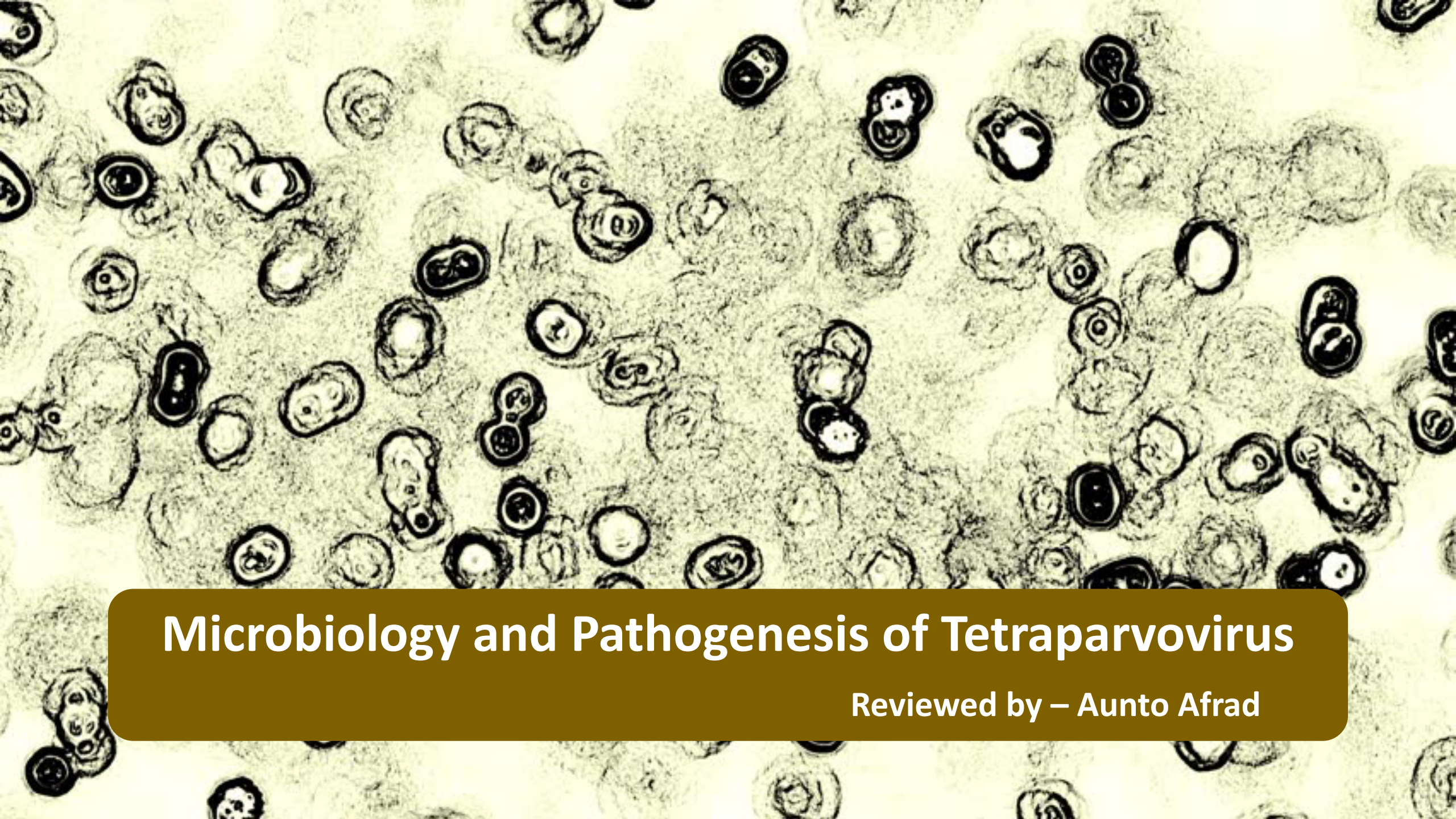
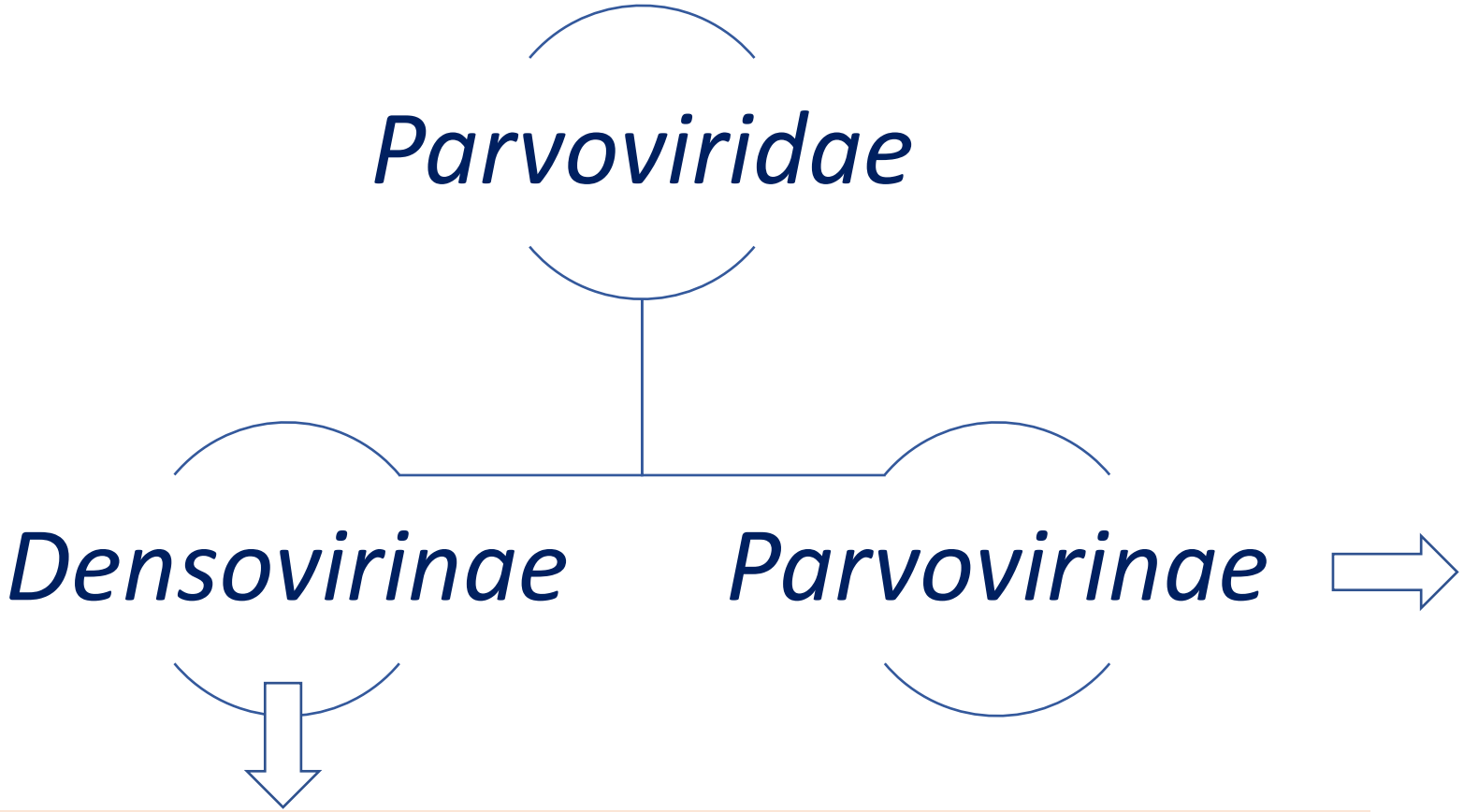


Microbiology and Pathogenesis of Tetraparvovirus

Reviewed by – Aunto Afrad

What is Tetraparvovirus?



Infect Arthropods (currently only known to infect insects, crustacea and echinoderms)

Infect Vertebrate: Mammals and Birds

Subdivided into eight genera, of which five include human pathogens

***Tetraparvovirus* (PARV4) is one of them**

doi: 10.1007/s00705-013-1914-1

Infection of Parvovirus: *at a glance*

The *Parvovirinae* subfamily has been subdivided into eight genera, of which five include human pathogens.

Amdoparvovirus* (Aleutian mink disease virus)*: Infect mink, fox, racoon dogs and skunk

***Aveparvovirus* (Chicken parvovirus):** Infect turkeys and chickens

***Bocaparvovirus* (Human bocavirus 1)** *:* Infect mammals from multiple orders, including primates

***Dependoparvovirus* (Adeno-associated virus):** Infect mammals, birds or reptiles

***Erythroparvovirus* (Human parvovirus B19)**: Infect mammals, specifically primates, chipmunk or cows

***Protoparvovirus* (Bufavirus):** Infect mammals from multiple orders, including canines and primates

***Copiparvovirus* (Bovine parvovirus 2):** Infect pigs and cows

***Tetraparvovirus* (Human parv4 G1):** Infect primates, bats, pigs, cows and sheep

Ref: ICTV. "Virus Taxonomy: 2017 Release"

TetraParvovirus (PARV4)

PARV4 was first reported in 2005 in a hepatitis B virus–infected injecting drug user (IDU).

There are currently six recognized species: *Chiropteran tetraparvovirus 1*, *Primate tetraparvovirus 1*, *Ungulate tetraparvovirus 1*, *Ungulate tetraparvovirus 2*, *Ungulate tetraparvovirus 3*, and *Ungulate tetraparvovirus 4*.

Small, non-enveloped, single-stranded DNA viruses, with an icosahedral capsid.

There is no in vitro culture system for PARV4, and it is unknown whether the virus can replicate autonomously.

Ref: J Virol. 2005 Jul;79(13):8230-6

Origin of PARV4 in Humans and Transmission

Is Mosquito the vector for tetra-parvovirus?

Three genotypes. Genotypes 1 and 2 (the latter originally termed PARV5) are predominant in Europe, North America, and Asia; genotype 3 is most widespread in Africa.

Genetic diversity within each genotype is minimal.

Chimpanzees and monkey species harbour the most closely related parvoviruses to PARV4.

The nonhuman PARV4-like variants were species-specific, despite frequent opportunities for transmission, including blood contact, between non human primates and human hunters.

Strongly associated with hepatitis C virus (HCV), chronic hepatitis B virus (HBV) and HIV infection

Parenteral transmission is also clearly possible independently from other blood-borne viruses, and PARV4 IgG has been reported in the absence of HIV, HBV, or HCV in the IDU population, in haemophilia patients, and in patients with a history of intra-muscular injections.

The potential for placental transmission has also been documented in a small series from Taiwan

Do Children have any unique signature?

- **There is currently no definitive clinical syndrome associated with PARV4 infection. PAV4 have been isolated from blood, liver, spleen, lymph node and bone marrow and have not been associated with disease in any of their known hosts to date.**
- **In the majority of instances, PARV4 viraemia appears to be self-limiting and asymptomatic.**
- **However, in a minority of reports, a range of possible disease outcomes are described in individuals with evidence of past or current PARV4 infection, including respiratory or gastrointestinal symptoms, hepatitis, rash, and encephalitis.**
- **Requires actively dividing cells to replicate, the type of tissue infected varies with the age of the animal.**
- **Notably, most of these studies describe small numbers of patients, with no clinical manifestation.**

Clinical Symptoms with PARV4 Infection

Reference	Characteristics and location of subject(s) with PARV4 infection[a]	Method of laboratory detection of PARV4 infection	Presenting clinical symptoms(s)
Benjamin et al., 2011 [21]	N = 2; children aged 2–3 years with suspected CNS infection; India.[b]	PARV4 DNA in CSF	Presumed encephalitis (fever and generalised convulsions).
Chen et al., 2011 [13]	N = 6; mother-infant pairs with nonimmune idiopathic hydrops in foetus; Taiwan.	Infants: five of six had PARV4 DNA in plasma.Mothers: four of six had PARV4 IgM; two of six had PARV4 IgG	Foetal hydrops (≥2 of ascites, pleural/ pericardial effusion, skin oedema, polyhydramnios). Two of six babies died.
Drexler et al., 2012 [16]	N = 13; Children with respiratory or gastrointestinal symptoms; Ghana.[c]	PARV4 DNA in nasal secretions (N = 8, median age 32 months) or faeces (N = 5, median age 43 months).	Upper/lower respiratory tract symptoms or gastrointestinal symptoms.
Jones et al., 2005 [1]	N = 1; homeless male IDU, Hepatitis B-positive, HIV-negative; United States.	PARV4 DNA in serum.	Fatigue, arthralgia, neck stiffness, pharyngitis, diarrhoea, vomiting, confusion, night sweats.
Sharp et al., 2012 [11]	N = 9; haemophilia patients aged 10–21 years seroconverting to PARV4 IgG positivity over a 5-year period (seven were already HIV-positive); HGDS cohort, US.	Conversion from PARV4 IgG negative to positive; two had transient positive PARV4 IgM. All were positive for PARV4 DNA in serum (viral titre $<10^3$–10^{10} copies/ml)	Rash in three subjects, unexplained hepatitis (but minimal disturbance of LFTs at the time of PARV4 IgG seroconversion).
Simmons et al., 2012 [9]	N = 193; subjects from Swiss HIV Cohort Study (www.shcs.ch/).	PARV4 IgG positive.	Early HIV-related symptoms (CDC-B symptoms).
Vallerini et al., 2008 [22]	N = 1; patient with Wegener's Granulomatosis on long-term steroid therapy; Italy.[b]	PARV4 DNA in serum.	Fever, anaemia (with erythroid hypoplasia on bone marrow biopsy), post-infectious glomerulonephritis, subsequent multiorgan failure.

Treatment

- **Currently, no vaccine exists to prevent infection by all parvoviruses, but recently, the virus's capsid proteins, which are non infectious molecules, have been suggested acting as antigens for improving of vaccines.**
- **Antivirals and human immunoglobulin-sourced treatments are usually for relief of symptoms.**

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Pearls

PARV4: An Emerging Tetraparvovirus

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We are left with important unanswered questions. What are the potential outcomes of infection with PARV4? Are there really multiple different modes of transmission? How frequently does viral persistence occur, and does this matter to the host? Further work is urgently needed to improve our understanding of this emerging infection.