Sheet number: 19

Refer to slide number: 2

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**Arbo Viruses**

* **We will cover the following:**
* Etiology
* Epidemiology and history
* Pathogenesis and Pathology
* Clinical Manifestation
* Diagnosis
* Treatment
* Prevention and Control
* The name of this virus originates from three words:

***Ar*** from arthropods (insects), ***Bor*** from borne. Hence these virsuses are transmitted to humans by arthropods.

* The WHO definition of Arbo viruses: “Viruses maintained in nature principally, or to an important extent, through biological transmission between susceptible vertebrate hosts by hematophagus arthropods or through trans-ovarial and possibly venereal transmission in arthropods.” In other words, these viruses are transmitted to humans by biting, feces or through their ovas.
* Arbo Viruses are classified into three groups.

1. Togaviruses: cause encephalitis mainly in horses (not humans). Examples : Eastern equine encephalitis, Western equine encephalitis, Venezuelan equine encephalitis.
2. Bunyaviruses. Examples: Sand fly Fever, Rift Valley Fever, Crimean- Congo Hemorrhagic Fever.

3) Flaviviruses. Examples: Yellow Fever, dengue, Japanese Encephalitis

* **Note:** These viruses are mainly found in animals but may be transmitted to humans.
* **Extra note for Slide no. 5:** the only virus seen in our area is the West Nile virus. It was isolated in Jordan.
* Structure of Arbo Viruses is typical. A negative stain was used in **slide no. 6.**
* **Extra notes on slide no. 7:**

-Both Togaviruses and Bunyaviruses have an envelope and hence are susceptible to ether and heat.

-Togaviridae anzd flaviviridae have a single stranded +ve RNA which means it’s a mRNA mainly.

-Bunyaviridae has a single stranded –ve RNA and must produce a mRNA in the host cell.

-Reoviridae has a segmented double stranded RNA. Different segments are noticed in this virus.

* **Slide 8:** The three proteins seen in the virus are used in the diagnosis.
* **Notes on slide no. 9:**
* E- glycoprotein is very immunogenic which means it can produce an immune response. If a vaccine is made this protein is used, however vaccine is very limited.
* Capsid is group reactive which means all Bunyaviridae have the same protein. While e-glycoprotein is species specific.
* M-protein is not very immunogenic but found embedded in the envelope.
* **Replication:**

These viruses enter through the membrane (especially if they are enveloped) and are associated with the host’s cell membrane. When they are inside they are decapsulated by proteolytic enzymes and the RNA is released. This genome will start producing its components using the cell’s machinery and then the complete virus is released by budding. The complete virus will have the cell membrane around it.

* **Transmission:**

Through three different arthropods:

* Mosquitoes, which transmit Japanese encephalitis, dengue, yellow fever, St. Louis encephalitis, EEE, WEE, VEE etc.
* Ticks, which transmit Crimean-Congo haemorrhagic fever, various tick-borne encephalitides etc.
* Sandflies, which transmit Sicilian sandfly fever, Rift valley fever
* **Examples of Arthropods on slide no12.**
* **Animal Reservoirs :**
* Birds; especially wild birds, are a reservoir for Japanese encephalitis, St Louis encephalitis, EEE, WEE.
* Pigs; Japanese encephalitis
* Monkeys; Yellow Fever
* Rodents ; VEE, Russian Spring-Summer encephalitis
* **Transmission (from slide no. 14)**
* **Transmission cycle:**
* Two types.
* For example, ‘Man-arthropod-Man’: If a human has a virus and was transmitted to an arthropod and then from arthropod the virus can go back to human.
* **Epidemiology:**
* Seasonal virus.
* Mainly in rainy forests because most Arthropods live there.
* If an infected animal survives, it will have lifelong immunity due to the presence of the proteins we talked about earlier.
* More than 530 species, 150 are pathogenic to humans.
* Pathogenesis:
* Generally, viruses have tropism to certain organisms. For example those causing encephalitis all have tropism to the brain.
* The response to the infection depends on the patient’s immunity status.
* When the arthropod transmits the virus through a bite, the virus undergoes an incubation period for about 2-3 days. During this period there are no symptoms except maybe itching at the site bitten. This virus then reaches the blood and then to different organs (to a vascular organ, the liver, macrophages, the spleen and lymph nodes..). During this period (incubation of 3-7 days), clinical signs and symptoms do appear including encephalitis in the brain, jaundice in the liver, and haemorrhage in the spleen... After that it might reach the CNS and cause impairment.
* There are two viremias. One after the infection and the second one after it reach the liver and other organs.
* **Pathogenesis(slide21):**
* Virus enters the macrophages, macrophages circulate in the blood, causing viremia.
* If the patient has an adequate immune response, the patient will experience a subclinical or mild systemic disease.
* If the patient’s immunity is impaired or weak, invasion of the CNS will occur and mortality rate is high.
* **Four stages of the disease (slide 22):**
* Prodromal stage, where there aren’t any clinical manifestations.
* Acute encephalitis stage
* Convalescence stage, if patient survives.
* Sequela stage; death.
* **Clinical Picture (slide23):**
* Rash especially at the infected area. This rash could be mixed with rashes originating from other types of viruses.
* Encephalitis
* Hemorrhagic fever
* The clinical picture is usually determined by the type of virus.
* **Pathogenesis and immunity (slide24):**
* Besides viral receptors, other antibodies may be a factor contributing to the spread of the virus. Antibodies coat the virus when reacting with it and this complex cannot be recognized by the immunity (as if it is now a self component). The virus in this state could spread much more easily.
* Antibody dependent cell cytotoxicity; where the infected cell is recognized by antibodies and those antibodies in the presence of complement will destroy infected cell. Destroying the infected cell would discontinue the virus’s replication process and the infection is aborted.

-note: the cell must have a receptor to the Fc portion for its invasion into the cell and causing an infection.

**Slide26:**

The main triad which is seen in those types of viruses is Fever/Rash/Arthritis.

**Transmission slide 29:**

Mainly the reservoirs are the birds and wild animals and sometimes the ovas of arthropod contains the virus itself and they lay their eggs anywhere and this could be a source of transmission.

**Slide 30:**

West Nile:

- Found in Jordan.

- Part of flaviviruses.

- Primary host wild birds

- Principle arthropod vector – mosquitoes.

- Geographic distribution: Africa, middle east, western Africa, Europe, Australia, north America, central America.

- the virus will be transmitted by an arthropod to the human being or to the birds here in Jordan it is mostly through birds this is due to migratory birds coming to al-azraq river.

**Slide 32/33:**

Laboratory tests we can look at antibody titer: hemagglutination inhibition, immunofluorescence, complement fixation, ELISA.

Definitive diagnosis is the isolation of virus from specimen mainly brain blood, skin.

We can also do serology, culture (we need tissue or animal culture and the specimen could be blood, CSF, or brain sample) or we could do direct detection by using electron microscopy.

**Prevention (slide34):**

-It's done by doing surveillance (if we have the virus or not and what type do we have) then we have to control the vectors by eradicating mosquitoes for example.

-personal protection: if someone wants to camp in a forest he must use an insect repellent.

- Vaccination is available for: yellow fever, Japanese encephalitis, Russian tick-borne encephalitis but mainly it is for yellow fever... anyone who wants to go to Africa he must be vaccinated by yellow fever because it is endemic there.

**Treatment (slide35):**

-Generally no effective treatment.

- Yellow fever vaccine is live attenuated.

**Slide 36:**

Epidemiological triangle

We have the host, virus, and vector if you break any of the lines of the triangle you will be breaking the infection. For example: treating an infected person, now even if he got bitten by the mosquitoes he won't transmit the disease.

**Slide 37** same as slide.

In summary, when we talk about this virus you should know that its structure is positive or negative, single or double stranded RNA. Pathogenesis, it is mainly an animal virus can be transmitted to humans. It is diagnosed by serology and nucleic acid. There is no treatment except for yellow fever vaccine.

**Retroviruses**

**Slides (42-44)**

-From its name it does reverse transcription starting from RNA then DNA then RNA protein so there is a reverse transcription to the virus.

-Mostly they are found in animals causing tumors.

-In humans in 1983 certain viruses were discovered HTLV3, LAV(HIV) by Robert gallo and luc montagnier.

-Generally nucleic acid of these viruses are either cis acting elements, Gag proteins, Pol proteins and Envelope proteins so it has a very complexed structure of proteins controlling this virus.

-Two life cyles.

-These viruses are ubiquitous found in all vertebrates; they have a large diverse family and cause HIV in humans, cats and some other animals.

- We don't have a specific definition and classification but mainly we depend on RNA structure.

-Transmission is either horizontal or vertical and it can be transmitted as free viral particles or through cell-cell contact.

- **History(slide45):**

It was first discovered in **1960** by howard temin and Baltimore they suggested the reverse transcription and they got a nobel prize.

In **1980** in japan they discovered Human T-cell leukemia virus we call it HTLV4.

In 1**982** HIV was discovered

In **1990** first gene therapy involving patients with deficiency in adenosine deaminase, virus was used as a vector to transfer a normal gene to a patient.

In **2006** Xenotropic murine leukaemia-related virus discovered.

**Slide 49**

**Members:**

1-Mainly they all cause tumours in animals, **Oncogenic Viruses**:

Avian oncoviruses: RSV, AMV, AEV, RAVs [ RAV- 0; RAV-1 ].

* + Murine oncoviruses: *e.g.,* MoMLV, A-MuLV.
  + Mammalian oncoviruses: *e.g*., FeLV, HaMSV, SSV .
  + Mouse Mammary Tumor Virus (MMTV); [ the only B- type particle ].
  + Mason-Pfizer Monkey Virus (MPMV); [ one of the few D-type particles ].
  + **Human T-Cell Lymphotropic Virus ( HTLV-1 & 2 ).**

2- **Lentiviruses:** HIV group

3- **Spumaviruses:** these generally produce foamy like cells in infected cells.

**Slide 50**

Genome is either simple or complex.

**Slide 51/52**

It has a very complex structure, containing envelope with glycoproteins projected to the outside ,dsRNA and capsomeres.

**Slide 53**

Genome is very complexed, containing Gag/Pol/Env these are the main structural proteins needed to produce the proteins of virus.

For example Gag encodes for: MA(matrix),CA(capsid),NC(nucleocapsid).

**Life cycle,** since the virus is enveloped the virus will attach and infuse with cell membrane of host cell then RNA will be released and produce the DNA by reverse transcriptase this DNA will be transmitted to nucleus and it will be integrated with host cell DNA, as replication starts the viral components will be produced, assembly and release of virus by budding (cell won't be destroyed).