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Journal of Virology and Pathogens

REVIEW ARTICLE

Fowl Pox Virus: Genome Biology and its Economic Importance

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Citation: Habtamu Demisse Kasa (2026) Fowl Pox Virus: Genome Biology and its Economic Importance, J Virol Pathog 2(1): 101

Abstract

Fowl pox virus belongs to genus avipoxvirus of the family poxviridae and cause a disease in chickens and other birds characterized by the formation of proliferative lesions and scabs on the skin, and diphtheritic lesions in the upper parts of the digestive and respiratory tracts. The virus replication occurs in the cytoplasm of the host cell and matured virion is extremely resistant to environmental conditions. Its distribution is world-wide and significant problem for small-scale and backyard flocks, as well as for intensive poultry commercial farming. The virus enters an epithelial cell and then spread from cell to cell aided by the production of epithelial growth factors which causes proliferation of cells. The disease transmitted from infected host by direct contact or biting insects, particularly mosquitoes and arthropods. Conformation suspected case was secured by virus isolation, serological test and molecular techniques. Fowl pox causes a transient drop in egg production and a reduced growth rate in birds and controlled by vaccination and following stable biosecurity based prevention.

Key words: Chickens; ELISA; Fowl pox virus; Replication; pathogenicity; Vaccination.

Introduction

Fowl pox is a disease of chickens and other birds caused by a DNA virus of the genus avipoxvirus of the family poxviridae [1]. The disease is often referred to as sore-head, canker, avian diphtheria, contagious epithelioma, or perhaps most commonly as chicken-pox [2]. This viral infection causes nodule on the skin and mucous membrane of the digestive and respiratory tracts of the chickens. It is a disease of economic importance listed by the world animal health organization and common in domestic birds farming system. It can commonly cause drops in egg production or retarded growth in younger birds [3].

Fowl pox disease has a world-wide distribution and its incidence is variable in different areas because of differences in climate, management and practice of regular vaccination [4]. Fowl pox has been controlled in developed countries. However, it is still a problem in most developing countries including Ethiopia and result serious economic impact across the countries [5].

Fowl pox disease exit as cutaneous or diphtheritic form on the chickens. The cutaneous form, also called dry form of the disease is characterized by the appearance of nodular lesions on the comb, wattles, eyelids, and other non-feathered areas of the body [6]. In the diphtheritic form (wet pox); slightly elevated white opaque nodules develop on the mucous membranes of the digestive and respiratory tracts of the chickens. The nodule on the mucous membranes rapidly increases in size to become a yellowish diphtheritic membrane. Lesions occur on the mucous membranes of the mouth, oesophagus, larynx or trachea [7].

The Fowl pox virus (FPV) transmitted by direct contact with infected chickens or by indirect contact with contaminated equipment or bedding [8]. It can also be spread by vectors, like mosquitoes (Culex and Aedes species). When infected mosquito with FPV bites another chicken, it can transmit the virus to that bird [9].

A presumptive diagnosis of FPV can be made based on observing the gross lesions on the infected body [10]. Confirmation of the cases is also accomplished by microscopic examination for the characteristic bollinger bodies. Virus isolation, serological results and polymerase chain reaction can furthermore be a means of confirming the disease [11].

Characteristic of Fowl Pox Virus

Morphology

The poxvirus genome contains a linear, double-stranded DNA molecule with a molecular size of 130-300 kbp. Fowl pox virus is belongs to Poxviridae family, in genus Avipoxvirus, subfamily of Chordopoxvirinae [12]. The virion involves of an electron--dense centrally located biconcave core or nucleoid with two lateral bodies in each concavity and surrounded by an envelope. The genome molecular size is 288 kbp and encodes about 250 genes [13]. Most of the necessary genes are located in the central part of the genome. The morphology of the FPV is brick shaped and measures about 330 × 280 × 200 nm [14].

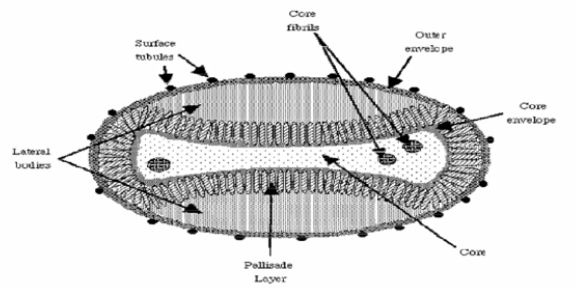

Figure 1: Schematic diagram of FPV

Replication

The replication of FPV occurs in the cytoplasm of the host cell. The virus is adequately complex and acquired all the functions essential for genome replication [15]. Fowl Pox virus gene expression and genome replication occur in enucleated cells, however maturation is blocked [16]. The viral receptors for are not known, but probably more than one on different cell types. Penetration process is complex and may also involve more than one mechanism. Uncoating stage has two step, first there was removal of the outer membrane, as the particle enters the cell and in the cytoplasm, the particle (minus its outer membrane) is additional uncoated and the core passes into the cytoplasm. After adsorption, penetration and uncoating, the virus followed to the bio syntheses of new virus from precursor materials [17].

Replication of the virus begins between 12-24 hours. This is happened basically by viral enzymes associated with the core and is divided into early and late gene phases. Early genes (account 50% of the genome) expressed before genome replication while late genes expressed after genome replication [18]. The incomplete virion then enters the inclusion body vacuole (originated from lipid granules of the cytoplasm) and there by obtains a membrane coat. The possible function of the inclusion body is to afford a precursor material for the lipid coat of the virion [19]. Finally, the Fowl poxvirus released from the cell of by budding process. The additional outer membrane of the virions was also obtained from the cell membrane [20].

Resistance to chemical and physical agents

Fowl pox is extremely resistant to environmental conditions. The virus can resist heat up to 100°C in for 5 minutes. It can also survive drying for several months even at room temperature. It can be conserved for numerous years by freeze-drying [21]. The virus can be destroyed at 60°c in 8 minutes or 35°c in 30-minutes. The keeping of the virus at 0oc-4°c in dried physical hold its availability for 2-years [22]. The virus is inactivated by acetic acid (1%), bichloride mercury, ethyl alcohol 75-95% in 30 minutes [23].

Epidemiology

Distribution

Fowl pox has long been recognized worldwide in chickens and known by distinctive dry, crusty, skin lesions, seen mostly on non-feathered areas of the chickens [24]. Fowl pox virus remains a significant problem for small-scale and backyard flocks, as well as for intensive poultry commercial farming. This infection is still prevalent in many poultry flocks, because the fowl pox virus can remain alive in four up to ten years, which contaminate the environment [25].

In Ethiopia, the FPV, known by local names “Fentata” and common all over the country and considered as major threat for Poultry production [26]. The greater economic loss in poultry production occurred by the disease in the country was due to poor disease prevention and control program [27]. The disease outbreak reported at North Gondar, SNNP, Oromia, Addis Ababa and other part of Ethiopia and caused high morbidity and mortality in chickens [28]. According to the poultry farmers, 19.5% of the cases signs recorded as eye-facial-head disease category were defined and scabby type of wound on featherless body of the chickens. While 27.5% were responded as red brown discoloration and swelling of wattle and comb with deaths observed [29].

Host range

Fowl Pox is viral disease of chickens, turkeys and other birds. The chicken and turkeys are considered as the only natural hosts while the experimental hosts can be any of the avian spices [30]. The existence of FPV infection in pigeons, house sparrows and

doves as experimental animals also reported [31].

Susceptibility

Chickens of all age groups are susceptible with FPV, but common cases observed at age of 3-5 months [32]. The study also observed outbreaks in battery brooded chickens; he also reported the disease in 6-weekes old chicks with lesion on feet and legs. There is also breed differences in susceptibility; chickens with large combs are more susceptible than those with small combs [33].

Pathogenesis

Fowl pox virus enters an epithelial cell and then spread from cell to cell aided by the production of epithelial growth factors which causes proliferation of cells. Some viruses enter the blood and cause viraemia and spread to internal organs [34]. In the chicken inoculated intradermally, the virus was first detected in the skin at the inoculated site on day two post inoculation (PI) and in the lung in day four followed by detectable viraemia on day five. In chickens, infected intratracheally, the virus was first detected in lungs on day two (PI) followed by viraemia on day four (PI) [35]. Following the infection, the virus was detected from liver, spleen, kidney and brain of birds. A virus was also isolated from an air sac and skin of affected birds. At necropsy finding, initially affected birds had cloudy air sacs and patchy pneumonia. Histologically, the lungs had proliferative necrotizing bronchitis [36].

The studies on one day-old chick's inoculation with FPV by the wing – web route, the virus is recovered from the inoculation site two- days (PI); from trachea, heart, thymus, spleen, esophagus, crop and proventriculus, at four days (PI) and from the brain 17 –days PI [37]. Vascular and cellular reactions studies using combination of histological and immunohistochemical techniques in skin induced by FPV showed lymphocytes were identified by staining techniques [38]. In the leukocyte migration test as early as 24 –hours after inoculation, population of neutrophils' and monocytes had been observed, and then they were later replaced by dense accumulation of lymphocytes and mononuclear macrophages forming lymphoid nodules [39].

Transmission

Contact transmission

Fowl Pox Virus can be transmitted by direct contact between infected and susceptible birds. The virus is transmitted through abraded or broken skin or the conjunctiva [40]. The virus is highly resistant to drying and may survive months to years in the dried scabs but sensitive to heat, phenol and other disinfectants [41]. Indirect contact transmission of the FPV can also occur via ingestion when food and water sources, feeders, cages, or clothing are contaminated with virus-containing scabs shed from the lesions of an infected bird. Indirect transmission can also occur via inhalation of FPV infected feather debris and air-borne particles [42].

Vector transmission

Mosquitoes are common mechanical vectors (there is no development of the virus inside the vector) transmitters of this disease. Culexpipiens and Aedesaegypti are capable of transmitting the disease from infected chickens [43]. Fowl pox virus is transmitted when a mosquito feeds on an infected bird that has viremia or when a mosquito feeds on virus-laden secretions seeping from a FPV lesion and then feeds on another bird that is susceptible to that strain of virus. A mosquito that fed on an infected bird is able to keep the virus in her salivary glands for up to 8 weeks [44]. Poultry farms that were heavily infested by fleas there were also transmission of viruses in which fleas may have acted as vectors in transmission of the virus [45].

The time of appearance and magnitude of vector populations varies from year to year, depending on annual weather conditions. This influences the appearance and severity of the disease in any given year [46]. Also some studies stated that incidence of the disease may be highest rainfall months [47].

Economic Significance

Fowl-pox is still an important disease to be considered by poultry farm owner. Mortality from fowl-pox is seldom of economic importance and it is low in healthy flocks but in laying flocks and in chickens in poor condition or under stress the disease may assume serious proportions with mortality rates of 50% or even higher [48]. The mortality rate is also higher in the diphtheritic form than in the cutaneous form, sometimes nearing 50% particularly in young chickens. The high rate of mortality may also occur mainly due to secondary infections caused later to FPV infection [49]. The Morbidity caused by infection of FPV ranged from 10-95%. The most critical loss from an outbreak of FPV is usually the loss of egg production in chickens, and the loss of body weight in chickens. Further, fowl-pox in a flock of breeder turkeys and chickens may cause a marked drop in fertility [50].

Clinical Sign

The incubation period (IP) of the FPV varies from 4-14 days. The course of the disease is usually long, it takes 3-4 weeks, and in case of complication it may prolongs to 8-9-weeks [51]. The disease exists in two forms; cutaneous (dry) and diphtheritic (wet) forms. Both forms may exist at the same time on chickens [52].

Cutaneous or Dry Form

The cutaneous form is the most commonly observed Sign of the disease. This form is characterized by the appearance of cutaneous eruptions or wart like nodules on the unfeathered parts of chicken, (comb wattle, eyelid, feet, cloaca aperture and under the wings) [53]. At first, the nodules appear as small, whitish foci which rapidly increase in size and become yellowish vesicle in color as they develop. The vesicle is a result of the separation of the surface layer of the skin with the formation of pockets of watery fluid rich in multiplying virus. In some instances closely adjoining lesions may merge and the large developing lesions are rough and gray or dark brown in color [54]. After about 2 weeks of development, the lesions may show area of inflammation at their base and become hemorrhagic. The lesion then undergoes a process of desiccation and scar formation which may last for another week or possible two weeks in uncomplicated cases the process ends with desquamation of the degenerated parts of the epithelial layer [55].

If the dry scab is removed, a moist sero-purulent exudate is found underneath, covering a bleeding, granulating surface. The specific process is often modified by the invasion of bacteria which propagate in the degenerated epithelium and may reach the deeper layer of mucous membrane where they catalyze necrotic processes with the formation of fibrinous deposits.

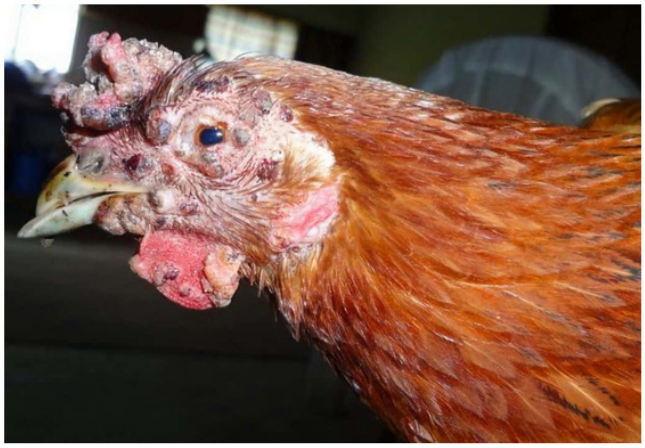

Figure 2: Dry form of FPV lesion [56]

Diphtheritic or Wet form

This type is not as common as the cutaneous form. The slightly elevated nodules begin on the mucous membrane of the mouth, oesophagus, larynx or trachea as white and opaque. These processes rapidly increase in size, often coalescing to become a yellowish, cheesy, necrotic material with the appearance of a pseudo membrane [57]. Diphtheritic membrane forms and may restrict air intake and result in labored breathing and possible suffocation. For this reason, the mortality rate is higher in the diphtheritic form than in the cutaneous form.

Figure 3: Diphtheritic form of FPV [58]

Diagnosis

Clinical diagnosis

Clinical features of infected chickens show multiple skin lesions varying from papules to vesicles on unfeathered part of body. Gross lesions in both the cutaneous and the diphtheritic forms, seen on live chickens and during necropsy, are usually sufficient to suspect FPV infection [59]. However, these signs are sometimes not sufficient for definitive diagnoses of FPV infection as other agents, such as papilloma virus and scaly leg mites show signs resemble to cutaneous form of the infection [60]. In addition to the above cases, mycotoxins may produce similar lesions in the skin [61]. A condition like candidiasis may give lesions in the oral cavity similar to the diphtheritic form of FPV infection. Infectious laryngotracheitis characterized by the presence of intranuclear inclusion bodies which is caused by a herpes virus also affect trachea of infected chickens should differentiated

from the diphtheritic form of FPV. It is therefore, crucial to secure samples and confirm the viral etiology of the condition [62].

Laboratory diagnosis

Microscopic examination

Fowl pox virus multiplies in the cytoplasm of epithelial cells with the formation of large intracytoplasmic inclusion bodies (Bollinger bodies) that contain smaller elementary bodies (Borrel bodies) [63]. The inclusions can be demonstrated in sections of cutaneous and diphtheritic lesions by the use of haematoxylin and eosin (HE), acridine orange or giemsa stains. The elementary bodies can be detected in smears from lesions, for example by the gimenez method, it conducted by the following procedures [64].

For smear preparation, place a drop of distilled water and the lesion (cutaneous or diphtheritic) on a clean slide. Then, prepare a thin smear by pressing the lesion with another clean slide and rotating the upper slide several times. Air dry and gently fix the smear over a flame. Stain the smear for 5–10 minutes with freshly prepared primary stain (8 ml stock solution of basic fuchsin mixed with 10 ml of phosphate buffer3, pH 7.5, and filtered through Whatman filter paper No. 1.). Wash thoroughly with tap water. Counterstain with malachite green (0.8% in distilled water) for 30–60 seconds. Wash the smear with tap water and then dry. Examine the smear under oil immersion. The elementary bodies appear red and are approximately 0.2–0.3 μm in size [65].

Transmission electron microscopy (TEM) may also reveal definite proof of FPV infection, by demonstrating the typical poxvirus morphology in infected bodies. FPV identification carried out by negative staining electron microscopy with 2% phosphor-tungstic acid (PTA) on infected cells [66].

Virus Isolation

Fowl pox virus can be isolated by inoculation clinical samples into embryonated chicken eggs or in cell cultures of avian origin [67]. Approximately 0.1 ml of tissue suspension of skin or diphtheritic lesions, treated with the appropriate concentration of antibiotics, is inoculated on to the chorioallantoic membranes (CAMs) of 9- to 12-day-old developing chicken embryos. Following inoculation of the embryos with the contamination free sample the eggs are incubated at 37°C for 5–7 days, and then examined for focal white pock lesions or generalized thickening of the CAMs [68]. Another method of isolation of FPV requires the excision and homogenization of clinical samples and inoculation of a homogenate supernatant onto a permissive cell culture, such as chicken embryo fibroblasts, chicken embryo kidney cells, chicken embryo dermis cells, or the permanent quail cell line (QT-35). The infection of FPV is confirmed by observing formation of CPE within 4-6 days post inoculation [69].

Serological Tests

Cell-mediated immunity (CMI) and humoral immunity play an important role in FPV infections and routine use of the CMI test is not convenient. Therefore, serological tests, such as virus neutralisation (VN), agar gel immunodiffusion (AGID), passive haemagglutination and fluorescent antibody tests as well as the Enzyme-Linked Immunosorbent Assay (ELISA), are used to measure specific humoral antibody responses against FPV [70]. The tests are time consuming, especially when carried out with large numbers of sera, and sensitivity appears to be low except ELISA test [71]. There are six closely related strains of avipoxvirus namely fowl pox, pigeon pox, quail pox, canary pox, psittacine pox, and ratite pox viruses [72]. Avian poxviruses are antigenically and serologically distinguishable from each other, although there is cross-relationship. This cross reactivity was observed passive haemagglutination and agar gel immunodiffusion [73].

Agar-Gel Immunodiffusion test: is a technique in which precipitating antibodies can be detected by reacting test sera against viral antigens. The antigen can be obtained by homogenisation of infected skin or CAM lesions as well infected cell cultures. The

lysed suspension is centrifuged and the supernatant is used as antigen. Gel-diffusion medium is prepared with 1% agar, 8% sodium chloride and 0.01% thiomersol. The viral antigen is placed in the central well and the test sera are placed in the peripheral wells [74]. It is important to include a positive and negative control serum. The plates are incubated at room temperature. Precipitation lines develop in 24–48 hours after incubation of the antigen with antibody. The test is less sensitive than the ELISA) [71]. In case of Passive Haemagglutination test, tanned sheep or horse red blood cells are sensitised with a partially purified fowl pox viral antigen prepared from infected CAMs or cells and incubated with biological samples to detect the presence of corresponding antibodies [75].

Virus Neutralisation test (VNT): This test done after virus or serum interaction, the residual virus activity may be assayed in embryonating chicken eggs or in cell cultures [76]. The assay detects antibody that is capable of inhibiting virus replication or in other words, antibody that can neutralize virus infection. VNT is a specialized type of immunoassay because it does not detect all antigen–antibody reactions. It only detects antibody that can block virus replication. This is significant because related groups of viruses may share common antigens, but only a fraction of these antigens are targets of neutralizing antibody [77]. Neutralizing antibodies develop within 1–2 weeks of FPV infection [78].

Immunoperoxidase test: This one also be conducted for conformation and specific staining of cytoplasmic inclusions is achieved, when horseradish-peroxidase-conjugated specific polyclonal antibody against fowl poxvirus is reacted with the hydrated sections of fowl pox-infected fixed tissues (CAM and skin) or cell culture [79]. The presence of the enzyme conjugate bound to the virus-infected cells is detected by adding a substrate, such as diaminobenzidine or aminoethylcarbazole, then oxidizing it in the presence of hydrogen peroxide which results in a reddish-brown color. The reaction is observed using a light microscope or naked eye [80].

Immunofluorescence antibody test: Is used to reveal specific intracytoplasmic fluorescence in infected cells. This test is commonly used and involves two steps: the antibody against fowl pox virus is reacted with the antigen in the infected cells, followed by a secondary fluorescein-isothiocyanate-labelled antibody against chicken gamma globulin (e.g. goat anti-chicken) [81].

ELISA test: Has been also developed to detect humoral antibodies to fowl pox virus. They are capable of detecting antibody 7–10 days after infection, but commercial kits for this test are not available [82]. ELISA is a faster and easier method to detect antibodies against FPV with high sensitivity, particularly when large numbers of sera are to be tested [83].

Molecular techniques

Diagnosis of FPV infections is conducted by demonstrating the presence of the virus in infected tissue samples, by microscopic examination or by serological assay. Demonstration of the virus in tissue samples can also carried out by isolation in cell cultures or in embryonated chicken eggs. These approaches of diagnosis were costly and consume time [84]. Recently, the hybridization of products obtained by the polymerase chain reaction (PCR) has been described the newly developed techniques for diagnosis of the FPV infection [85]. This technique is based on the enzymatic amplification of a part of the viral genome by means of thermostable DNA polymerase using specific primer [86]. A primer was used by PCR for the detection of FPV infection is 4b gene sequence of the FPV strain HP44 [87]. By repeated cycles of denaturation, annealing and extension it is possible to amplify specific parts of DNA so that a few copies of DNA fragment accumulate to microgram quantities which can then be readily visualized in gels electrophoresis running. The sensitivity and specificity can be enhanced further by hybridization after southern transfers [88]. Restriction endonuclease analysis also is a useful method for comparing closely related DNA genomes and can be used for comparison of field isolates and vaccine strains of fowl pox virus [89].

Prevention and Control

Vaccination

Fowl-pox vaccination when properly carried out has proved highly successful in protecting chickens from the FPV. The vaccination should have no protection for a bird on which fowl-pox lesions have started to develop [90]. There are two kinds of pox vaccines that are available for poultry which are pigeon-pox vaccine and fowl-pox vaccine. Fowl-pox vaccine is the type that is almost universally used [91]. The length of immunity following the use of pigeon-pox vaccine on chickens and turkeys is so short (below six month) for such reason this type of vaccine is not recommended. However, in case of fowl pox vaccine the length of immunity is long and stays for 6-12months and which is commonly used as prophylaxis against the FPV [92]. The fowl-pox vaccine is produced in two different ways. The virus may be propagated on the chorioallantoic membranes of a growing chick embryo or cell culture of avian origin [93].

Bio-security based prevention

Biosecurity based plan to prevent the entry of FPV agent onto a farm is necessary to minimize the disease impacts. This prevention strategy for fowl pox virus includes regulating vector transmission at the farm by controlling mosquitoes and other vector population by using chemicals or avoiding the stagnant water around the farm [94]. Farm disinfection is also a critical part on the preventing the spread of the FPV. It must be done correctly to kill disease organisms. This would include washing the farm and area around the poultry houses thoroughly. This is followed by applying the disinfectant according the recommendations of the manufacturer [95]. Finally, the house needs to remain empty for 2- 3 weeks prior to reintroducing chickens and the feed that remained from the previous flocks must never be re used [96].

Outbreak control

During disease outbreak, affected bird should be segregated immediately and the remaining birds must be vaccinated at earliest possible [97]. As in most viral infections, there is no specific treatment for FPV infections in birds. Available treatments include the use of iodine-glycerin application on proliferating skin lesions to aid healing and antibiotics to control secondary bacterial infections [98].

Conclusion

Fowl pox virus categorized under Poxviridae family, in genus Avipoxvirus, subfamily of Chordopoxvirinae. The virus genome contains a linear, double-stranded DNA molecule with a molecular size of 130-300 kbp. The virus causes disease of economic importance for the poultry industry, and wild birds. The virus is adequately complex and acquired all the functions essential for genome replication. The virus can resist heat up and can also survive drying for several months even at room temperature. Fowl pox virus remains a significant problem for poultry commercial farming and can remain alive in four up to ten years, which contaminate the environment and cause mortality and morbidity in chickens. The virus because huge economic loss and this prevented by vaccination when properly carried out has proved highly successful in protecting chickens from the disease.

List of Abbreviations

CAMs Chorioallantoic Membranes

CFC Chicken Fibro Blast Cell

DNA Deoxyribonucleic Acid

ELISA Enzyme Linked Immune Sorbent Assay

FPV Fowl Pox Virus

Kbp Kilo Base Pairs

OD Optically Density

OIE Office of International des Epizootics

PBS Phosphate Buffered Saline

PCR Polymerase Chain Reaction

PI Post Inoculation

VNT Virus Neutralization Test

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