**Paramyxoviridae**

- **Enveloped viruses with a negative single stranded nonsegmented RNA genome**.
- They have special relationship with:
  1. **Orthomyxoviridae**:
     a. Related to pathogenesis (when respiratory infection takes place it will be localized or spread to other tissues)
     b. The function of the surface glycoproteins; having structures that can agglutinate erythrocytes, and neuraminidate activity.
  2. **Rhabdovirus**:
     - Genome organization and gene expression are similar.
  - **They encode and package their own RNA transcriptase**.
  - **They range in size from 150-350 nm** (variety in size >> pleomorphic).
  - **Classification**:
    - They retested in 1993.
RNA viruses

- **Structure**:
  - Spherical
  - Enveloped, the surface is decorated with spikes (envelope glycoproteins).
  - These spikes are 10-15 nm in length, and divided into two types:
    1. Those which are utilized in binding (attachment) to the susceptible cells (HN, H, G)
    2. Those which are utilized in fusion to adjacent cells (F)

*Very remarkable and common characteristic to all paramyxoviruses is the formation of the multinucleated giant cells. Ex: Respiratory syncytial virus was given this name because of the pronounced activity to fuse with adjacent cells and form multinucleated giant cells.*

**Regarding attachment proteins, viruses may:
1. Have hemagglutinin and neuraminidase activity > HN
   - ex: paramyxovirus, rubella (i.e. all parainfluenza viruses and mumps)
2. Have hemagglutinin alone > H
   - ex: morbilligenus (i.e. measles)
3. Lack both > G
   - ex: pneumovirinae (i.e. RSV)

*** Fusion proteins are present in all members of paramyxoviridae

- **Genome**:
  SSRNA, non-segmented, helical, size > 15 – 13 nucleotide and is associated with three proteins that make the transcription complex.
  *transcription complex composed of:
  1. **NP (nucleoprotein)**: acts to encapsidate the RNA genome which protect RNA from degradation by RNA!! (and it must be associated with the genome in order of the transcription to occur.
  2. **P (phosphoprotein)**: a-associate with NP (forming complex) and with the genome acting as a template for transcription and translation.
    - b-associated with L.
RNA viruses

3-L: it is the polymerase of the virus .. (it’s size and it’s localization in nucleus indicate this), %50 copies for each virion.
So, there are ... NP, NP-P, P-L, L.

- **Matrix**:
  Underlie the envelope. Responsible for morphogenesis of the virus (organization morphogenesis by allowing the acquisition of the envelope). Responsible also for the release of the virus.
  *The most abundant one is >>> N
  It is responsible for the anchorage (binding, connection) the RNA (core) to the envelope.
  So, it is responsible for the integrity of the virus.
  Virus that doesn’t have protein matrix N can’t release from the cell.

Virus that doesn’t have protein matrix N can’t release from the cell. If such defect takes place like in measles, the virus wouldn’t be able to release > with the consequence of cell destruction >> forming SSPE (subacute sclerosing panencephalitis).
  
  explanation: After infection with a virus, such defect (in N protein) results in the persistence of the measles virus in the brain cells (CNS), such persistence causes damage to the cells in the form of demyelination resulting in SSPE.
  
  About SSPE: - it is very fatal disease
  - no cure
  - incubation period (3-8) years ... pathologic changes require 3-8 years to become evident then disease manifestations start and death result in a short period after starting manifestations. (patients will be totally paralyzed then dead)

All in all, there are six major proteins (2 > Surface, 3 > Core, 1 > Matrix). There are other proteins which differ from one virus to another (1 or 2 or 3 ...etc.) of which in each virus, they are (SH, C, V, W, I, D, NS and NS2).
RNA viruses

Now, we’ll discuss each virus ...

**Parainfluenza virus:**

- ssRNA virus
- Enveloped (with HN,F envelope glycoproteins), pleomorphical morphology, 150-200 nm in diameter.
- 5 serotypes:
  - 1, 2, 3 >> Pathogenic (causing significant diseases).
  - 4a, 4b >> Nonpathogenic (may cause infection but without disease).
- No immunity (no common group antigens).
- Closely related to mumps virus.
- Are responsible for 30-40% of the respiratory infections in children below one year (infants), remember that this pathogenicity just for 1,2,3 types.
- They are second only to RSV as a cause of serious RT disease in infants and children (HPIV13).

**Respiratory Syncytial virus:**

- The most important pathogen in children and infants worldwide causing lower RT disease >> Major killer.
- Causes annual epidemics, affecting mainly children in nurseries and care centers (especially during cold months), Attack Rate = 100% (every child in the center will be infected if the virus is introduced into that center).
- The virus can also cause disease in immune-compromised patients and elderly.
- Nosocomial spread can take place.
- Difficult to study (pathogenesis is not fully understood), why?
  - Because, we don’t have animal models (natural illness occur only among humans) >>poor in tissue culture.
- The virion is highly unstable (can’t be maintained for a long period of time because cycles of freezing and thawing rapidly inactivate the virus,,, and in the lab we need these cycles in order to loose viability.
- It can survive on surfaces for up to 6 hours, and on gloves for less than 2 hours.
RNA viruses

- Loosing viability is due to: 1- Freezing and thawing cycles 2- acidic conditions 3- treatment by disinfectants.
- It encodes a larger number of mRNAs than do the paramyxoviruses (10 compared with 6 or 7).
- Additional genes are:
  SH: 3rd glycoprotein of the envelope.
  M2: 2nd in matrix.
NS1 and NS2 (nonstructural proteins 1,2).
  - Although six proteins appear to correspond (N, P, M, G/H/HN, F and L) only F and L exhibit unambiguous sequence relatedness between the two subfamilies.
  - Variation in the G glycoprotein:
    This glycoprotein is for attachment, it is the target for neutralizing antibodies, and in RSV variation in it leads to 2 subtypes (RSV-A and B) ... leading to partial immunity (no complete protection).
- RSV utilizes ICAM-1 as its receptor.

**Mumps virus:**
- Causes a disease of children called Mumps; it is an infection of parotid and salivary glands (parotitis) causing facial expression that gives the name to the virus.
  - to mump: means to grimace or grin which is an ugly twisted expression of the face (pain, edema, slanting to a side)
- Virion: 120-200 nm in diameter
- 8 major proteins (Additional: V (viral) and S (soluble))
- 1 serotype
  - Natural infection causes long life immunity because the virus is present in one serotype
  - Although, the RNA viruses undergo mutations but this virus remains relatively stable and that’s why it is of one serotype.
    (i.e. no effective mutations > relatively stable > one serotype > long life immunity).
- There is a vaccine, but many countries don’t utilize it because the infection is not that much dangerous during childhood, but !! if the infection is delayed it might be associated with significant complications especially CNS complications.
RNA viruses

- Mumps has remarkable predilection for the CNS tissue (meningitis, encephalitis, meningoencephalitis), and that’s why many countries the vaccination against mumps!

*** This vaccine is given with Measles and Rubeola >> MMR vaccine .. and it’s a life attenuating vaccine.

**Measles virus:**

- Relatively new disease of humans the probably evolved from animal morbilli virus (rinderpest) and it is related also to canine distemper virus.
- Abu-Bacr AlRazi (10th century) was the first who distinguish measles from smallpox (he described measles as an independent entity).
  ** He referred to measles as (الحصبة), he derived this name from (الحصى الملتهبة) describing the characteristic skin rash of the measles, and regarded it as a modification of smallpox.
- Very infectious virus >> almost always infection will develop disease (asymptomatic or subclinical infection don’t exist in measles).
  ** One of the major 4 viruses where we don’t have asymptomatic or subclinical infections, which are: Measles, Influenza, Rabies and Smallpox.
- Virion: similar to other members of paramyxoviridae but it lacks neuraminidase activity (i.e. has only H).
- Membrane cofactor protein (MCP) or CD46 is the receptor for the virus.
- Measles virus is a stable monotypic virus with some degree of variability (strains).

**Human Metapneumovirus (Hmpv):**

- The first description was in 2001, van den Hoogen and colleagues reported that they had isolated a paramyxovirus from 28 young children in the Netherlands identified as a new member of the metapneumovirus genus by:
  1- Virological data of the virus.
  2- Sequence homology of its genome.
  3- Gene constellation.
Previously, avian pneumovirus was the sole member of this recently assigned genus, hence the provisional name for the newly discovered virus: human metapneumovirus.

- Features:
  - -ve stranded RNA virus
  - Paramyxoviridae family.
  - Related to avian pneumovirus and turkey rhinotracheitis virus.
  - Causative agent of respiratory tract disease in humans (similar to RSV).
  - As common as RSV and parainfluenza viruses.
  - Most children seropositive by age of 5 (every child will be infected at least once).
  - 2 genetic clusters of hMPV may represent different serotypes.

**Rubella virus:**

- Rubella = Rubeola = الحصبة الألمانية
- Rubella virus is a member of the togaviridae but unlike most other togaviruses, rubella virus has no known invertebrate host (not transmitted by arthropods), and the only known natural reservoir for rubella virus is man.
- It’s related to measles in pathogenesis. It was named firstly by German physicians in 1800s as a distinct from measles >> German measles.
- Rubella was regarded as a trivial insignificant cause of disease until it was first associated in 1942 with congenital malformations, when a physician from Australia described facing a congenital cataract following an epidemic of Rubella.
- Congenital Rubella Syndrome: is a very serious disease that is associated with (myocardial, CNS, eyes, ...etc) abnormalities.
- First isolated as a virus in 1962.
- A vaccine was developed in 1969.
- Rubella virus is a spherical, icosahedral, enveloped particle that measures 60-70 nm in diameter.
- It has a +ss RNA genome of about 10,000 nucleotide that is encased by multiple copies of the capsid protein (C). Two glycoproteins, E1 and E2, are embedded in the envelope.
  - E1 is projected and most abundant, E2 is laying beneath.
  - Neutralizing antibodies are directed against both (E1 & E2).
RNA viruses

**Rhabdoviridae:**

- An important family of viruses that infect wide range of hosts (insects, reptiles, humans ...)
- A large number of member viruses that are serologically unrelated.
- Most lethal viral disease >> Rabies
- Mortality = 100 %
  - when disease manifestations start >>> Death .
  - Prevention (before clinical manifestations) is the treatment of Rabies .
- Rabies belongs to the genus lyssa virus (rabies in Greek means mad or frenzy).
- mad and frenzy .... Because the aggressive behavior of the dog .
- It is bullet shaped, enveloped and has a diameter of 75X180 nm.
- Genome:
  - helical and associated with protein (N).
  - ssRNA, non-segmented.
- Proteins: G, M, L, N, NS ... The same proteins of paramyxoviridae.
  ** Remember the relationship between paramyxoviridae and (rhabdo and ortho).**
- Can be seen using electronmicrograph.
- The virus has striated appearance because of the envelope glycoproteins.
- Virions bud from the endoplasmic reticulum of the infected cell.
- Replication of rhabdoviruses is followed by cell death except for rabies virus which is nonlytic causing no discernable damage to the infected cell.
- little pathology seen but it causes disseminated encephalitis that is highly fatal.
- But if rarely examined .. no pathology is seen, no inflammatory response and pathology is seen unlike other encephalitis cases. (unique characteristic).
- Rabies causes formation of inclusion bodies in the cytoplasm of infected cell causing Negri bodies ... the detection of which is a characteristic and is utilized as a base of diagnosis.
  ** Because we can’t make this way of diagnosis in infected humans .. we can take a specimen and infect for example mice and demonstrate the presence of Negri bodies.
- The virus can reach CNS via the retrovir axoplasmic flow and then it is disseminated back to highly innervated site. The virus can recover from highly innervated site easily with nonaggressive procedure.
(i.e. The virus infects striated muscle, replicates there and goes to the CNS .. then disseminated by sensory nerves (highly innervated regions)... So, if you want to make a diagnosis.. best clinical specimens that is easy to be obtained in non-aggressive way are from: Saliva, Cornea, Skin biopsy.

Corona viruses

- In 1930s first recognition of the virus when avian infectious bronchitis was first differentiated from other illnesses of chicken, then the virus was isolated (Schalk and Hawn, 1931) Recovery of virus in the Laboratory (Beaudette and Hudson 1937).
- In 1965 human corona virus was discovered (Tyrrell and Bynoe), and the virus has distinctive morphology that gives its name >> Corona (crown like appearance)

** This shape is due to the distribution of the surface glycoproteins; here S glycoprotein is responsible for that appearance, why? because these proteins are: 10-20 nm long and stud the viral envelope.
- The virus is **enveloped** with at least 2 glycoproteins:
  M: matrix
  S: binding site of the virus and target for neutralizing antibodies.
  EH (for group 2 corona virus): Hemagglutinin and Esterase function.
  ** This type of corona virus (2) is similar to influenza C virus that has HEF.
  So, it’s believed that this glycoprotein was acquired from influenza C virus during an infection with corona and influenza C together (RT infection)
- **Copy Choice Mechanism**: a mechanism that is associated with corona virus RNA polymerase in which this polymerase jumps from one strand of RNA (that is being copied, as a template) to another strand and continue copying.
- **Classification**:
  - until 2002 corona virus was classified into 3 groups:
    1- Human corona virus 2292
    2- Human corona virus OC43 (remember! HE)
    3- Doesn’t contain a human virus.
RNA viruses

- In 2002 new corona virus was discovered > SARS , which caused the pandemic of respiratory tract illness that spread all over the world with mortality approaching 14% .
- Then this discovery was followed by a discovery of 2 more corona viruses that cause lower RT diseases .
- And currently , we have a corona virus that is causing a disease in Qatar , Saudi Arabia and Jordan .. ( 9 cases and 2 deaths in Al-Zarqa’a )
- The Genome of corona virus has a sequence then >> 200-500 nucleotides of non-coding sequence then >> 2 overlapping frames that code for the enzymes : protease and polymerase then >> the structure of SMN .

Similar genome organization for the 3 corona viruses : Protease followed by SMN .

- Genus >> Coronavirus
  - Species >> HCoV-229E , HCoV-OC43 , HCoV-NL63(was discovered later ) , HCoV-HKU1 , SARS- CoV ,,,, , the currently circulating one is EMC .

- Responsible for about 10-20% of common colds
  - re-infection is common
  - infections year-round, most prevalent in fall and spring
  - incubation period about 2 to 5 days .

Best wishes with finals 😊
Hadeel Abudari