

VIRUS-INDUCED DISEASES

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Summary

Virus-induced diseases affect a wide range of living organisms, ranging from microorganisms to humans. Examples are offered of diseases caused by viruses that infect plants, animals, and humans. Some viruses affect humans directly, whereas others affect humans indirectly. Examples of viruses affecting humans directly are smallpox, measles, rubella, mumps, varicella-zoster, hepatitis A, B, C, and D. Some of the virus-induced diseases have available vaccines, while others do not. Examples are provided of virus-induced cancers, as well as insect-borne viral disease. The Bibliography provides references to information that is electronically accessible.

1. Introduction

Viruses are the smallest infectious agents (20-300 nm in diameter), containing only one kind of nucleic acid (RNA or DNA) in their genome. Viruses are inert in extra-cellular environments (outside a living cell). They can only replicate in the living cell, as they are parasites at the genetic level. The host range for a given virus may be broad or extremely limited. Viruses are known to infect unicellular organisms, such as mycoplasmas, bacteria and algae and all higher plants and animals.

From a broad perspective, there are virus-induced diseases that affect humans directly as well as indirectly. Examples are provided, with references for an in-depth study of this vast area. The following examples have been selected in order to identify particular state-of-the-art strategies affecting life support systems.

2. Viruses Which Affect Humans Indirectly

One example of virus-induced disease, which has a broad economic impact, concerns the overpopulation of rabbits, especially in Australia where crops have been extensively destroyed. Efforts to control the rabbit population have included the transmission of myxoma virus or more recently calicivirus to eliminate the rabbits. Certain viruses are extremely species specific, for example, rabbit calicivirus which causes rabbit calicivirus disease (RCD) in European rabbits and in domestic strains derived from this species (*Oryctolagus cuniculus*) in over 40 countries throughout the world.

It is nonpathogenic to humans and other domestic animals. RCD causes rapid development of blood clots in major organs such as heart, lungs and kidneys. These clots block blood vessels and result in death from heart and respiratory failure. Calicivirus has been successfully used to control rabbits in Australia, which cause extensive damage to crops. This form of pest control, which uses one organism to control the number of another, is called biological control.

Another good example of biological control is the use of a bio-engineered virus to destroy the fungus that causes chestnut blight in chestnut trees whose growth has been almost completely eliminated by the fungus in the Appalachian region of the United States. Current strategies include the dissemination of bio-engineered viruses to destroy the fungus, in the hope that there will be re-growth of economically important chestnut trees.

3. Viruses Affecting Humans Directly

Virus-induced diseases affecting humans encompass an enormous variety of agents that cause a spectrum of diseases. Examples follow of diseases that are amenable to control by vaccine strategies, and some others that have escaped such strategies until now.

3.1. Virus Induced Diseases Which Have Useful Vaccines

3.1.1. Smallpox

Smallpox has been eradicated globally since 1975 through the use of vaccinia virus administered intradermally. The World Health Organization (WHO) campaign to eradicate smallpox started in 1967, and the last Asiatic case was reported in Bangladesh in 1975; the last natural victim was reported in Somalia in 1977, and the WHO officially declared that smallpox had been eradicated in 1980.

Another example of a virus-induced disease that can be eliminated through the use of a vaccine is poliomyelitis caused by poliovirus, which is an RNA virus classified as an enterovirus, and which is transmitted through the fecal-oral route. Poliomyelitis is an acute infectious disease that in its serious form affects the central nervous system. The destruction of motor neurons in the spinal cord causes flaccid paralysis, however, most Poliovirus infections are sub-clinical. In 1988, the WHO established a target to eradicate polio by the year 2000 by using Salk formalin inactivated vaccine and Sabin live attenuated vaccine. Current WHO guidelines recommend the use of the Salk vaccine administered intramuscularly, followed by the trivalent Sabin vaccine administered orally.

3.1.2. Measles

Measles (rubella) is an acute, highly infectious disease caused by the measles virus which is an RNA virus belonging to the paramyxoviridae family. The initial infection is clinically silent. The prodromal phase begins after an incubation period of 8 to 12 days, and is characterized by fever, runny nose, sneezing, conjunctivitis (eyes that are red and sensitive to light), and hacking cough. The risk of infecting others is highest during the prodromal phase.

Two to three days before the onset of a rash, koplik spots (the characteristic feature of measles) appear inside the mouth. These are small red, irregular spots with blue-white centers. The rash begins three to four days after the prodromal symptoms. Once the rash develops, the prodromal symptoms disappear, except for the cough. The rash typically begins on the forehead at the hairline behind the ears, and on the upper part of the neck, and then spreads downwards until it reaches the feet.

The rash begins to fade by the third day in the same order in which it appeared, and vanishes in about 14 days. Complications are common with measles, and may be quite serious. The most common complications of measles include otitis media (middle ear infection), pneumonia and encephalitis. Pneumonia is the most frequent, life-threatening complication of measles. Pneumonia is more common in young children, whereas encephalitis is more common in adolescents and young adults. Acute post infectious measles encephalomyelitis is the most common neurologic complication of measles. A

second form of measles encephalitis, subacute sclerosing panencephalitis is a rare and delayed complication of measles, that occurs in about 1 in 300 000 cases. Measles is an important cause of blindness in developing countries. The eye lesions of measles are usually self-limited, but in malnourished children with vitamin A deficiency, they may progress to corneal ulceration and blindness. Recovery from a natural infection confers lifelong immunity. The incidence of measles has been dramatically reduced in the USA and other developed countries through the use of a live attenuated vaccine. The vaccine is given as a part of measles, mumps, rubella cocktail (MMR), with one dose given at the age of 15 months and a second at the age of 11-12 years; nevertheless, measles is still a leading disease of young children in many developing countries.

3.1.3. Rubella

Rubella (German measles, 3-day measles) is an acute illness characterized by low fever, rash, joint aches, swollen glands, especially behind the ears and in the back of the neck, that affects children and young adults. Rubella is caused by an RNA virus, which belongs to the togaviridae family. It is the mildest of the common viral exanthems, however infection during early pregnancy may result in abnormalities of the fetus, including congenital malformations and mental retardation. It can be prevented by an intramuscular injection of a live attenuated vaccine given as a part of the MMR cocktail that is given to children and women of childbearing age who are susceptible to rubella. Women should not receive the vaccine if they are pregnant or planning to become pregnant within three months.

3.1.4. Mumps

Mumps is caused by an RNA virus belonging to the family paramyxoviridae. Mumps is an acute contagious disease characterized by an enlargement of one or both parotid glands. Other organs that may be involved include the pancreas, testis and ovaries, as well as the central nervous system. It can be prevented by the use of a live attenuated vaccine given as a part of the MMR cocktail.

3.1.5. Varicella-Zoster

Varicella-Zoster virus (VZV) is a DNA virus belonging to the herpesviridae. VZV is the causative agent of two diseases, varicella (chicken pox) and zoster (shingles). Primary infection with VZV causes chicken pox. Chicken pox is a highly contagious disease characterized by fever and a rash lasting about five days. The rash is characteristically more concentrated on the trunk and head than on the extremities. Chicken pox is usually self-limited. Zoster is mainly a disease of adults. The prerequisite for developing zoster is a previous infection with VZV.

After primary infection, the virus persists in the sensory ganglion of the central nervous system. Reactivation after many years leads to infection and tissue damage to the dermatome served by the infected ganglion. Reactivation of the virus usually occurs in immune-compromised individuals, however it can occur in healthy young adults due to a transient fall in immunity to VZV due to another viral infection or stress. Chicken pox can be prevented by the use of a live attenuated vaccine, which is now given routinely

to children in the USA.

Hepatitis means inflammation of liver. The most common cause of hepatitis is infection with one of the five viruses called hepatitis viruses: A, B, C, D and E. All of these viruses can cause acute disease, with symptoms including yellowing of skin, dark urine, extreme fatigue, nausea and vomiting. Some of these viruses can cause a chronic carrier state in which the patient is never free of the virus, and after many years may develop cirrhosis of the liver or hepatocellular carcinoma (liver cancer). Hepatitis B is a virus of this type, and is the cause of the most serious type of viral hepatitis.

3.1.6. Hepatitis B

Hepatitis B virus is a DNA virus belonging to hepadnaviridae. Hepatitis B virus (HBV) causes the most serious type of hepatitis. HBV is transmitted from person to person through sexual contact, sharing of contaminated needles by IV drug abusers, transfusion of unscreened blood or blood products, and from an infected mother to infant through perinatal infection. The incubation period from exposure to the virus and appearance of symptoms varies from 60 to 180 days. Acute infection can be asymptomatic or it can present with jaundice, gastrointestinal symptoms, such as nausea, vomiting, severe anorexia, and fever. Some patients may experience a serum sickness-like illness consisting of urticaria, rash, arthralgias, or arthritis; 95% of otherwise healthy patients recover from hepatitis B infection completely. Less than one percent develop massive liver necrosis, but a larger number (5% to 10%) develop chronic hepatitis. Chronic hepatitis may evolve into cirrhosis, liver failure, or hepatocellular carcinoma.

Safe and effective vaccines have been developed for preventing hepatitis B, consisting either of highly purified and inactivated hepatitis B surface antigen obtained from serum of chronic carriers, or a recombinant preparation using hepatitis B surface antigen synthesized in microorganisms. The vaccine is administered in three doses, a single dose initially, and boosters at 3 months and 6 months later. This vaccine is now given to all infants, children under 12 years and to high risk adults, such as health care professionals, intravenous drug users etc. This is the first vaccine that is believed to be able to prevent a major cancer.

3.1.7. Hepatitis A

Type A Hepatitis is caused by an RNA virus belonging to the picornovirus family. Outbreaks of type A hepatitis are common in families, institutions, summer camps etc. The mode of transmission is the fecal-oral route. The consumption of raw oysters obtained from water polluted with sewage has also resulted in several outbreaks of hepatitis A. The acute illness itself is diverse in its clinical manifestations and course. In the majority of cases, there are no apparent symptoms, or a nonspecific flu-like syndrome. Symptoms usually subside, but hepatitis A virus infection has been implicated in some cases of acute cholestatic hepatitis and may exhibit a relapsing and protracted course. Preventive measures include personal hygiene and prevention of fecal contamination of food and water. An inactivated vaccine is available which is recommended for people traveling to endemic areas.

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Biographical Sketches

Hema Dantuluri received her Bachelors degree in Medicine from Deccan College of Medical Sciences, India. She is currently doing a residency in Internal Medicine at Muhlenberg Regional Medical Center, and is working on a Masters in Public Health at the University of Pittsburgh. Dr. Dantuluri was involved in research at the Pittsburgh Cancer Institute, and worked with Dr. Koros in the Infectious Diseases and Microbiology Department on cultured human tumor cells for analyses using monoclonal antibodies and indirect immunofluorescence and flow cytometry. Dr. Dantuluri also worked with Dr. Ishwad in the Department of Human Genetics on a study comparing the gene expression patterns in uterine leiomyomas and leiomyosarcomas to elucidate pathways that mediate their progression.

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