

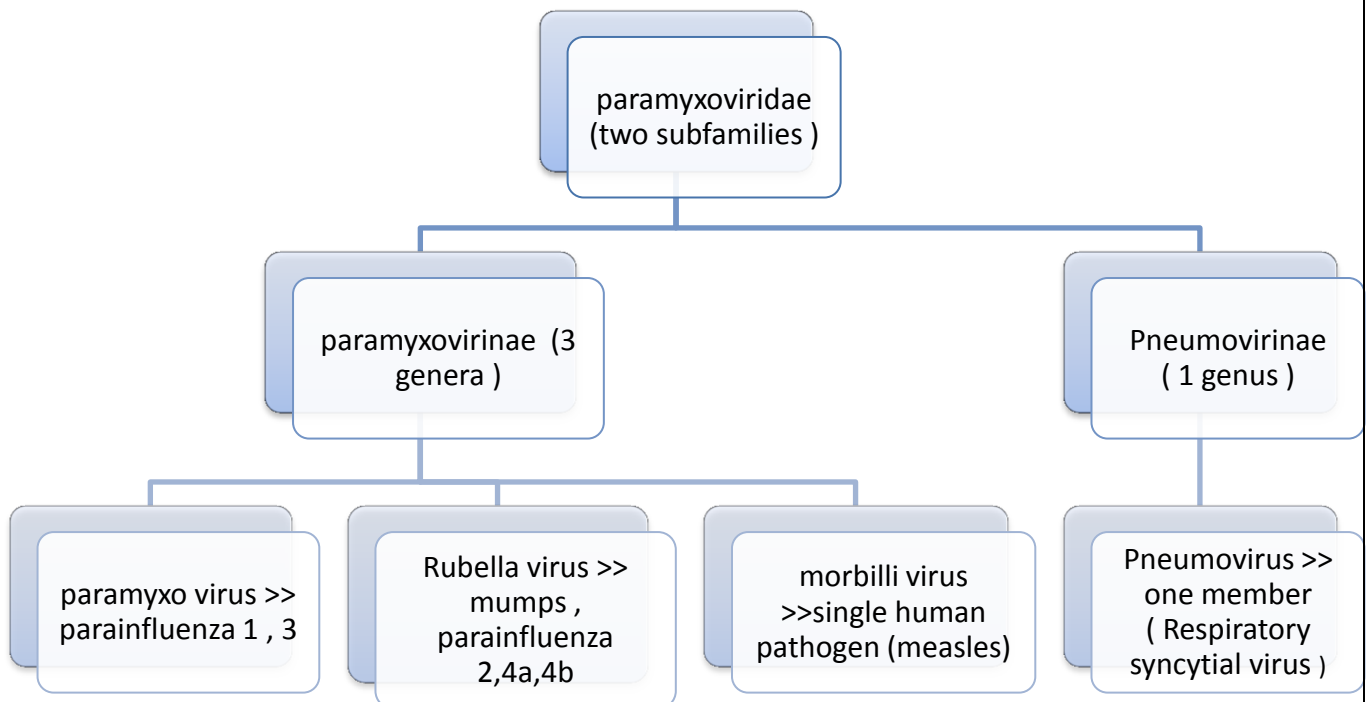
Paramyxoviridae

- **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- Rahbdovirus :**

Genome organization and gene expression are similar .
- **They encode and package their own RNA transcriptase .**

Because the genome is of -ve polarity .
- **They range in size from 150-350 nm (variety in size >> pleomorphic) .**
- **Classification :**

They retested in 1993 .



- **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 : paramyxo , rubula (i.e. all parainfluenza viruses and mumps)
- 2- Have hemagglutinin alone > H
ex : morbilli genus (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 .

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) .

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 .

- 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) ... أبو كعب
- 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 .

- 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).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) .

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) الحمى التاجية
 - ** 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 .

- 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 .
- *S and M : glycoproteins ...N : nucleoprotein .

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 😊

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