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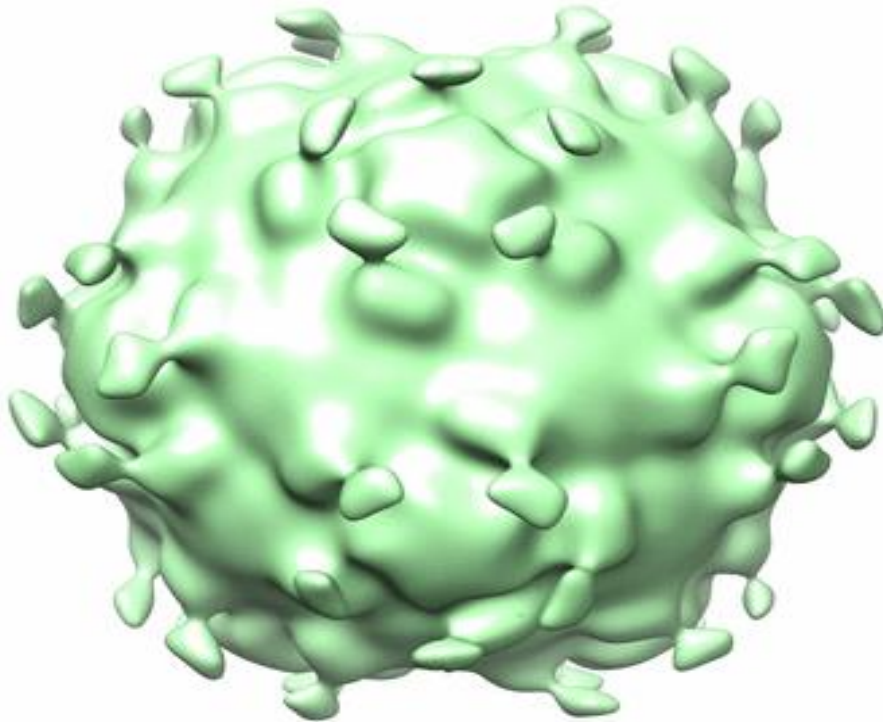
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نورة الدوسري

بحث من متطلبات مقرر (حق 450)

"Poliomyelitis"



Introduction

Poliomyelitis is a viral disease. it effects primarily children under the age of five years Near the beginning of the 20th century epidemics of the acute central nervous system disease known as poliomyelitis began to occur in the United States and Europe. These outbreaks came as a surprise to the medical community, which viewed the disease as a rarity. The causative agent of this disease, poliomyelitis virus (later shortened to poliovirus) was identified in 1908. Research on the virus over the next 40 years provided information on antigenic types, pathogenesis, and immunity that ultimately lead to the development of two effective vaccines. A consequence of the introduction of these vaccines in the early 1960s was that investigation of

the pathogenesis of poliomyelitis ceased. Instead, studies on the molecular biology, structure, and genetics of poliovirus flourished. The identification of the cell receptor for poliovirus allowed the development of transgenic mice susceptible to poliovirus, an advance that revived interest in understanding how the virus causes disease. Work on poliovirus pathogenesis is now done with a sense of urgency as global eradication of polio approaches. There are three types of poliovirus and many strains of each type. The virus enters through the mouth and multiplies in the throat and gastrointestinal tract, then moves into the bloodstream and is carried to the central nervous system where it replicates and destroys the motor neuron cells. Motor neurons control the muscles for swallowing, circulation, respiration, and the trunk, arms, and legs. Human nerve cells have a protruding protein structure on their surface whose precise function is unknown. When poliovirus encounters the nerve cells, the protruding receptors attach to the virus particle, and infection begins. Once inside the cell, the virus hijacks the cell's assembly process, and makes thousands of copies of itself in hours. The virus kills the cell and then spreads to infect other cells.

Classification of poliovirus

Poliovirus is classified as an:

Genus : (enterovirus) within **family**: (*Picornaviridae*) , a family that contains many human and animal pathogens. All three serotypes of poliovirus cause paralytic disease.

Species: (poliovirus)

Structure of genome

The virus is composed of an ssRNA genome and protein capsule

Types : three types : PV1 ,PV2 ,PV3 .

Differentiated by the type of capsid protein .

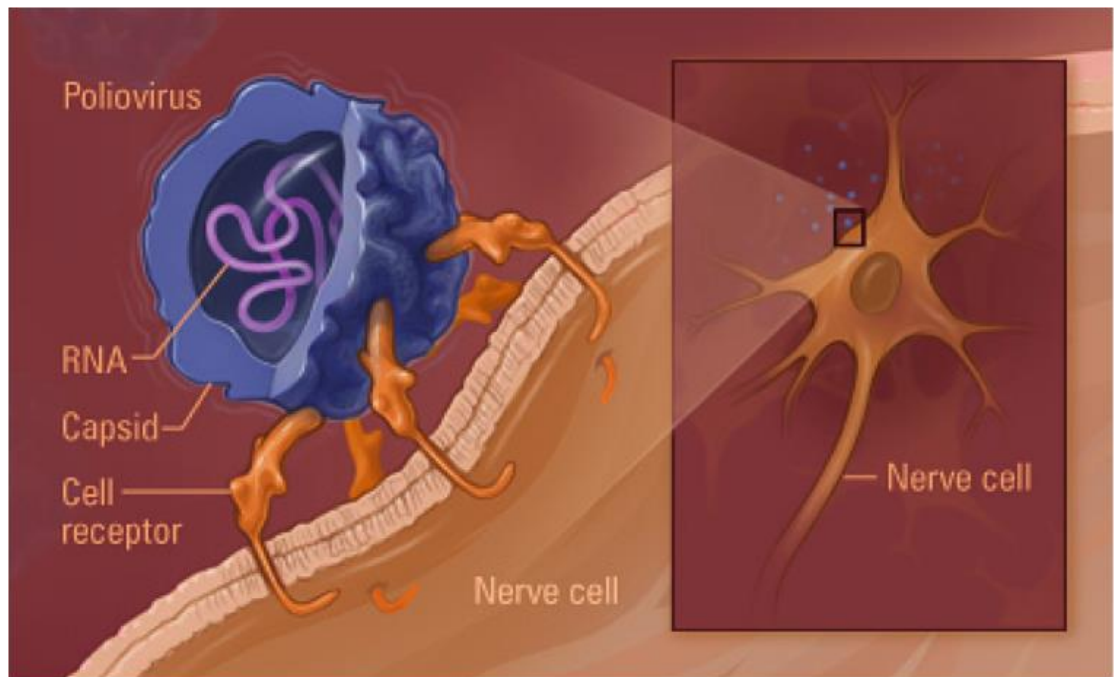
PV1 is most common encountered from &the one most commonly associated with the paralysis .

Size : 30 nm diameter .

The viral genome, a single-stranded,positive-sense (+)-strand RNA approximately 7500 nucleotides in length, is enclosed in a nonenveloped capsid comprising 60 copies of four different polypeptides arranged with icosahedral symmetry.

- Often called the simplest significant virus- first isolated in 1909 by karl Landsteiner and Erwin popper .

- Egyptian paintings depicted the effects of polio by showing otherwise healthy individuals with withered limbs .



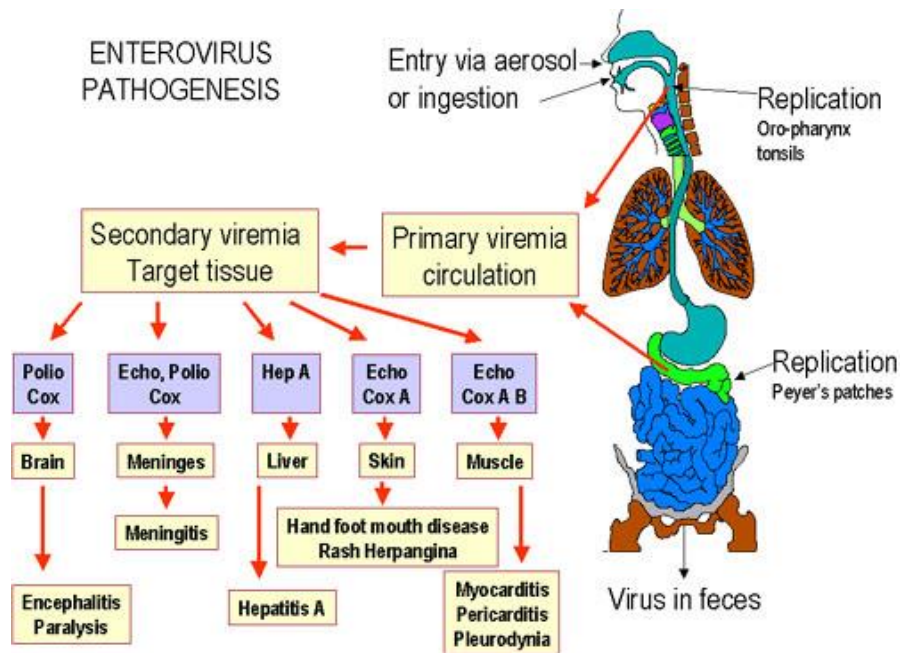
Pathogenesis

1-The virus enters through the mouth, and primary multiplication of the virus occurs at the site of implantation in the pharynx and gastrointestinal tract.

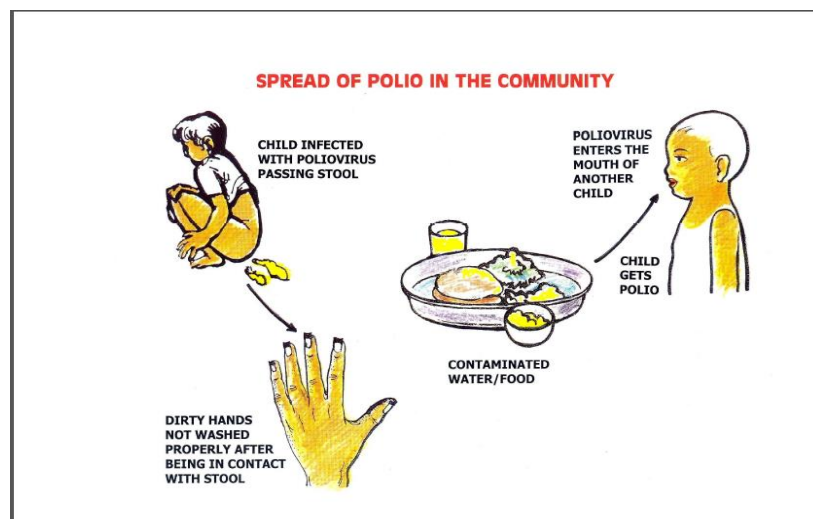
The virus is usually present in the throat and in the stool before the onset of illness.

One week after onset there is less virus in the throat, but virus continues to be excreted in the stool for several weeks.

The virus invades local lymphoid tissue, enters the bloodstream, and then may infect cells of the central nervous system. Replication of poliovirus in motor neurons of the anterior horn and brain stem results in cell destruction and causes the typical manifestations of poliomyelitis.



Transmission: Intimate contact with infected persons. Where sanitation is good, oral-oral, and respiratory may be more important than fecal-oral spread; it rarely occurs through milk and water where good sanitary conditions prevail. Transmission from mother to newborn has been reported. Immunodeficient patients may excrete virus for prolonged periods. In temperate climates, poliovirus infections are most common in the summer and fall.



Protomer of poliovirus capsid

The capsid of poliovirus is made up of 60 subunits which contain four protein chains each. Shown here is one subunit (or protomer) containing:

VP1 (302 amino acids)

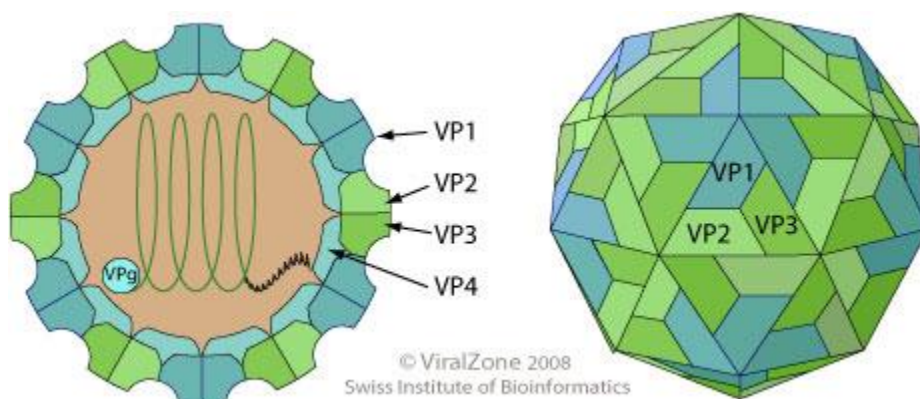
VP2 (272 amino acids)

VP3 (238 amino acids)

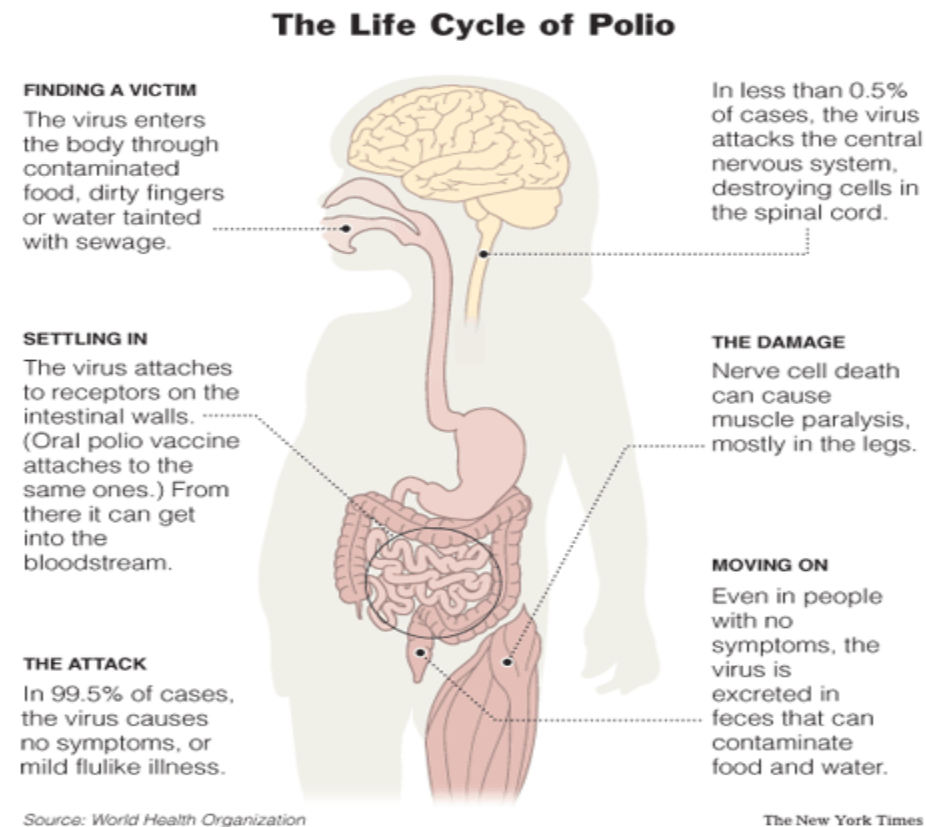
VP4 (68 amino acids)

Note a gap in **VP1** between amino acids 10 and 20. Residues 11-19 could not be modelled because of too great mobility in the viral crystal (this holds for some other terminal residues, too). Inserted into **VP1** is a hydrophobic molecule (modelled here as palmitic acid), which is assigned some role in interaction with the virus receptor and subsequent uncoating of the particle. This molecule is surrounded by hydrophobic amino acids mainly from **VP1** and the neighboring **VP1**. **VP4** is synthesized along with **VP2** and cleaved off only when the complex (VP0) is inserted into the capsid. The PDB entry notes the myristyl residue at the amino terminus of VP4 as #1.

The choice of which viral proteins constitute a protomer is somewhat arbitrary and made here in analogy to plant viruses with similar structure. The atomic structure data are deposited in the PDB in the configuration shown here. One 5-fold axis is placed north and one 3-fold Axis to the south. However, you might as well choose the 'road map'-view by selecting the right hand side **VP3**.



Replication cycle:

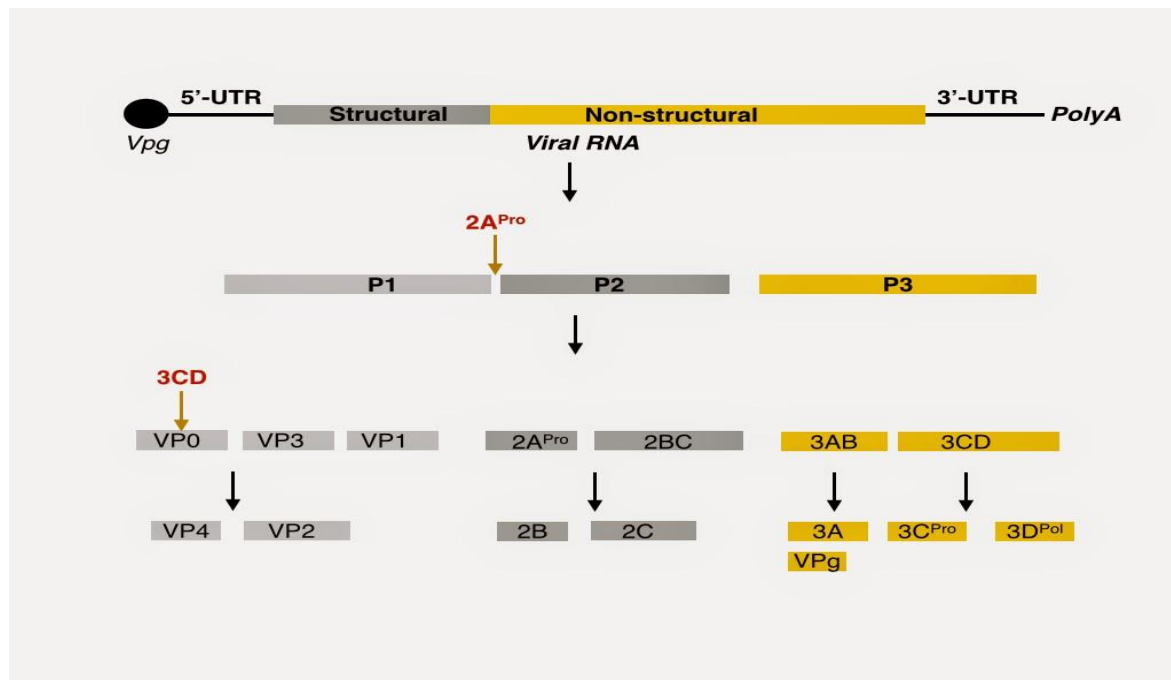


(<https://www.youtube.com/watch?v=hzpBBWiuItc>) video

Assembly and egression:

Poliovirus (PV) mRNA has a long 5 nontranslated region (5 NTR) without a 5 cap. A cloverleaf RNA structure at the 5 terminus of PV mRNA forms ribonucleoprotein (RNP) complexes with poly(rC) binding proteins (PCBPs) and with viral protein 3CD. A C24A mutation in the 5 cloverleaf inhibits the binding of PCBP and renders PV mRNA susceptible to degradation by 5' exonuclease. An internal ribosome entry site (IRES) within the 5 NTR of PV mRNA requires eukaryotic initiation factor 4G (eIF4G) to mediate translation initiation, and accumulating evidence indicates that eIF4G likely interacts directly with the IRES. PV 2A protease (2APro) expression during the course of PV mRNA translation leads to the cleavage of eIF4GI and eIF4GII. Cleavage of eIF4Gs by 2APro prevents cap-dependent host mRNA translation and thereby contributes to the conversion of host mRNA polysomes to predominantly viral mRNA polysomes in infected cells. Cleavage of eIF4Gs by 2APro may abrogate some RNA-protein-protein-RNA bridges

between the 5 and 3 termini of mRNAs while leaving intact other potential RNA-protein-protein-RNA bridges . In addition to interactions with the 5' cloverleaf, PCBP_s interact with stem-loop 4 of the PV IRES to mediate the initiation of translation .PCBP_s may also contribute to RNA-protein-protein-RNA bridges between the 5 and 3 termini of PV mRNA



(<https://www.youtube.com/watch?v=9zYuppTdBKw>) video

Symptoms:

polio viral disease invades the nervous system, and can cause total paralysis in a matter of hours of time

The initial symptoms of the disease in fever, fatigue, headache, vomiting, stiff neck and pain in the extremities

These symptoms may be mild, so it is difficult for the doctor diagnosed as polio, but severe injuries it may same as the previous symptoms but are Atakhtvi, starts stiffness in the muscles of the back and neck and become weak muscles and movement difficult. The pain occurs in both the back and legs, especially if you become Members of this tight or lying. the man is unable to stand or walk if it managed to Parkinson's disease



DAIOGNOSIS AND CYTOPATHIC EFFECT:

Laboratory Diagnosis:

The laboratory diagnosis of polio is made by isolation of the polio virus from stool, throat specimens, urine or CSF (rare). Stool cultures are most likely to yield the organism. Acute and convalescent serologic tests can be done, but may be difficult to interpret because the rise in titer may occur prior to paralysis. (Washington State Department of Health-2011)

The current method of diagnosis is polymerase chain reaction (PCR) for detection of poliovirus, which can be isolated from samples of stool, throat swabs, blood, and cerebrospinal fluid (CSF). Stool samples of the infected person are the primary sample source. The virus is excreted intermittently for a long period of 1 to 2 months after infection. In all, 80% of exposed people excrete the virus in the first 2 weeks, which declines to around 25% in the third week. Therefore, 2 samples of stool must be collected ideally at an interval of 24 hours within 2 weeks' time for maximizing the chances of isolation of virus.¹¹ Presence of the virus in

the oropharynx is usually early in the infection. The virus can rarely be isolated from CSF in cases of aseptic meningitis. During first phase of viremia (3-5 days after infection), virus can be isolated from blood, but it is not of diagnostic importance.

Cell Culture

Initially the virus was cultivated in Rhesus and Cyanomolgus monkey cell lines, but these methods are not preferred now. At present, human cell lines like human amnion cell line and human embryo cell line are generally preferred methods. In India, polio laboratories work on RD cell line, which is derived from human rhabdomyosarcoma and L20B cell line, which are very specific for poliovirus. Virus growth is determined by its cytopathic effect on the cell lines. This usually occurs within 7 days of inoculation. If the cytopathic changes are seen only in RD cell line, inoculation is done in L20B cell line to confirm poliovirus. The isolate is then subjected to neutralization tests using specific antisera for serotyping. Tests are also done to confirm whether the isolate is a wild strain or a vaccine-derived one. These tests are called intratypic differentiation tests. These are either based on the principle of enzyme-linked immunosorbent assay or based on the hybridization techniques.

Serology

A 4-fold rise in antibody titer is essential for confirmation of the infection. Neutralizing antibodies appear very early in the disease process and persist for life.

Molecular Methods

Samples like CSF and serum give a poor yield of virus in culture. In addition, cell culture is technically laborious and time consuming. These

challenges have been addressed by the addition of PCR in the armamentarium of diagnostic tests. It has revolutionized the isolation of poliovirus. Polio-specific PCR primers have been designed, which help in the isolation of the virus.

Genetic sequencing of the virus is essential to determine its origin and mode of transmission in cases of outbreak. When the world today stands on the brink of polio eradication, immediate identification of the genome of the outbreak isolate is imperative. Whether it is a recirculating strain or an imported one, the knowledge will help in curbing transmission.(T. Jacob John -2014)

CNTROLIN THE VIRUS:



Management:

In the earlier times, when the epidemics of polio were frequent, there was absolute lack of knowledge regarding the management aspects of this crippling disease. Acute cases required immediate relief from pain, and rehabilitation was a challenge for chronic cases with deformities. Various strategies to manage these cases were in vogue at that time. A lot of experimentation was also involved. One of the earliest descriptions

regarding management strategies of polio is the heroic work of Sister Elizabeth Kenny (an Australian nurse). She used hot packs to relieve muscle spasms in early stages of the disease and discouraged the practice of prolonged immobilization of affected limbs. A large number of patients were benefited.

The first modern rehabilitation center dedicated to patients with polio was set in 1926 by President Franklin Theodore Roosevelt in the United States .

Later, new inventions were introduced to offer relief to the sick patients. One such instrument was the Iron Lung Machine. It was used in patients with respiratory paralysis to prolong their lives by assisted respiration. The drawbacks were the mammoth size, technical adjustments, and cost factor.

Modern medicine has contributed tremendously to the management of polio. In the recovery stage, remedial exercises are prescribed to assist the paralyzed muscles. Appropriate orthotic devices have been designed to prevent deformities due to muscle imbalance. Various sessions of intense physiotherapy are necessary for rehabilitation and recovery. Surgical management includes tendon transplant, contracture relieving surgeries, and joint replacement surgeries. Ilizarov technique, an orthopedic technique used to stabilize and rehabilitate the limb has also been now increasingly used for correction of deformities. .(T. Jacob John -2014)

Management of a Case:

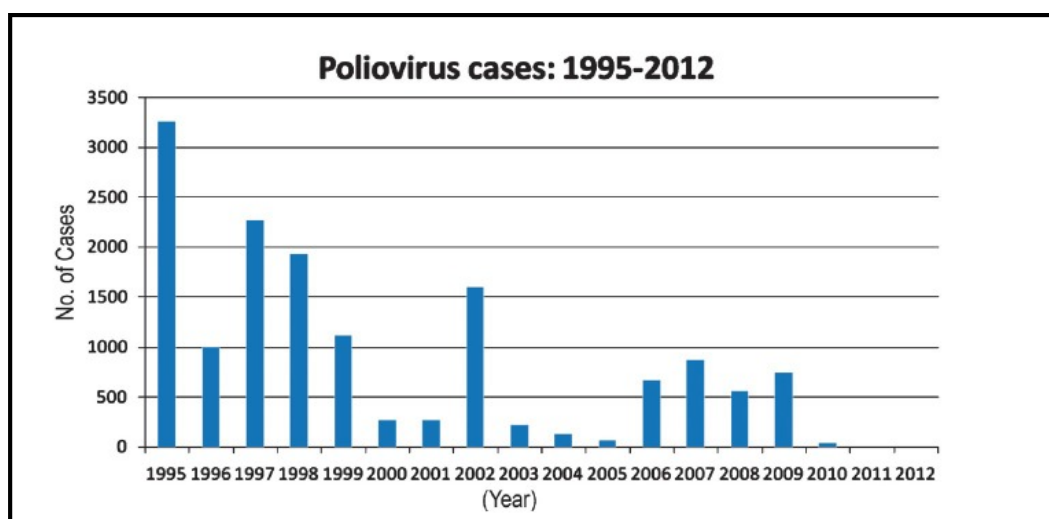
1*Isolation with routine practices and contact precautions for hospitalized patients .

3* Household measures are felt to be of little use since the infection has usually spread by the time the first case is suspected. It is still important, however, to implement routine practices and contact precautions.

3* Throat discharges, feces, and contaminated articles should be handled using routine practices and contact precautions. In areas where there is modern sewage disposal, feces and urine can be discharged directly into the sewers. (Alberta Health and Wellness-2011)

RESEARCH COVERES :

1*epidemiology of the poliovirus in INDIA:



In 2003, the ‘under-served strategy’ was introduced as part of better communication efforts in Uttar Pradesh to reach out to and get support of marginalized sections of the society especially those living in poor Muslim communities, lacking access to basic sanitary and healthcare services, and were often missed in tOPV rounds, and thus were more likely to receive fewer doses⁶¹. The strategy was aimed at engaging universities, religious leaders and groups, local associations and individuals from underserved Muslim communities to broaden ownership

and accountability for polio eradication. An improvement in poliovirus surveillance quality was seen in 2004.

The extremely poor efficacy of OPV - 'failure of vaccine' - permitted WPV transmission in western U P and in Bihar in spite of high tOPV coverage. Thus, >95 per cent of children with polio had earlier received at least four tOPV doses.

There was a polio outbreak in 2006, with 648 cases of type 1 and 28 of type 3, again most cases occurring in UP and Bihar. The population immunity gap was found primarily in infants and very young children (<2 yr) due to very low UIP coverage with tOPV and insufficient opportunities to receive mOPV1 in pulse campaigns . To compensate for low routine coverage, the PPI campaigns had been increased to 10 per year, and neonates and very young infants were specially targeted.

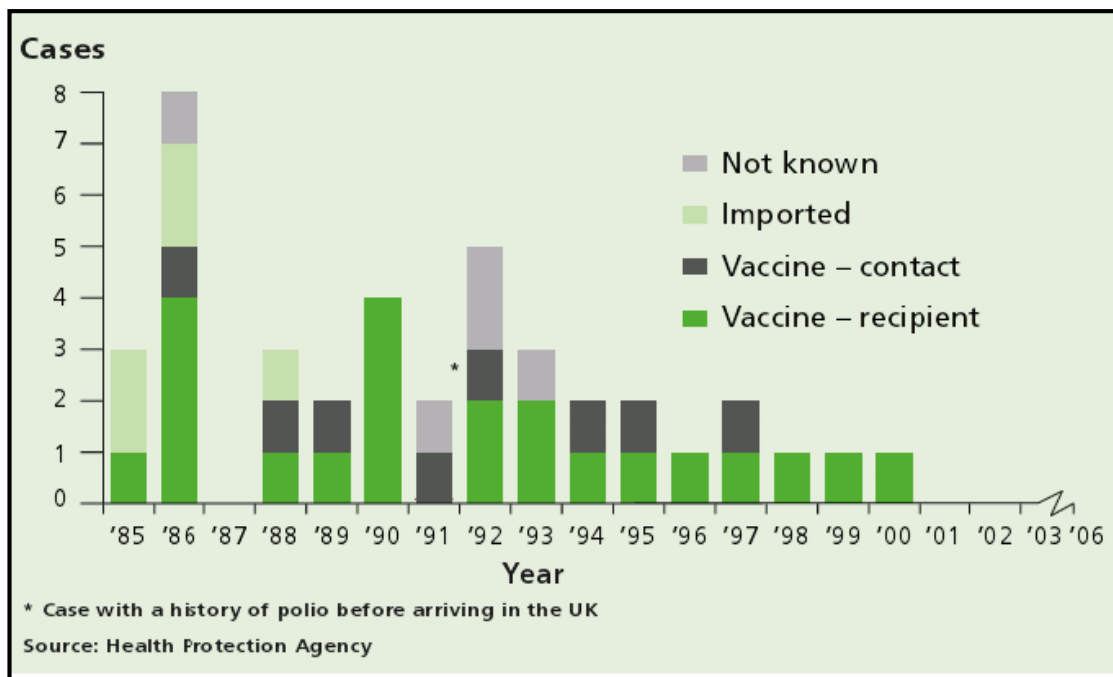
In 2008, Kosi River bank communities in Bihar were identified as a key reservoir of WPVs Plan was drawn up to intensify and focus efforts in Kosi River areas. High-risk blocks were mapped, and additional stay points built for enhanced supervision and efforts in the hardest-to-reach areas where children were being missed .

As no WPV was identified throughout the high-transmission season in 2012, India is regarded as free of WPV polio. This places the WHO SEA Region, of which India is a member, on track to be certified polio-free as early as 2014. Certification of polio eradication occurs at three levels.

The National Certification Committee will collect all relevant documentation not only to confirm the absence of WPV circulation but also to ensure that no laboratory is keeping any clinical specimen likely to contain poliovirus or any past laboratory virus isolate or virus stock for research or diagnostic studies. India has a mechanism to ensure such laboratory containment under the ICMR. WHO does not certify individual countries but a Region. The SEA Regional Certification Committee will review all information and will consider certification after three consecutive years have passed from the very last WPV isolate in the region (January 13, 2011). Therefore, we may expect Regional Certification some time after January 2014. Once that happens SEA Region joins the other already certified Regions, (Pan American, Western Pacific and European). Eastern Mediterranean Region (with Afghanistan and Pakistan) and African region (with Nigeria) will remain to achieve WPV elimination and certification, hopefully in 2015 or 2016. Only after all Regions are so certified will the Global Certification Committee recommend to WHO to declare the world free of WPVs.(T. Jacob John and Vipin M. Vashishtha-2013)

2*epidemiology of the poliovirus in UK:

During the early 1950s, there were epidemics of poliomyelitis infections with as many as 8000 annual notifications of paralytic poliomyelitis in the UK.



Until 2004, OPV was used for routine immunisation in the UK because of the continuing risk of importation of wild virus. Both OPV and IPV provide excellent individual immunity. In addition, OPV provides community benefit as contacts of recently immunised children could be protected through acquisition of vaccine virus. OPV also promotes antibody formation in the gut, providing local resistance to subsequent infection with wild poliomyelitis virus. This reduces the frequency of symptomless excretion of wild viruses. The risks of wild polio virus being imported and the benefits of OPV need to be balanced against the risks of VAPP from OPV use and the efficacy of IPV. Since 2004, this balance favours the use of inactivated polio vaccine for routine immunisation in the UK. (Green Book Chapter 26 v2_0 -2013)

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