Clinical Findings:

A- Rubella: It is a milder, shorter disease than measles. After an incubation period of 14-21 days, a brief prodromal period with fever and malaise is followed by a maculopapular rash, which starts on the face and progresses downward to involve extremities. Posterior auricular lymphadenopathy is characteristic. The rash typically lasts 3 days.



B- Congenital rubella syndrome: the significance of rubella virus is not as a cause of mild childhood disease but as a teratogen. When a non-immune pregnant woman is infected during the 1st trimester, especially the 1st month, significant congenital malformations can occur as a result of maternal viremia and fetal infection. The increased rate of abnormalities during the early weeks of pregnancy is attributed to the very sensitive organ development that occurs at that time. The malformations are widespread and involve primarily the heart (e.g., patent ductus arteriosus), the eyes (e.g., cataracts), and the brain (e.g., deafness and mental retardation). Congenitally infected infants have significant IgM titers and persistent IgG titers long after maternal Ab has disappeared.

Lab Diagnosis:

- Virus can be grown in cell culture, but it produces little CPE, it is usually identified by its ability to interfere with echovirus CPE. If rubella virus is present in patient's specimen and has grown in the cell culture, no CPE will appear when the culture is superinfected with an echovirus.
- Rising Ab titer 4-fold or greater between acute-phase and convalescent-phase sera in the hemagglutination inhibition test or ELISA.
- Observing the presence of **IgM** Ab in single acute-phase serum sample may help in diagnosis.
- Pregnant woman exposed to rubella virus, the presence of **IgM** Ab indicates recent infection, whereas a 1:8 or greater titer of **IgG** Ab indicates immunity and protection of the fetus.
- If recent infection has occurred, an **amniocentesis** can reveal whether there is rubella virus in amniotic fluid, which indicates definite fetal infection.

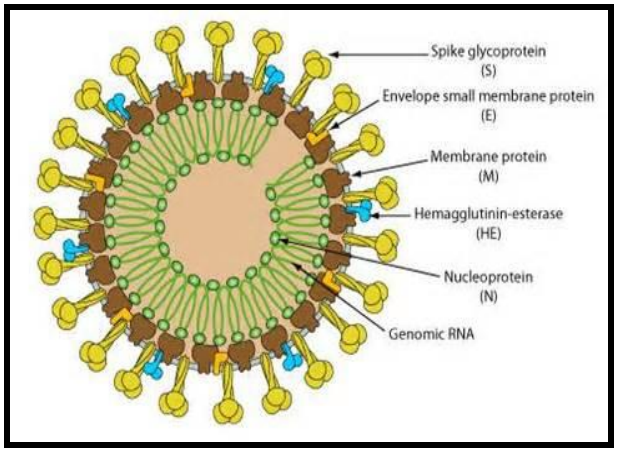
Treatment and prevention:

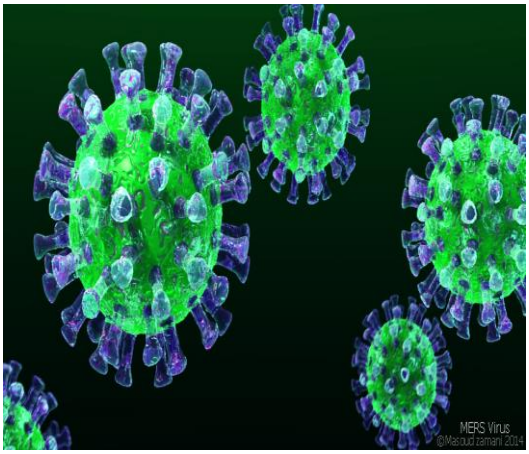
- No antiviral therapy.
- Immunization with live attenuated vaccine with measles, mumps and Rubella (MMR) subcutaneously at age of 15 months, 18 months, before entry the school. To unimmunized young adult woman if they are not pregnant and will use contraception for the next 3 months. Vaccine is a live one it should not be given to immunocompromized patients or to pregnant woman.
- Vaccine has caused significant reduction in the incidence of rubella and congenital rubella syndrome. It induces respiratory IgA interrupting the spread of the virus by nasal carriage.
- Immune serum globulins IG can be given to pregnant woman in 1st trimester, but it may fail to prevent fetal infection.

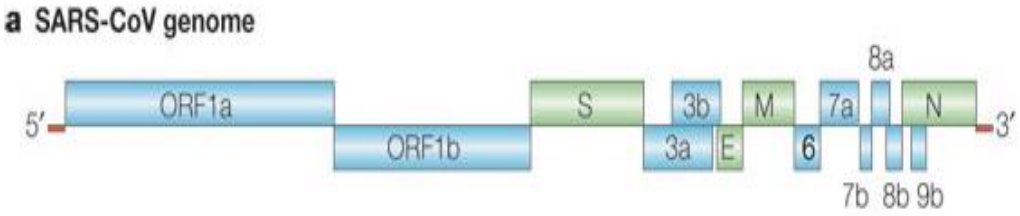
Corona viruses: Is a genus of animal virus belonging to the family Coronaviridae. The name "coronavirus" is derived from the Latin *corona*, meaning crown or halo, and refers to the characteristic appearance of virions under electron microscopy (E.M.).

Important properties of Corona viruses

- Enveloped particles measuring about 120-160nm in diameter.
- Genome is single stranded- positive sense RNA (26-32kb).
- Helical nucleocapsid, 28-30 nm, contains 60 subunits.
- The viral structural protein include a phosporelated nucleocapsid (**N**), membrane glycoprotein (**M**) serve as a matrix protein embedded in the envelope lipd bilayer and interacting with the nucleocapsid, Spike protein(**S**). Some viruses like human coronavirus OC43 have hemagglutinin (HE).







The human coronaviruses cause common colds in adults primarily in the winter and early seasons and have been implicated in gastroenteritis in infants. A novel coronavirus was identified as the cause of a worldwide outbreak of a Severe Acute respiratory Syndrome (SARS) in 2003 and others.

Novel human coronaviruses Following the high-profile publicity of SARS outbreaks, there has been a renewed interest in coronaviruses among virologists

For many years, scientists knew about only two human coronaviruses HCoV-229E and HCoV-OC43.

- The discovery of SARS-CoV added a **third** human coronavirus.

- By the end of 2004, three independent research labs reported the discovery of a **fourth** human coronavirus. It has been named NL63, NL, and the New Haven coronavirus by different research groups. The three labs are still arguing over which one discovered the virus first and has the right to name it.

- Early in 2005, a research team at the University of Hong Kong reported finding a **fifth** human coronavirus in two patients with pneumonia. They named it Human coronavirus HKU1.

- In September 2012, a **sixth** new type of coronavirus was identified, initially called Novel Coronavirus 2012, and now officially Middle East respiratory syndrome coronavirus (MERS-CoV).

- In 30 Oct. 2013, there were 124 cases and 52 deaths in Saudi Arabia. After the Dutch Erasmus Medical Centre sequenced the virus, the virus was given a new name, Human Corona Virus-Erasmus Medical Centre (HCoV-EMC). The final name for the virus is Middle East respiratory syndrome coronavirus (MERS-CoV).

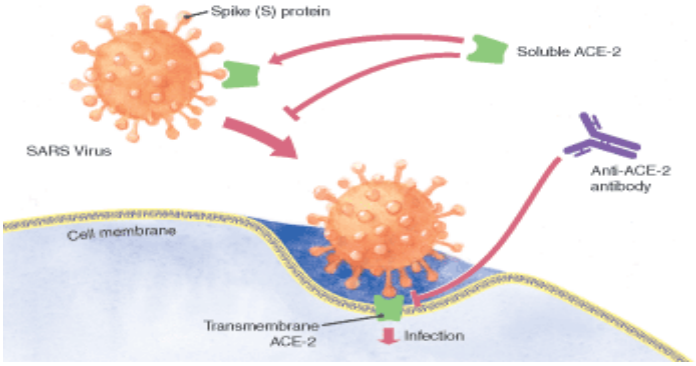
- In December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the first known case was identified in Wuhan, China as Coronavirus disease 2019 (COVID-19) caused by this virus.

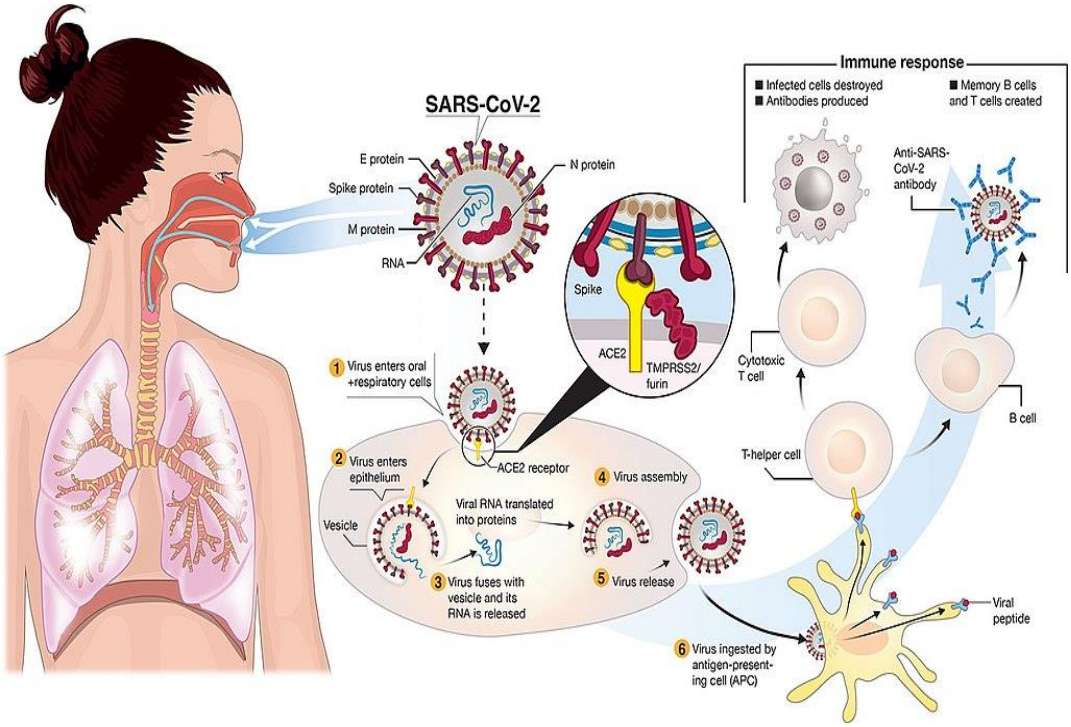
Mode of transmission

1-The main way to viral spread is by close person-to-person contact the virus that causes SARS-1 and -2 is thought to be transmitted most readily by respiratory droplets.
2-The virus also can spread when a person touches a surface or object contaminated with infectious droplets and then touches his or her mouth, nose or eye.
3- In addition it is possible that the SARS virus might spread more broadly through the air (airborne spread) or by other ways that are not now known.

Replication cycle

The virus attaches to receptors (angiotensin-converting enzyme 2, or ACE2) on target cells by glycoprotein spikes on the viral envelope (either by the S or HE). Then particle is internalized, probably by absorptive endocytosis. The S protein glycoprotein may cause fusion of the viral envelope with the cell membrane, RNA act as mRNA, and then newly replicated genome RNA associated with viral protein in cytoplasm. The particles acquire an envelope by budding through the plasma membrane and release





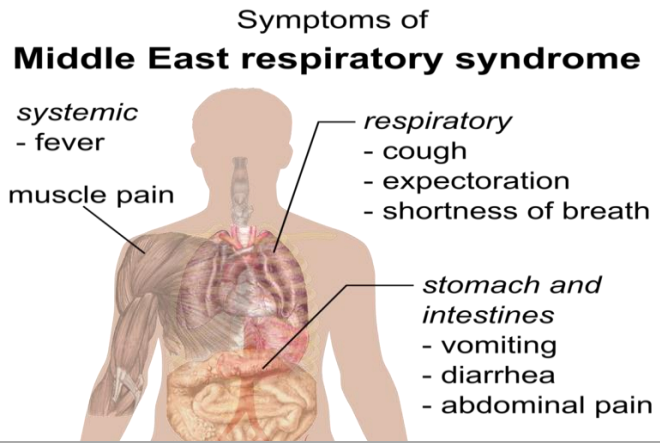
Disease caused by coronaviruses

Coronaviruses primarily infect the upper respiratory and gastrointestinal tract of mammals and birds. Seven different currently known strains of coronaviruses infect humans. The much publicized human coronavirus, SARS-CoV-1 and -2 which causes SARS, has a unique pathogenesis because it causes both upper and lower respiratory tract infections.

Coronaviruses are believed to cause a significant percentage of all common colds in human adults. The significance and economic impact of coronaviruses as causative agents of the common cold are hard to assess because, unlike rhinoviruses (another common cold virus), Coronaviruses can cause pneumonia, either direct viral pneumonia or a secondary bacterial pneumonia, and bronchitis, either direct viral bronchitis or a secondary bacterial bronchitis.

Symptoms of SARS

The incubation period for SARS is 4-5 days. In general SARS-1 and -2 begins with a high fever (temperature more than 38°C), headache an overall feeling of discomfort and body aches, some people also have mild respiratory symptoms at the outset about 10-20% of patients have diarrhea, after 2 to 7 days, SARS-1 and -2 patients may develop a dry cough and pneumonia.



Complications

Pneumonia, viral sepsis, acute respiratory distress syndrome, kidney failure, cytokine release syndrome, respiratory failure, pulmonary fibrosis, paediatric multisystem inflammatory syndrome, long COVID.

Laboratory diagnosis

1- Isolation of virus in cell culture has been difficult. The SARS-1 virus was recovered from oropharyngeal specimens using vero monkey kidney cell.
2- Detection of viral antigen in respiratory secrections by using the ELISA test or molecular techniques.
3- Antibody detection to virus in a single serum specimen, a four - fold or greater increase in SARS-CoV-1 and -2 antibody titer between acute and convalescent phase
4- Detection of virus RNA by RT-PCR.

Prevention

There are several types of vaccine ageist covid-2019.

	Medicinal Ingredient	Number of Doses	Recommended Time Between Doses	First Shot Efficacy	Second Shot Efficacy
Pfizer-BioNTech	mRNA	2	Recommended: First dose, then the second dose 21 days later NACI: Four months	52.4 per cent effective, then 92.3 per cent effective after 14-21 days	95 per cent effective in preventing COVID-19 one week later, with immunity developing over time
Moderna	mRNA	2	Recommended: First dose, then the second dose 28 days later NACI: Four months	80.2 per cent effective, then 92.1 per cent effective after 14 days	94.1 per cent effective in preventing COVID-19 two weeks later
AstraZeneca	Adenovirus vector vaccine	2	Recommended: First dose, then the second dose 4-12 weeks later NACI: Four months	76 per cent effective after 22-90 days	82 per cent effective when the second dose is taken 12 weeks or more after the first dose, with immunity developing over time
Johnson & Johnson	Adenovirus vector vaccine	1	N/A	66 per cent effective in preventing symptomatic COVID-19 disease two weeks later, with immunity developing over time	N/A