SYSTEMATIC VIROLOGY

RNA VIRUSES

BY

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2) Bunyaviridae

Bunya comes from Bynyamwera is the name of a place in Uganda, where the type species virus was isolated.

Commom charachteristics:

1. The viruses in this family are medium sized, spherical, enveloped measuring 60-100 nm in diameter.
2. Contain helical neucleocapsid.
3. The genome is –ve sense ssRNA which is in 3 pieces, each held in a circular configuration, and there is an associated transcriptase, they replicate in the cytoplasm and matures by budding into smooth surfaced vesicles in the Golgi or nearby region.
4. Bunyaviruses because of their segmented genome, they undergo genetic reassortment, which may produce “antigenic shift". Some strains have been shown to undergo antigenic drift as well.
5. Most bunyaviruses are arthropod (arbo)- or rodent-borne, i.e. transmitted via arthropods e.g.(mosquitoes) or from infected rodents.

Rift Valley fever (Enzootic hepatitis)

Definition:

Rift Valley fever (RVF) is an acute viral disease that can cause severe disease in domestic animals (such as buffalo, camels, cattle, goats and sheep) and humans. Disease in these species is characterized by fever, severe illness, abortions, and a high morbidity and mortality rate especially in young animals.

Etiological agent:

Rift Valley fever (RVF) virus is of the family Bunyaviridae within the genus Phlebovirus. Only one serotype is recognised but strains exist of variable virulence.

Resistance to physical and chemical action:

Temperature: In serum, inactivated by 56°C for 120 minutes and after several months at 4°C.

pH: Resistant to alkaline pH, but inactivated by pH <6.8.

Chemicals: Inactivated by ether and chloroform.

Disinfectants: Inactivated by strong solutions of sodium or calcium hypochlorite (residual chlorine should exceed 5000 ppm).

Survival: Survives in freeze dried form and aerosols at 23°C and 50–85% humidity. Virus maintained in the eggs of certain arthropod vectors during inter-epidemic periods. Can survive contact with 0.5% phenol at 4°C for 6 months.

Host affected:

•Cattle, sheep, goats, dromedaries, several rodents.

•Wild ruminants, buffaloes, antelopes, wildebeest, etc.

• Humans are very susceptible (major zoonosis).

Mode of transmission:

•Direct contact: occurs in humans when handling infected animals and meat.

•Mechanical transmission by various mosquitoes vectors has been demonstrated in laboratory studies.

Source of infection:

•Nasal discharge, blood, vaginal secretions after abortion and mosquitoes.

•Aerosols and consumption of raw milk and infected meat.

Clinical signs: Incubation period (1 – 6) days.

1-Cattle

- **Calves** (highly susceptible):
  - ✓Fever (40–41°C), inappetence, weakness and depression.
  - ✓Bloody or fetid diarrhoea.
  - ✓More icterus than in lambs.
- **Adults** (moderately susceptible):
  - ✓Often inapparent infection, but some acute disease.
  - ✓Fever lasting 24–96 hours.
  - ✓Dry and/or dull coat.
  - ✓Lachrymation, nasal discharge and excessive salivation.
  - ✓Anorexia, weakness.
  - ✓Bloody/fetid diarrhoea.
  - ✓Fall in milk yield.
  - ✓The abortion rate may reach 85% in the herd.

2- Sheep

- **Newborn lambs** or under 2 weeks of age (extremely susceptible):
  - ✓Biphasic fever (40–42°C); fever subsides just prior to death.
  - ✓Anorexia; in part due to disinclination to move.
  - ✓Weakness, listless.
  - ✓Abdominal pain.
  - ✓Rapid, abdominal respiration prior to death.
  - ✓Death within 24–36 hours.
- **Lambs over 2 weeks of age (highly susceptible) and adult sheep:**
  - ✓Peracute disease: sudden death with no appreciable signs.
  - ✓Acute disease more often in adult sheep.
  - ✓Fever (41–42°C) lasting 24–96 hours.
  - ✓Anorexia, weakness, listlessness and depression.
  - ✓Increased respiratory rate.
  - ✓Vomiting, bloody/fetid diarrhoea.
  - ✓Mucopurulent nasal discharge
  - ✓Icterus may be evident in a few animals.
  - ✓In pregnant ewes, ‘Abortion storms’ with a rates approaching 100%.

3-Humans

People with RVF will either show no symptoms or develop a mild illness. Influenza-like syndrome: fever (37.8-40°C), weakness, myalgia (muscle pain), backache, dizziness, liver abnormalities, and weight loss. In some patients, the illness can progress to haemorrhagic fever, encephalitis, or ocular disease (inflammation of the eye, blindness). Most people recover within four to seven days. Approximately one percent (1%) of humans infected with Rift Valley fever dies of the disease.

Post mortem lesions:

•Focal or generalised hepatic necrosis (white necrotic foci of about 1 mm in diameter).

•Congestion, enlargement, and discoloration of liver with subcapsular haemorrhages.

•Brown-yellowish colour of liver in aborted fetuses.

•Enlargement, oedema, haemorrhages and necrosis of lymph nodes.

•Congestion and cortical haemorrhages of kidneys and gallbladder.

•Haemorrhagic enteritis.

Diagnosis:

1-Sample:

•Heparinised or clotted blood. Plasma or serum.

•Tissue samples of liver, spleen, kidney, lymph node, heart blood and brain from aborted foetus.

•Specimens should be submitted preserved in 10% buffered formalin and in glycerol/saline and transported at 4°C.

2-Virus isolation:

The samples are inoculated into:

A. Embryonated chicken egg: via C.A.M and yolk sac thickening of the membrane, but without pocks formation.
B. Laboratory animals: intracerebral inoculation of mice – hamsters - 1-2-day-old lambs shows CPE.
C. Tissue culture inoculation: (as Vero, CER, BHK-21, mosquito line cells or primary calf, lamb and goat kidney) shows acidophilic intracytoplasmic inclusion bodies (Dauney- Hudson – Garnham bodies).

3-Viral antigen identification:

•In tissue suspensions by complement fixation and immunodiffusion.

•In cryostat sections or in impression smears of liver, spleen and brain by immunofluorescence.

•Antigen detection in blood by immunodiffusion and enzyme immunoassay.

4-Serological tests

Prevention and control: No specific treatment.

Symptomatic treatment in severe human cases.

Vaccination:

1) Inactivated virus vaccine:

•A formalized vaccine prepared from the pantropic virus grown in monkey tissue culture and killed by formalin.

•This type of vaccine used in man and pregnant animals and annual vaccinated.

2) Attenuated virus vaccine (Smithburn strain):

- One inoculation confers immunity lasting 3 years.
- Residual pathogenicity for pregnant ewes (abortion).
- Pathogenic for humans.

In Egypt:

- Tissue culture inactivated vaccine, which contains the local "Zagazig strain" and cultivated on CER cell line (chicken embryo rough) then inactivated by formalin and adjuvanted with aluminum hydroxide gel is used for vaccination of cattle (2ml) and sheep (1 ml) subcutaneously.
- Revaccinate 6 months post first dose, then annually.

3) Togaviridae

- Toga comes from the Latin word cloak or gown, which refers to the envelope.
- **Common characteristics:**

1. Virons are spherical 40-70 nm in diameter, have a lipid bilayer envelope.
2. The nucleocapsid is icosahedral.
3. The genome is non segmented, + ve ssRNA & the genomic RNA serves as messenger RNA and is infectious.
4. Most of these viruses have a natural habitat in specific arthropod and vertebrate host to fulfil their life cycle. The vertebrate hosts are usually mammals, birds, domestic animals and human beings.
5. In the family Togaviridae there are four genera i- Alphavirus- arthropod viruses and non-arthropod ii- pestivirus iii) arterivirus and iv- rubivirus. Most members of all genera cause serious diseases in domestic animals excepting rubivirus which contain human rubella virus.

1) Bovine viral diarrhea (BVD)

Definition:

- Bovine Viral Diarrhea (BVD) is a very common infectious fatal viral disease of cattle, sheep and other even-toed ungulates, caused by Bovine Viral Diarrhea Virus (BVDV). BVD has been long considered a disease of the respiratory, gastrointestinal and reproductive organ but it is now believed to cause primary reproductive symptoms, with lesser effects on the other organ systems.

Aetiology:

- BVDV is a pestivirus in the in the family Togaviridae and is closely related to classical swine fever and ovine Border disease viruses. BVDV occurs in two forms: noncytopathogenic (99%) and cytopathogenic (for cell cultures (1%). There are two antigenically distinct genotypes (types 1 and 2), and virus isolates within these groups exhibit considerable biological and antigenic diversity.

Resistance to physical and chemical action:

- **Temperature**: Maintained in a lyophilized or frozen (-70) for many years.
- **pH**: Stable at pH 5.7 – 9.3.
- **Chemicals**: Inactivated by ether and 0.4%ß-propiolactone.
- **Disinfectants**: Inactivated by ether and chloroform and trypsin.

Host affected:

- Cattle of all ages, but more common in young stock. Sheep and goat.

Mode of transmission:

- Direct contact with infected cattle.
- Ingestion of contaminated food or water with infected feaces.
- Vertical transmission from infected mother to her foetus.

Source of infection:

- The BVD virus is usually brought in by replacement animals or their unborn calves if it has not previously been found on the farm.
- Replacement animals can shed the virus in the air, manure and in body secretions.

Clinical signs: Incubation period → 10-14 days.

1-An acute infection: describes cattle that are exposed to the virus and develop an immune response to the disease. Cattle that become acutely infected may exhibit visible signs of disease. Calves exhibiting signs of illness may show **respiratory** or **gastrointestinal symptoms**. Signs of respiratory disease include fever, nasal discharge, lethargy and mild coughing. Gastrointestinal signs may or may not be present. These signs may include diarrhea, poor appetite, weight loss and high mortality.

2-Fetal form:

- If an unprotected cow acquires a BVD infection while she is pregnant, there are several possible outcomes, depending on the stage of pregnancy when she is infected.
- A normal calf could be born to a cow that becomes infected during late gestation (>180 days). This occurs when the fetus has a competent immune response in utero, and it would be born without any negative results.

- An infection during early pregnancy (120 days) can result in more detrimental outcomes. During this period, early embryonic death, abortion, fetal mummification or a calf born with a persistent infection are all possibilities.
- Fetuses exposed to BVD at 150 days or more of gestation could be born with congenital defects. These defects may lead to poor brain development, eye abnormalities, structural malformations and stunted growth. Calves born with congenital defects usually have difficulty standing and walking and may exhibit an early death due to a poor ability to nurse the dam. Abortion, stillbirth and mummified foetus can occur.

3-Fatal (fulminating) form: characterized by:

- Fever (40-41.5°C).
- Profuse salivation, diarrhea and recumbancy.
- GIT erosions.
- Dehydration and decrease lactation.
- Cessation of rumination and leukopenia.

Post mortem lesions:

- Congestion, haemorrhages, edema and erosions of the mucosal membranes, including the intestine and abomasum.
- Irregular, small and shallow oral lesions on the tongue, dental pad, pharynx and oesophagus.
- Cataracts, renal degeneration and neuritis of the optic nerves.
- Cerebellar hyperplasia.

Diagnosis:

a) Samples: Nasal or pharyngeal brush swabs, faeces, blood, liver, lymph nodes and intestine.

b) Virus isolation:

- The samples are inoculated into cell culture (Bovine embryonic skin, muscle and kidney cells) shows cytopathic strains with plaque formation.
- Non-cytopathogenic strains are identified by immunodiffusion.

c) Virus identification:

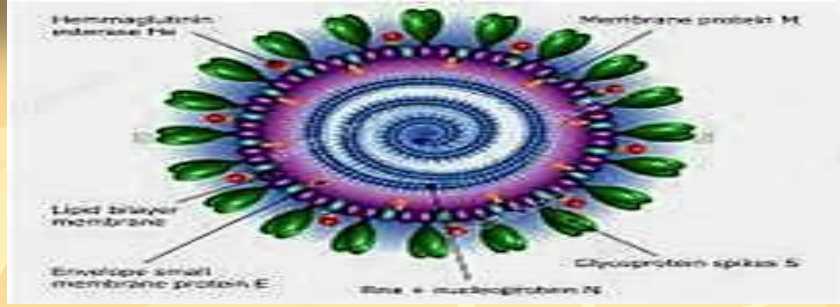
Vaccination in Egypt:

A) Live attenuated vaccine:

- Given alone or in combination with IBR and PI-3.
- Given at 4-6 moth after calving and then annually.
- It is contraindicated for pregnant cattle to avoid abortion.

B) Killed virus vaccine, is used for immunization of calves against BVDV, it produces high titre of neutralizing antibodies and the vaccinated animals are resistant to the virulent virus.

4) Coronaviridae



The characteristic club shaped surface projections studding the virion envelope (in Latin Corona mean Crown) have given the family its name.

Common characteristics:

1. Coronaviruses are pleomorphic, enveloped, measre about 100-120nm in diameter with unique club shaped peplomers projecting from envelope which give the virus the crown shape.
2. The nucleocapsid is helical in symmetry.
3. The genome consists of one molecule of infectious linear, non- segmented, +ve sense ssRNA.

4- Coronaviruses replicate in cytoplasm. The virions bud into cisternae acquiring lipid membrane from cell and subsequently transported and accumulated in Golgi vesicles.

5- Coronaviruses have 2 specific structural glycoproteins (E1-E2).

a) E1 structural protein:

- Is a transmembrane molecule that is deeply embedded in the envelope.
- Antibodies directed against E1 may neutralize the virus in the presence of complement.

b) E2 structural protein:

- Give rise to the typical club shaped projections 20 nm in length, which provide the crown shape of the virus.
- The glycoprotein contains epitopes to which neutralizing antibody and cell mediated immunity is directed and is also responsible for viron binding to the host cell membrane.

1) Avian infectious bronchitis

Definition:

- The virus causes IB is an acute, contagious disease, infections, mainly in chickens and is a significant pathogen of commercial meat and egg type birds characterised primarily by respiratory signs in growing chickens. In hens, decreased egg production and quality are often observed. Some strains of the virus are nephropathogenic and produce interstitial nephritis and mortality.

Aetiology: Avian infectious bronchitis (IB) is caused by coronavirus infectious bronchitis virus (IBV).

Resistance to physical and chemical agents:

1- Tempereture: Inactivated at 56 ºC for 15 min and stable at cold temperature.

2- pH: Variable in stability in acidic pH, some strains survive at pH 3 for 3 hours at 4 ºC.

3- Lipid solvent: inactivate the virus.

Host affected: Chickens (natural host) of all ages, but mainly at 2-4 weeks.

Mode of transmission:

- Inhalation via the respiratory tract "droplet infection".
- Direct contact with diseased bird.
- Indirect transmission through feed racks, water troughs and equipments.

Source of infection: Excretions as respiratory discharge for 4 weeks and faeces for 3 weeks of infected bird.

Clinical signs:

- In broiler chicks of between two and six weeks of age, the main clinical signs seen are **respiratory disease** characterizes by difficulty in breathing, tracheal rales, coughing and sneezing with or without nasal discharge. Feed consumption and body weight are markedly reduced. Clinical signs in uncomplicated infections can be of short duration, commonly lasting less than seven days. Secondary infections due to *Escherichia coli* often follow, thereby accentuating the respiratory signs.

- Infectious bronchitis virus infection at a **young age** and after **maturity** can both lead to **reproductive problems** in hens. **In adult chickens** clinical signs may not be present or may take the form of a mild respiratory disease with coughing, sneezing and rales which can go unnoticed unless the flock is examined carefully. A decline in egg production usually follows within seven to twelve days. The severity of the decline in egg production varies according to the stage of lay at infection and the strain of virus involved. Typically, these declines are between 3% and 10%, but reductions of up to 50% have also been observed. In some flocks, a decline in egg production will be the only feature. However, in many flocks the decline in egg production is also associated with eggs of smaller size and inferior shell and internal egg quality, seen as soft-pale shelled and misshapen eggs, and eggs with thin albumen.

Postmortem lesions:

- Catarrhal tracheitis, bronchitis and lung congestion.
- The length and weight of the oviduct are reduced or damaged.

Diagnosis:

a) Sample:

- **For acute respiratory disease,** swabs from the upper respiratory tract of live birds or tracheal and lung tissues from diseased birds should be harvested, placed in transport medium containing penicillin (10,000 IU/ml) and streptomycin (10 mg/ml) and kept on ice and then frozen.
- For birds with nephritis or egg-production problems, samples from the kidneys or oviduct, respectively, should be collected in addition to respiratory specimens.

b) Virus isolation: Samples are inoculated into:

- Allantoic cavity of embryonated chicken egg 9-11 days old shows dwarfing, curling and death of the embryo, may accompany with liver necrosis, pneumonia and nephritis.
- Tissue culture as chicken embryo kidney cell culture shows syncytium formation.

c) Virus identification:

Treatment and control:

- Non – specific treatment by replacing drinking water with electrolyte solution as soon as respiratory signs appear.
- Strict isolation of affected flock of chicken.

- **Vaccination:** The only practical means of controlling IB is vaccination, which is routinely used throughout the intensive poultry industry. The following factors are a feature of IB vaccination:

a) Vaccinal immunity is not long-lasting and re-vaccination is necessary.

b) The selection of an appropriate antigenic type for the region is important, given the existence of wide antigenic variation.

c) Timing and method of vaccine application will vary for different flocks and may require adjustment according to practical experiences.

- **Live vaccines** are in **widespread** use. These vaccines represent IBV strains that have been **passaged** in **embryonated chicken eggs** to achieve a reduction in virulence for the respiratory tract. Consequently, depending on the level of attenuation, IBV vaccines can be either mild or virulent. Live IBV vaccines are administered by either coarse spray, aerosol or drinking water, depending upon the vaccine used. Embryo vaccination is not practiced, but vaccines suitable for such a purpose are in development. Vaccination of day-old chicks at the hatchery, with vaccines of low virulence, is practiced in most countries since this is a simple way of handling the birds. More virulent vaccines are used for booster vaccination at approximately seven to ten days, usually in the drinking water.

5) Orthomyxoviridae

The virus family Orthomyxoviridae consists of one genus made up of influenza A, influenza B and influenza C on the basis of shared antigens by complement fixation and immunodiffusion tests. Influenza type A naturally occurs in human, equine, swine and birds, while B and C affect only human.

Influenza viruses

Gr: Ortho = direct and Myxo = mucous, viruses in this family have a direct affinity for mucous membrane.

Common characteristic:

1- A virus consists of roughly spherical or filamentous enveloped particles which measure 80-120 nm in diameter.

2- The nucleocaspid is helical and is enclosed within a protein matrix. The protein matrix is enclosed by a lipid membrane which is covered by two types of glycoprotin spikes which haemagglutinin and neuraminidase activities are associated.

- Neuraminidase (N) mushroom shaped and facilitates virus release from infected cells.
- Haemagglutinin (HA) rod shape and binds to the cell surface receptor to initiate infection. Ab against HA neutralizes viral infectivity.

3- The virus genome is a -ve sense single stranded RNA in eight segments which is associated with a viral transcriptase.

4- The neucleocapsid is helical in symmetry with 3 polymerase peptide (PB1, PB2, PA) associated with each segment of the RNA.

5- Influenza virus A is the cause of flu pandemics and is divided into subtypes all of which share a common nucleoprotein and matrix protein, but differ in their haemagglutinin (HA) and neuraminidase (N) of which 13 subtype of H (H1-H13) and 9 subtypes of N (N1-N9) are identified.

6- Antigenic shift and drift in influenza A viruses. Antigenic variation is a common in influenza viruses due to changes in HA and NA. Antigenic variation continually occurs in type A, less in type B while type C which is antigenically stable. The viral HA, and to a lesser extent the NA, are major targets for the immune response, and there is ordinarily little or no cross-protection between different HA or NA types.

Influenza A viruses are very diverse, and two viruses that share a subtype may be only distantly related. The high variability is the result of two processes, **mutation** and **genetic reassortment**. Mutations cause gradual changes in the HA and NA proteins of the virus, a process called '**antigenic drift**'.

Genetic reassortment can cause more rapid changes. The influenza A genome consists of 8 individual gene segments and when two different viruses infect the same cell, gene segments from both viruses may be packaged into a single, novel virion. This can occur whenever two influenza viruses replicate in the same cell, whether the viruses are adapted to the same host species (e.g., two different avian influenza viruses) or originally came from different hosts (for instance, an avian influenza virus and a swine influenza virus). An important aspect of reassortment is that it can generate viruses containing either a new HA, a new NA, or both. Such abrupt changes, called '**antigenic shifts**,' may be sufficient for the novel virus to completely evade existing immunity. After a subtype has become established in a species and has circulated for a time, antigenic shifts and drift can produce numerous viral variants.

1) Avian influenza (Fowl plague – Fowl pest)

Definition:

Avian influenza (AI) is acute, highly fatal contagious disease affecting the respiratory, enteric or nervous system of wild and domestic birds.

Aetiology:

- Avian influenza virus (H5N1), caused by the influenza virus Type‘A’ which belongs to Orthomyxoviridae.
- There are many strains of AI viruses and generally can be classified into two categories: low pathogenic (LPAI) that typically causes little or no clinical signs in birds and highly pathogenic (HPAI) that can cause severe clinical signs and/or high mortality in birds.

Host affected:

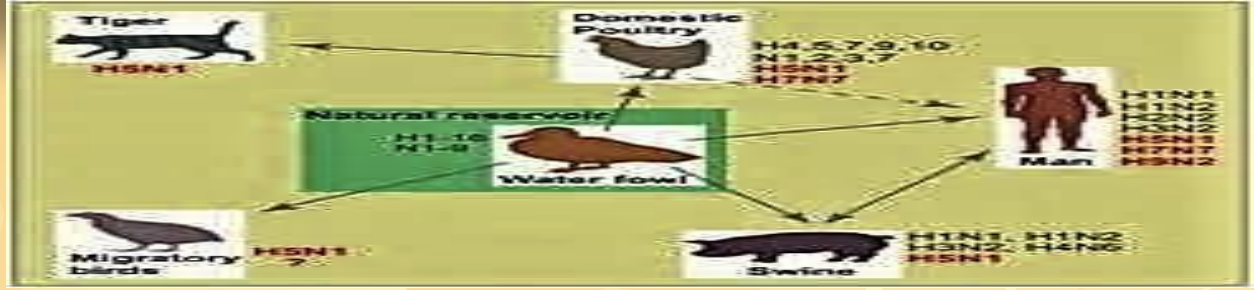
- Wild birds in aquatic habitats are thought to be their natural reservoir hosts.
- Food producing birds (chickens, turkeys, quails, guinea fowl, etc.), as well as pet birds and wild birds.
- The virus has also been isolated from mammalian species, including humans, rats and mice, weasels and ferrets, pigs, cats, tigers and dogs.

Resistance to physical and chemical agents:

- The virus is one of the resistant poultry viruses. It is ether sensitive.
- Temperature: destroyed by exposure to 55°C.

Mode of transmission:

- Ingestion or inhalation of the virus.
- Fecal – water- cloacal route. Fecal – water- oral route.
- Vertical transmission through infected birds.



Source of infection:

- Clothing that come in contact with infected birds.
- Feaces of infected birds.
- Infected birds.

Clinical signs:

In the mild form, signs of illness may be expressed only as ruffled feathers, reduced egg production, or mild effects on the respiratory system.

In the severe form of the disease, the virus not only affects the respiratory tract, as in the mild form, but also invades multiple organs and tissues that can result in massive internal haemorrhaging. Some or all of the following clinical signs are evident in birds infected with a highly pathogenic strain of AI (including H5N1 strain):

•Quietness and extreme depression.
•Sudden drop in production of eggs, many of which are soft-shelled or shell-less.
•Wattles and combs become swollen and congested.
•Swelling of the skin under the eyes.
•Coughing, sneezing and nervous signs.
•Diarrhoea.
•Haemorrhages on the hock.
•A few deaths may occur over several days, followed by rapid spread and a mortality rate that can then approach 100% within 48 hours.

Post-mortem lesion:

•Edema and cyanosis of the head, wattle and comb; excess fluid (which may be blood-stained) in the nares and oral cavity; edema and diffuse subcutaneous hemorrhages on the feet and shanks; and petechiae on the viscera and sometimes in the muscles.
•Foci of necrosis in the skin, combs, wattles, spleen, liver, lung, kidneys, intestine and pancrease.
•Petechial haemorrhages of the cardiac muscle, abdominal fat, mucosa of proventriculus and inner suface of the sternum.
•Fibrinous exudates in air spaces, oviduct, peritoneum and pericardial sac.

Diagnosis:

1- Clinical signs. 2- Post-mortem lesions.

3- Laboratory diagnosis:

a) **Sample**:

- Swabs from trachea, lung, air sacs, sinus exudates and cloaca.
- Serum from affected and contact birds.

b) **Virus isolation:**

The samples are inoculated into:

1- Embryonating chicken eggs (10-11 days) virus replicates in the embryonic tissues and membranes death of the embryo in less than 48 hrs.

- Haemagglutination test using RBCs detects the virus in egg fluid.

2- Tissue culture as (chicken or monkey kidney cells) CPE in the form of plaques over the agar overlay.

c) **Virus identification:**

•Virus can be identified as influenza A viruses with agar gel immunodiffusion (AGID), antigen-detection ELISAs or other immunoassays, or by a molecular test such as RT-PCR.

•They can be subtyped with specific antisera in hemagglutination and neuraminidase inhibition tests, by RT-PCR, or by sequence analysis of the viral HA and NA genes. RT-PCR assays can detect influenza viruses directly in clinical samples, and real-time RT-PCR is the diagnostic method of choice in many laboratories2, Viral antigens can be detected with ELISAs including rapid tests.

Control:

- Careful husbandry to prevent introduction of the virus into the flock.
- New birds shouldn't be introduced into a started flock until tested.
- Eggs for hatching should come from flocks free from virus.
- Prevention of exposure to infected birds.
- Careful precautions to prevent direct or indirect contact with mild, migratory or exotic birds.
- Turkey farms must be free from pigs, which act as a virus reservoir.

Treatment:

There is no specific treatment for influenza virus infections in animals. Poultry flocks infected with HPAI viruses are depopulated (this is generally mandatory in HPAI-free countries), while the disposition of infected LPAI flocks may differ, depending on the specific virus and the country.

Vaccination:

Avian influenza vaccines include both **traditional inactivated whole virus vaccines** and **newer recombinant vectored vaccines**. Most vaccines are produced for chickens, although they may be validated for use in turkeys, and their effectiveness can differ in other species. In addition to **suppressing clinical signs**, some vaccines are **capable of increasing resistance to infection**, and **decreasing virus excretion** and **transmission**. Appropriate vaccines are rarely available due to antigenic variation and diversity of the subtypes.

2) Swine influenza (Pig influenza – hog flu)

Definition:

Swine influenza is a highly contagious viral infection of pigs, which is a respiratory disease characterized by coughing, sneezing, nasal discharge, elevated rectal temperatures and in some instances associated with reproductive disorders such as abortion.

Aetiology:

•Swine influenza is caused by influenza A viruses in the family Orthomyxoviridae with a segmented RNA genome. Influenza A viruses are further characterised by subtype by the two major surface glycoproteins, haemagglutinin and neuraminidase.

Aetiology:

•One relatively stable subtype, classical and avian H1N1, was the etiologic agent of most swine influenza. The most common subtypes of influenza virus in swine are H1N1, H1N2, and H3N2. Other subtypes that have been identified in pigs include rH1N7, avian (av) H4N6, avH3N3 & avH9N2.

•Pigs act as mixing vessels on which have a receptors in their respiratory tract that will bind swine, human, and avian influenza viruses, resulting in development of new influenza viruses when swine, avian, and/or human influenza viruses undergo genetic reassortment in pigs.

Host affected:

•Swine influenza viruses (SIV) are found mainly in pigs, but they have also been found in other species, including humans, turkeys, and ducks.

Source of infection & Mode of transmission:

•Infected pigs may begin excreting swine influenza viruses within 24 hours of infection, and typically shed the viruses for 7-10 days.

•Contact with swine influenza virus containing secretions such as nasal discharges and aerosols created by coughing or sneezing of infected pigs.

•Swine flu can be transmitted from pig to pig or from pigs to man

•Human to human transmission in case of swine flu infection can also occur.

Resistance: Although influenza viruses are enveloped, some of these viruses have been reported to survive for long periods in the environment, particularly when the temperature is low. Mammalian influenza viruses seem to be relatively labile, but can persist for several hours in dried mucus.

Temperature: Influenza viruses can be inactivated by heat of 56°C for a minimum of 60 minutes (or higher temperatures for shorter periods) as well as by ionising radiation.

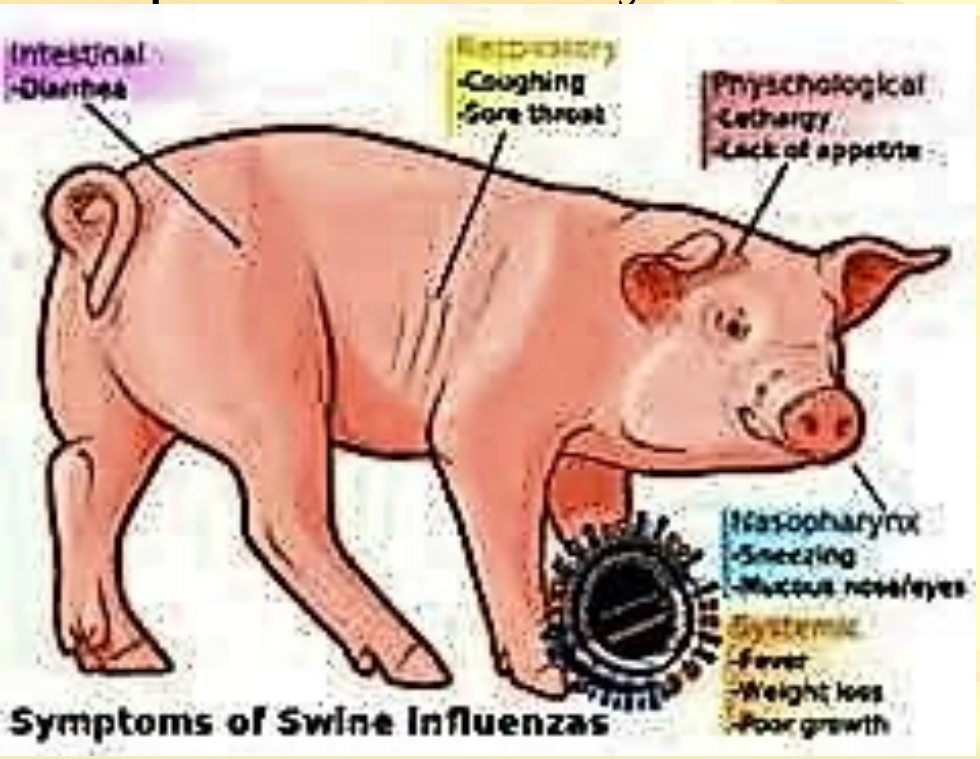
pH: Inactivated by low pH (pH 2).

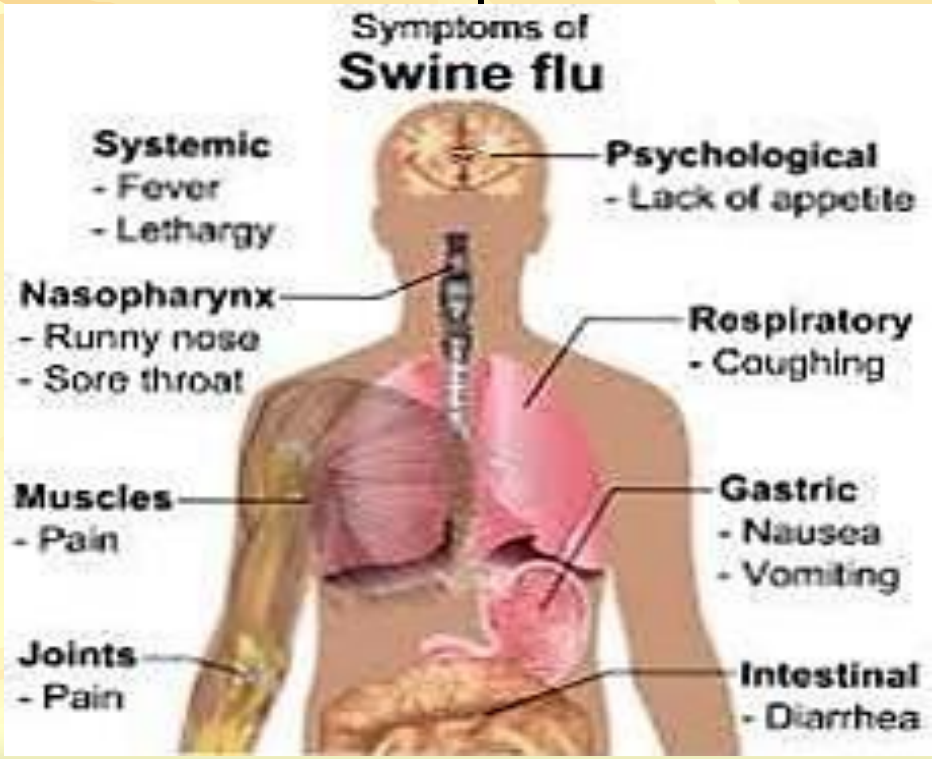
Chemicals/ Disinfectants: Susceptible to a wide variety of disinfectants, including sodium hypochlorite, 70% ethanol, oxidising agents, quaternary ammonium compounds, aldehydes (formalin, glutaraldehyde, formaldehyde), phenols, acids, povidone-iodine and lipid solvents.

Clinical signs:

- The clinical signs usually appear within 1 to 3 days in pigs, and most animals recover within 3-7 days if there are no secondary infections or other complications. Morbidity rates can reach 100% with SIV infections, while mortality rates are generally low.
- Swine influenza is an acute upper respiratory disease characterized by fever, lethargy, anorexia, weight loss, and laboured breathing. Coughing, sneezing, and nasal discharge are commonly seen.
- Conjunctivitis is a less common clinical sign. Abortions may also occur. Some strains can circulate in pigs with few or no clinical signs. Complications may include secondary bacterial or other viral infections. Severe, secondary potentially fatal bronchopneumonia is occasionally seen.
- Turkeys infected with swine influenza viruses may develop respiratory disease, have decreased egg production, or produce abnormal eggs.

•In humans, when infections have been reported, symptoms observed generally resembled seasonal influenza, and included: fever (which is usually high, but unlike seasonal flu, is sometimes absent), upper respiratory disease, acute respiratory disease, or pneumonia. Very rare fatalities have been reported.





Diagnosis:

1- Clinical signs. 2- Laboratory diagnosis:

a) Sample: Swabs from nasal discharges- infected lung tissue.

b) Virus isolation:

Inoculate samples into:

1- Embryonating chicken eggs (10 -11 days) in the allantoic cavity and amniotic sac incubate at 35- 37 °C for 3-4 days, death of the embryo after 24 hours.

2- Tissue culture as Madin- Darby canine kidney (MDCK), primary swine (kidney- testicle- lung or tracheal cells) CPE in the form of plaques over agar overlay.

c) Virus identification:

•Haemagglutination test using turkey or chicken RBCs, positive haemaggltination.

•Serological tests (paired sera should be collected 10–21 days apart. a four-fold or greater increase in titre between the first and second sample is suggestive of a recent SIV infection).

✓ Haemagglutinatin inhibition (HI) & Neuraminidase inhibition (NI) tests.

✓ Immunofluorescence. Enzyme-linked immunosorbent assay (ELISA).

•Direct electron microscopy.

•RT- PCR is the method of choice for diagnosing H1N1 virus.

Treatment:

•Broad spectrum antibiotic to prevent bacterial pneumonia & other secondary infections in influenza weakened pig's herds.

•In man antiviral drugs as Tamiflu (oseltamivir) or Relenza (zanamivir) make the illness milder & the patient feel better faster.

•Oseltamivir & Zanamivir are neuraminidase inhibitors, they prevent new viral particles from being released by infected cells.

•The 2009 flu pandemic vaccines are the set of influenza vaccines that have been developed to protect against the pandemic H1N1/09 virus.

Two types of influenza vaccines are available:

•**TIV** (flu shot (injection) of **t**rivalent (three strains; usually A/H1N1, A/H3N2, and B) **i**nactivated (killed) **v**accine) or

•**LAIV** (nasal spray (mist) of **l**ive **a**ttenuated **i**nfluenza **v**accine.)' not recommended for individuals under age 2 or over age 50'

-Both these types of vaccine are usually produced by growing the virus in chicken eggs.

- The vaccines have a several advantages such as safe, having a similar safety profile to the normal seasonal influenza vaccine and providing a strong protective immune response

6)Rhabdoviridae

Animal rhabdoviruses (from Greek rhabdo means rods).

Common characteristics:

1-The virus are oblong particles with one rounded and one planar end, which makes the virus particle to look a bullet.

2- The virus particles are varying sizes, length 130-380 nm and diameter between 50-95 nm.

3- It's envelope consists of lipid bilayer with surface spikes which elect neutralizing and haemagglutination inhibiting antibodies.

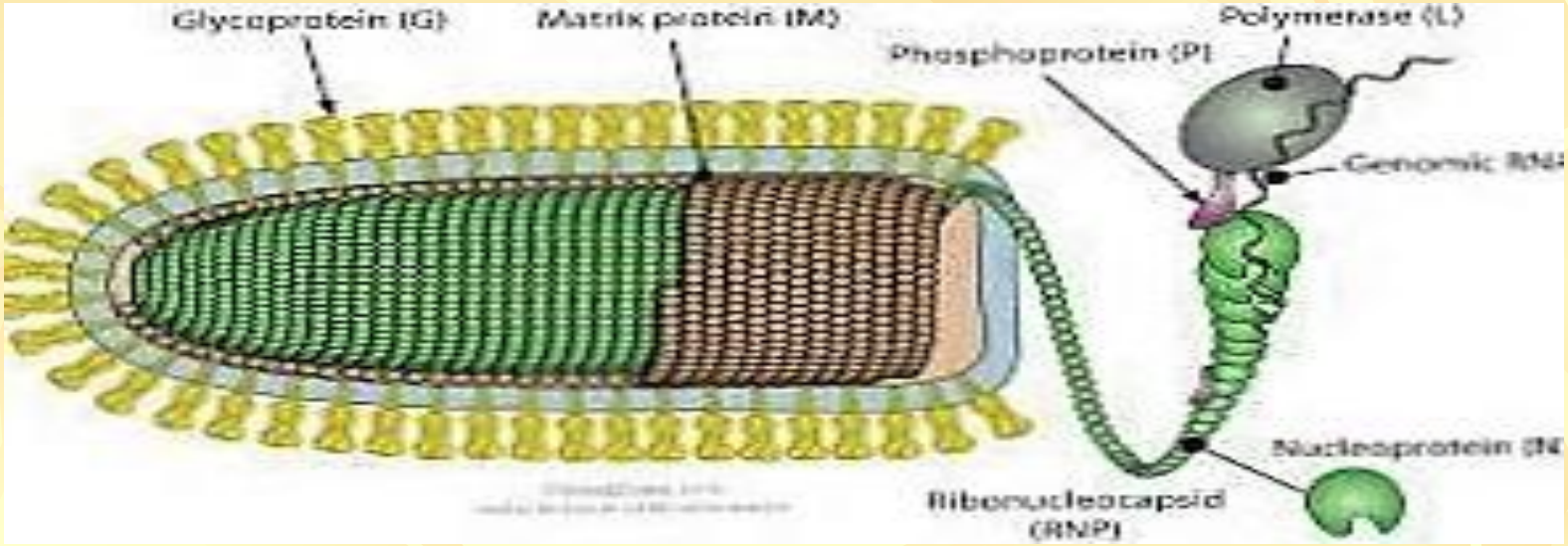
4- It contains a linear, non-segmented, -ve single stranded RNA genome.

5- Contains helical nucleocapsid.

6- Viron contains RNA dependent RNA polymerase.

7. Rhabdoviridae is divided into 2 antigenically distinct genera:

- Vesiculovirus which includes Vesicular stomatitis virus, the only virus in this genus.
- Lyssa virus, Rabies virus is the only member of veterinary importance. The other animal pathogens in this family haven't an established group is Bovine ephemeral fever.



1) Vesicular Stomatitis (VS)

Definition:

- It is a benign contagious vesicular disease in cattle, pigs, horses, deer and occasionally in man. The disease is characterized by the formation of vesi-cles in the mucosal lining of the mouth, tongue, teats, skin of the coronary band and in the interdigital spaces of the foot. The signs of this disease are almost identical to three other important diseases of animals: foot and mouth disease, swine vesicular disease and vesicular exanthema of swine.
- **Aetiology:** Vesicular stomatitis virus which belongs to Family Rhabdoviridae.
- **Host affected:**
  - Horses, donkeys, mules, cattle, swine, and man can be affected by VSV. Horses are usually affected the most severely.
  - Sheep and goats are resistant and rarely show signs of disease.

Resistance to physical and chemical agents:

- Vesicular stomatitis virus is inactivated at 58° C for 30 min.
- Stable between pH 4.0 and 10.0.
- Sensitive to formaldehyde, ether and other organic solvents; chlorine dioxide, formalin (1%), 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde, 2% sodium carbonate, 4% sodium hydroxide, and 2% iodophore disinfectants, all effective disinfectants.
- Inactivated by sunlight; survives for long periods at low temperatures, The virus can be preserved for years at -70°C and by freeze-drying under vacuum.

Mode of transmission:

- VSV can be transmitted by insects (vector), especially sand flies and black flies.
- It can also be transmitted by direct contact with infected animals and contaminated objects known as fomites.

- **Source of infection:**
- the disease spreads between animals through contact with saliva or fluid from ruptured sores from infected animals to healthy animals.

Clinical signs: The signs are similar to those of foot and mouth disease (FMD), with which it can easily be confused (but horses are resistant to FMD and susceptible to VS).

- Incubation period is up to 21 days.
- Fever (103-104° F) is present in all infected animals.
- Lesions range from mild punctate erosions on the dental pad to blanched raised or broken vesicles of various sizes in the mouth, which progress to severe ulcers involving tongue and oral mucosa 4 to 6 days post infection.

Horses: upper surface of the tongue, surface of the lips and around nostrils, corners of the mouth and the gums.

Cattle: tongue, lips, gums, hard palate, and sometimes muzzle and around the nostrils.

Pigs: snout.

- Lesions involving feet of horses and cattle are not exceptional.
- Teat lesions occur in dairy herds.
- Foot lesions and lameness are frequent in pigs.
- Recovery in few days up to 2 weeks.

Complication: loss of production and mastitis in dairy herds due to secondary infections, lameness in horses.

- Morbidity rates vary between 5 and 70 %; mortality is rare.

Postmortem lesions: Vesicles filled with clear serous fluid, ulcers, erosions, and crusting of muzzle and lips; limited to the epithelial tissues of mouth, nostrils, teats and feet.

Diagnosis: **Sample**: Vesicular fluid, Saliva, Epithelial tissue covering the vesicles placed in buffered glycerol or frozen.

- Virus isolation inoculation into:
  - Embryonated chicken eggs show cytopathic effect and visible plaques.
  - Laboratory animals such as mice lead to fatal encephalitis.
  - Tissue culture as (chick fibroblasts, pig kidney, BHK-21, Vero cells, bovine fetal spleen cells) shows intracytoplasmic inclusion bodies.
- Virus identification:

2) RABIES (Hydrophobia)

- The Greeks called rabies lyssa or lytta, which means frenzy or madness. They named human rabies hydrophobia, which means fear of water, a symptom shown by rabies victims.

Definition:

- Rabies is an acute fetal zoonotic viral disease that affects the central nervous system of warm-blooded animals, primary of wild and domestic canines, secondary of other mammals including humans. The disease has a long incubation period (six months) and symptoms may take several weeks to appear after infection. However, once symptoms appear, rabies is always fatal in animals.

Host affected:

- Hosts are usually Canidae, including dogs (responsible for more than 99% of all human deaths from rabies), foxes, coyotes, wolves and jackals; also cats, skunks, raccoons, mongooses, and other biting animals. Blood sucking rats as Vampire bats, which act as reservoirs.
- Man and all warm-blooded animals, including birds, cattle, camel, sheep, goat, equines, rodents and pigs).

- Susceptibility to infection depends on (virulence of the strain- quantity of the virus in the rabid animal saliva – susceptibility of the species).
- A bite or a scratch introduces virus-laden saliva from a rabid animal.
- The incubation period ranges from a few days to several years (most commonly 3-8 weeks).

Etiologic agent: Rabies virus is related to genus Lyssaviruses of the Rhabdoviridae family.

- **Antigenic properties:**
- There is only one immunological type of rabies virus and specific antibodies are readily detected by S.N.T, C.F.T and agar gel diffusion tests.

Biological forms of rabies virus:

1- Street virus:

- Isolated from naturally infected animals.
- It infects by peripheral inoculation causing encephalitis.
- All laboratory animals are susceptible by intramuscular and intracerebral inoculation.
- The incubation period is (3- 8 weeks).
- It produces intracytoplasmic inclusion bodies in the brain (Negri bodies).

2- Fixed virus:

- This results from repeated passage (40-80) of the virus in the brain of laboratory animal particularly (rabbit).
- It is attenuated strain and causes encephalitis only when inoculated intracerebrally.
- The incubation period is short (4-6) days.
- Inclusion bodies are absent or found with difficulty.

Resistance to physical and chemical agents:

1- It is inactivated by

- Heating at 56 °C for 30 min.
- 1% formalin, 3% cresol and 0.1 % β- propionolactone.
- Repeated thawing and freezing.
- Exposure to ultraviolet rays, proteolytic enzymes and acid pH.

2- The virus persists viable in brain tissue for 7-10 days at room temperature and for several weeks at 4 °C.

Mode of transmission:

- Biting of a rabid animal.
- Biting of a vampire bat.
- Direct contact with:
- Saliva of rabid animals when there are wounds or abrasion in the skin.
- Tissue and organs of infected carcass.
- Indirect contact with contaminated equipments used during post mortem examination.

Source of infection:

- Saliva of rabid animal in prodromal phase between 10-15 days before the appearance of clinical signs.
- Tissue and organs of rabid animals specially brain.
- Contaminated articles, especially those used during post mortem examination.

Pathogenesis:

- The virus is introduced through the bite of a rabid animal in its saliva then multiplies locally and travels via the peripheral nerves to the CNS where it multiplies, causing fatal encephalitis (Negri bodies) then travel down in the peripheral nerves to the salivary glands passing in the saliva.

Clinical signs:

- Incubation period 10 days- 2 years, depending on:
  - Severity of the bite and its distance from the brain.
  - The amount of the virus inoculated.
  - Incubation period in young animals is shorter.

Clinical forms: There is no viraemia.

a) Furious rabies or excitative form, characterized by:

- Fever, dilatation of the pupil and photophobia.
- Profuse salivation.
- Animals may be anxious, highly excitable and/or aggressive with intermittent periods of depression.
- With the loss of natural caution and fear of other animals and humans, animals with this form of rabies may demonstrate sudden behaviour changes, and attack without provocation.

- As the disease progresses, muscular weakness, incoordination and seizures are common.
- Difficult in swallowing and drinking due to painful spasms of pharyngeal muscles (hydrophobia).
- Death results from progressive paralysis.

b) Dumb rabies or paralytic form, characterized by:

- Animals may be depressed or unusually docile.
- The animal will often have paralysis, generally of the face, throat and neck, causing abnormal facial expressions, drooling and inability to swallow.
- Paralysis may affect the body, first affecting the hind legs. The paralysis progresses rapidly to the whole body with subsequent coma and death after 2-4 days from the onset of the paralytic stage.
- **In humans**, early signs can include fever or headache. As the disease progresses, symptoms may include confusion, depression, sleepiness, agitation or paralysis of the face, throat and neck. Death generally results from progressive paralysis.

Pathological lesions:

- Neuronal degeneration and glial proliferation in the brain stem, cerebral cortex and thalamus.
- Non purulent encephalomyelitis with perivascular cuffing.
- The presence of acidophilic intracytioplasmic inclusion bodies (Negri bodies) is particularly abundant in nerve cells in Ammon's horn of the hippocampus.

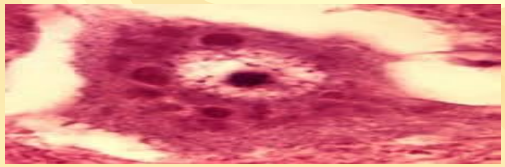
Diagnosis:

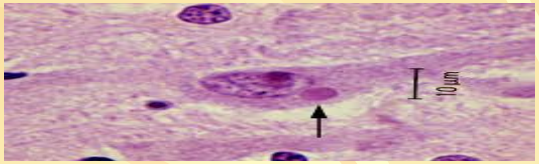
- Immediately after the bite the animal should be captured and observed for 10 days.
- If no symptoms appear during this period the diagnosis of Rabies is excluded.
- If the animal dies or symptoms appear the animal is sacrificed and diagnosis is done.

Sample: Brain tissue placed in 50% glycerol saline to preserve the virus.

Virus isolation:

- The sample is inoculated into:
  A. Laboratory animal: I/C or I/M inoculation into (Rabbit- Guinea pigs- white mice) paralysis and death.
  B. Chicken embryo: the virus is inoculated via C.A.M, allantoic cavity and yolk sac inoculated embryos are smaller than normal and usually dies.
  C. Tissue culture: the samples are inoculated into primary or continuous culture of (chick embryo, mouse, rabbit, dog and human cells -BHK-21) shows plaque.





Virus identification:

1. Antigen detection by direct immunofluoresence in brain tissue.
2. Detection of (Negri bodies) in stained brain smear.
3. Specific antibodies against rabies can be detected by VNT in mice.
4. Detection of haemagglutination produced by Rabies virus when propagated on (BHK-21) cells maintained in media containing 0.4% bovine serum albumin.
5. RT- PCR applied to brain tissue.

Management and prophylaxis:

- Case management of bitten patients by:
- Immediate and thorough cleaning of the wound with soap and water, antiseptic as (1/1000 perchloride of mercury - absolute alcohol) and irrigated with a virucidal agent as poviodine, iodine solution and do not suturing the wound.
- Administer tetanus vaccine and antibiotic to control bacterial infection.
- Post-exposure prophylaxis by vaccination and passive immunization with rabies immune globulins is required in the following cases:
  1. In case of a bite by a wild or domestic animal which is not available.
  2. In severe bite in the head and neck even if the animal is available due to short incubation period.
  3. If the diagnosis is established in captured animal.
  4. Bite or non bite, exposure to bats.
  5. Exposure to infected saliva through abrasions or scratches.

Vaccination:

1- Inactivated virus vaccine: BHK-21 (Low egg passage) used to protect rabies in dogs, cats, and other animals.

2- Modified live virus vaccines:

- Porcine tissue culture origin (HEP, street Albama Dufferin SAD) strain and (ERA strain) to vaccinate dogs every 3 year and cattle, horses, sheep, goats every year.
- Canine cell line origin (High egg passage) (Flury strain) was used to vaccinated dogs every 3 years and cat every year.

3- A recombinant viral vaccine: Consisting of vaccine virus carrying the rabies glycoprotein gene successfully immunized animals when orally administered.

In Egypt: Avianized rabies vaccine is used which is live attenuated, freeze dried vaccine contain flurry strain low egg passage (LEP) with 40-50 passage, propagated in embryonated eggs inoculated Intramuscular given to dogs not less than 6 months ages and vaccinate annually.

3) Bovine Ephemeral Fever (Three–Day Sickness)

(Bovine Epizootic Fever, Three–Day Stiffsickness, Dragon Boat Disease)

- **Definition:**
- Bovine ephemeral fever is an acute, arthropod-borne disease of cattle. The disease characterized by the sudden onset of fever, nasal discharge, stiffness, disinclination to movement accompanied by lameness, abortion and loss in milk production, high morbidity and very low mortality. Recovery usually occurs within three to four days of the onset of clinical signs.
- **Aetiology:**
- Bovine ephemeral fever virus has been classified as the type species of the genus Ephemerovirus in the Rhabdoviridae.

Host affected:

- Cattle, water buffalo, sheep, water buck and wildebeest.
- Cattle in good condition are usually affected more severely, but mortality is low.

Resistance to physical and chemical agents:

- The virus is inactivated by - Heat at 56 °C for 10 minutes.
  - High pH (12) and low pH (2.5).

Mode of transmission:

- Arthropod-borne disease, mechanical transmission by insect vectors.
- The disease is not transmitted by direct contact, bodily secretions, or aerosol droplets.
- Carriers are not known to occur.

Clinical signs:

- The incubation period under normal conditions is very short: 36–48 hours, but the average is three to four days.

- The disease causes a sudden rise in temperature and affects the general state of health. There is a similar sudden fall in temperature, culminating in a general recovery after three to five days without complications. Hyperthermia generally occurs in two phases.
- During the first peak of fever, the clinical signs are discreet and hard to detect. In more severely affected animals there is sudden fever with temperatures reaching 40–41°C, as well as depression, loss of appetite, anorexia, stiff gait, salivation and nasal discharge, inflammation of the joints, rapid pulse and respiration rate, shivering and oedema of the subcutaneous muscles, eye sockets and head.
- The animal, sometimes lying in sternal recumbency and sometimes on its side, shows some reflexes, but these gradually disappear as the disease progresses.
- Loss of the swallowing reflex, lack of rumination, constipation and profuse salivation becomes evident.
- Total loss of reflexes followed by coma leads to the death of the laterally recumbent animal. However, that these clinical signs may also disappear as suddenly as they appeared.

- The second peak of fever occurs 12–24 hours after the first, affecting the lungs (tachypnea, rattling) and causing lacrimation.
- Secondary complications may include signs of pneumonia and pulmonary emphysema, abundant discharge, stiffness of the limbs, arthritis, lameness and lasting paresis, forcing the animal into prolonged sternal recumbency. This phase of hyperthermia may last from two to four days.
- In addition to hyperthermia, other clinical signs may appear or persist, such as subclinical mastitis leading to a sharp reduction in milk yield, abortion in 5% of pregnant females and infertility in bulls. Generally speaking, animals in good physical condition (fat, good milkers) show more severe signs than lean animals and non-lactating females.
- The disease can lead to death in some individuals following a gradual loss of reflexes, or to cessation of swallowing and rumination. But other individuals recover in five to six days without complications (pulmonary emphysema, locomotor ataxia, persistent stiffness of the limbs). Milk yield in recovered milking cows is always lower than it was prior to the disease.

Post mortem lesions:

- Serofibrinous polyserositis, of varying degrees, in the articular synovial membranes and in the thoracic and peritoneal cavities is characteristic of the disease.
- Serous surfaces may also show signs of bleeding and oedema to varying degrees. The oedema fluid in the thoracic or abdominal cavity contains fibrin.
- In the joints, this periarticular inflammatory fluid is yellow or brown and gelatinous in appearance.
- Other lesions may also occur, such as pulmonary and lymph node oedema, inflammation of the parietal and visceral pleura, pericarditis (especially at the base of the heart), necrosis at certain points of the skeletal muscles, and, sometimes, emphysematous lesions of the lungs, mediastinum and subcutaneous connective tissue.

Diagnosis:

1. Clinical signs.
2. Post-mortem lesions.
3. Laboratory tests:

- **Sample:**
  - To prevent the spread of the disease proper authorities and authorized laboratories should be contacted and samples should only be sent under secure conditions.
  - Blood samples should be collected during a fever spike and one to two weeks later.
- **Virus isolation:**
  - Blood samples are inoculated into suitable tissue culture as (BHK–21, bovine kidney, hamster lung, Vero) shows intracytoplasmic inclusion bodies.
  - Intracerebral inoculation of suckling mice with blood of infected animal shows intractoplasmic inclusion bodies.
- **Virus detection: (serology)**

Differential Diagnosis:

- Rift Valley fever, foot and mouth disease, botulism, blackleg, bluetongue, babesiosis.

Prevention and control:

1. Notification of authorities.
2. Quarantine and Disinfection by Sodium hypochlorite which effectively destroy ephemeral fever virus; however, disinfection is relatively unimportant in preventing the spread of this virus.
3. Contact with potential insect vectors must be avoided.

Vaccination:

- Live virus attenuated vaccine prepared by serial passage in the brain of mice.
- Cell culture formalin inactivated adjuvant vaccine.

Differential Diagnosis:

- Rift Valley fever, foot and mouth disease, botulism, blackleg, bluetongue, babesiosis.

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II) Unclassified agents

Bovine Spongiform encephalopathy (BSE

Mad Cow disease, Scrapie in sheep,
Kura or creutzfield Jacob disease in man.

Definition:

It is an infectious and chronic degenerative condition of the CNS of bovine, sheep, goat and even human characterized by fatal spongy neurodegeneration in the brain and spinal cord caused by a small and uncharacterized agent.

Aetiology:

BSE is a member of the transmissible spongiform encephalopathies (TSEs), a group of neurodegenerative disorders caused by **prions**, infectious proteins that appear to replicate by converting a normal cellular protein into copies of the prion. Composed entirely of protease resistant proteins (PrP) with no detectable nucleic acids, which differentiate it from viruses. Electron Microscopy reveals filaments rather than virus particles.

Pathogenesis of disease production:

When these proteins are in normal α- helix configuration PrP^{C} they are non pathogenic, but when they undergo misfolding and their configuration change to β- pleated sheet PrP^{SC}, they aggregate into filaments that disrupt neuronal functions and result into the symptoms of the disease.

Characters of prion-mediated diseases:

- Have a long incubation period and a chronic progressive course with dementia and ends fatally.
- Confined to CNS, causing neurodegeneration (amyloid) and spongiform changes due to neuronal vacuolation and neuronal loss.
- No inflammatory or immune response to these diseases as they are normal body proteins.

Transmission:

•BSE is usually transmitted when an animal or human ingests tissues, mainly the brain, transplanted tissues and contaminated surgical instruments containing the BSE prion.

•Young animals may be particularly susceptible: some studies suggest that most cattle become infected with BSE during the first six months of life.

•Sheep are, likewise, most susceptible to experimental (oral) inoculation during the first few months of life, especially during the first few weeks.

Zoonotic potential:

Humans occasionally develop variant Creutzfeldt Jakob disease after eating prion-containing tissues from an infected animal. To date, all known cases have been caused by the classical BSE prion. Whether H-BSE and L-BSE can cause disease in people is still uncertain.

Resistance to physical and chemical agents:

Temperature: - Preserved by refrigeration and freezing.

- Inactivated by autoclaving at 134 – 138 C°

-Resist temperature used for cooking, so it transmitted by ingestion.

2- **pH**: stable over a wide range of pH.

3- **Disinfectant**: - NaoH for >1hr at 20 C° for surfaces & overnight for equipments.

- Phenol and ether

4-Survival if -Protected within tissue preserved in aldehyde.

- Protected within dried organic matter.

- Present in post mortem tissues after wide rendering processes.

Clinical signs:

Animals with BSE may demonstrate some of the following symptoms:

- The disease has a long incubation period about 4 years.
- Nervous or aggressive behaviour.
- Depression.
- Hypersensitivity to sound and touch, twitching, tremors.
- Abnormal posture.
- Lack of coordination and difficulty in rising from a lying position;
- Autonomic dysfunction: of rumination, bradycardia, altered heart rhythm.
- Pruritis: occur, but not usually a prominent sign.
- Weight loss, or; decreased milk production.

Postmortem lesions: The histopathologic lesions are confined to the CNS. Neuronal vacuolation and non-inflammatory spongiform changes in the gray matter are characteristic of the disease in cattle. These lesions are usually, but not always bilaterally symmetrical.

Diagnosis:

1. Sample "frozen as soon as possible after death".
   - Whole brain. Brain stem or medulla.
   - Cervical spinal cord or caudal medulla: for PrP^{SC} detection.
2. Detection histologically of spongiform and amyloid (neurodegeneration) changes in brain biopsy mainly in grey matter.
3. Imumohistoclemical analysis of brain tissue for PrP^{SC} detection.
4. Electron micrscopy examination for detection of scrapie-associated fibrils (SAF).
5. Monoclonal antibody based assay detect prion proteins in tonsillar and lymphoid tissues.
6. Elecro encephalogram shows periodic" triphasic spikes" sharp wares.
7. No serological test due to absence of detectable immune responses in BSE, as they have normal body proteins.

Treatment: No effective treatment, so clinically suspected cases must be killed by lethal injection to avoid damage to brain tissue sampled for diagnosis.

Prophylaxis:

1. Free countries safeguards on importation of live ruminant species and their products.
2. Countries with cases in cattle:

- Slaughter and proper disposal of infected cattle.
- Controls on recycling of mammalian protein.

3. Laboratory workers should wear appropriate protective clothing.