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RESEARCH ARTICLE

MUTON – NEW THEORY FOR VIRAL ORIGIN

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ABSTRACT

Aim: To introducenew theory of viral origin "Muton" and the available data on the virus origin, types, pathogeneses, and treatment.
Methods: An analytic descriptive study, conducted to show new theory of viruses origin, and explore the published reports and article in international journals depending of PubMed search engine from June 2016 to August 2016.
Conclusions: Viruses impact all forms of life. When the cell exposes to the vanishing power, most components sometimes vanish leaving only core and sheath protein. This nucleus is a viral cellulous called Muton caused by vanishing the living cell and the core which is usually called (DNA) of the transformed cell. Virus separates (DNA) of the original cell from it and the Virus installs it's (DNAC) inside the cell. The origin of viruses remains a debatable topic. Early pioneers of virology studied bacteriophages, plant viruses such as TMV, and smallpox virus that caused large numbers of outbreaks and mortalities throughout recorded human history.

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INTRODUCTION

Virus, an infectious agent of small size and simple composition that can multiply only in living cells of animals, plants, or bacteria. The name is from a Latin word meaning "slimy liquid" or "poison" (Nquist, 2007; Branch, 1939 and Van Regenmortel, 2000). Viruses are chunks of genetic information—either DNA or RNA—wrapped in proteins and sometimes covered with a membrane (Villarreal, 2004). Unlike bacteria, viruses cannot make more of themselves: to reproduce, they rely on the cells they infect (Lwoff, 1966). Viruses have proteins on their surfaces that act like keys. The proteins attach to receptors on a cell, providing a way for the virus to get in. Once inside, viruses hijack the cell's internal machinery to reproduce. When released from the cell, the new viruses attack other cells and continue the infection (Figure 1) (Lodish *et al*., 1995 and Walker, 2006). Viruses were originally distinguished from other infectious agents because they are especially small (filterable) and because they are obligatory intracellular parasites —that is, they absolutely require living host cells in order to multiply (White *et al*., 1994) However, both of these properties are shared by certain small bacteria, such as some rickettsia. The truly distinctive features of viruses are now known to relate to their simple structural organization and their mechanism of multiplication. Accordingly, viruses are entities that (Lucas, 2010):

- Contain a single type of nucleic acid, either DNA or RNA.
- Contain a protein coat (sometimes itself enclosed by an envelope of lipids, proteins, and carbohydrates) that surrounds the nucleic acid.
- Multiply inside living cells by using the synthesizing machinery of the cell.
- Cause the synthesis of specialized structures that can transfer the viral nucleic acid to other cells.

Viruses have few or no enzymes of their own for metabolism; for example, they lack enzymes for protein synthesis and ATP generation. To multiply, viruses must take over the metabolic machinery of the host cell. This fact has considerable medical significance for the development of antiviral drugs, because most drugs that would interfere with viral multiplication would also interfere with the functioning of the host cell and therefore are too toxic for clinical use (Gottschalk, 1957). The current article aimed to introduce new theory of viral origin "Muton", and explore the available data on the virus origin, types, pathogeneses, and treatment.

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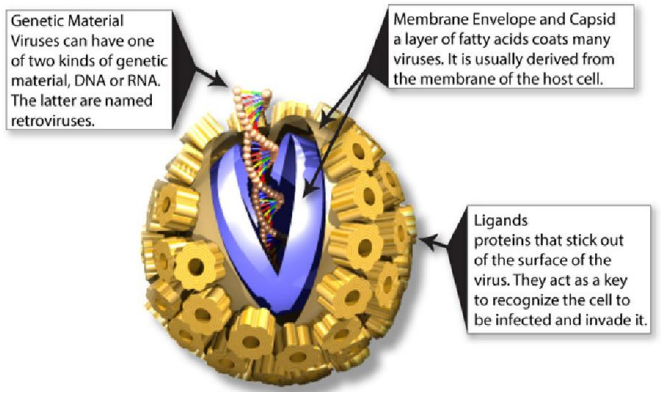


Figure 1. Structure of Viruses

History and Theories of Viral Origin

Viruses are too small to be seen with a light microscope and cannot be cultured outside their hosts. Therefore, although viral diseases are not new, the viruses themselves could not be studied until the twentieth century. In 1886, the Dutch chemist Adolf Mayer showed that tobacco mosaic disease (TMD) was transmissible from a diseased plant to a healthy plant. In 1892, in an attempt to isolate the cause of TMD, the Russian bacteriologist Dimitri Iwanowski filtered the sap of diseased plants through a porcelain filter that was designed to retain bacteria (Lechevalier, 1972).

One hundred years ago, researchers could not imagine submicroscopic particles, and thus they described the infectious agent as contagiumvivumfluidum—a contagious fluid. By the 1930s, scientists had begun using the word virus, the Latin word for poison, to describe these filterable agents (Kruger, 2000). The nature of viruses, however, remained elusive until 1935, when Wendell Stanley, an American chemist, isolated tobacco mosaic virus, making it possible for the first time to carry out chemical and structural studies on a purified virus. At about the same time, the invention of the electron microscope made it possible to see viruses. The question of whether viruses are living organisms has an ambiguous answer (Kay, 1986). Life can be defined as a complex set of processes resulting from the actions of proteins specified by nucleic acids. The nucleic acids of living cells are in action all the time. Because viruses are inert outside living host cells, in this sense they are not considered to be living organisms. However, once viruses enter a host cell, the viral nucleic acids become active, and viral multiplication results. In this sense, viruses are alive when they multiply in the host cells they infect (Lwoff, 1957). From a clinical point of view, viruses can be considered alive because they cause infection and disease, just as pathogenic bacteria, fungi, and protozoa do (Ewald, 1994).

Depending on one's viewpoint, a virus may be regarded as an exceptionally complex aggregation of nonliving chemicals, or as an exceptionally simple living microorganism (Nquist, 2007; Villarreal, 2004 and Grant, 1963). Where did these viruses come from? Could a cough or sneeze be a sign of a close encounter with a tiny visitor from outer space? The late Sir Fred Hoyle (1915– 2001)—a world-renowned astronomer known for being controversial—and his former student Nalin C. Wickramasinghe proposed the panspermia hypothesis (Burbidg *et al*., 2002). This hypothesis asserts that viruses or other microorganisms are raining down upon earth and contaminating it. Hoyle and Wickramasinghe proposed that these outer space microbes were responsible for originating life on earth and cause massive contagion flowing in from space. They speculated that influenza pandemics occurred in our history when solar winds during sunspot peaks caused the viruses to be swept down through the earth's atmosphere. Hoyle speculated that diseases tend to strike during the winter season because cooler weather generates stronger downdrafts. Almost all members of the scientific community have dismissed the panspermia theory. Most scientists believe that cosmic radiation would almost certainly destroy germs in space (Wickramasinghe, 2004). Three other theories have been proposed to explain the origin(s) of viruses (Figure 2) (Flint, 2009) the regressive theory (a), the cellular origin theory (b), and the coevolution theory (c).

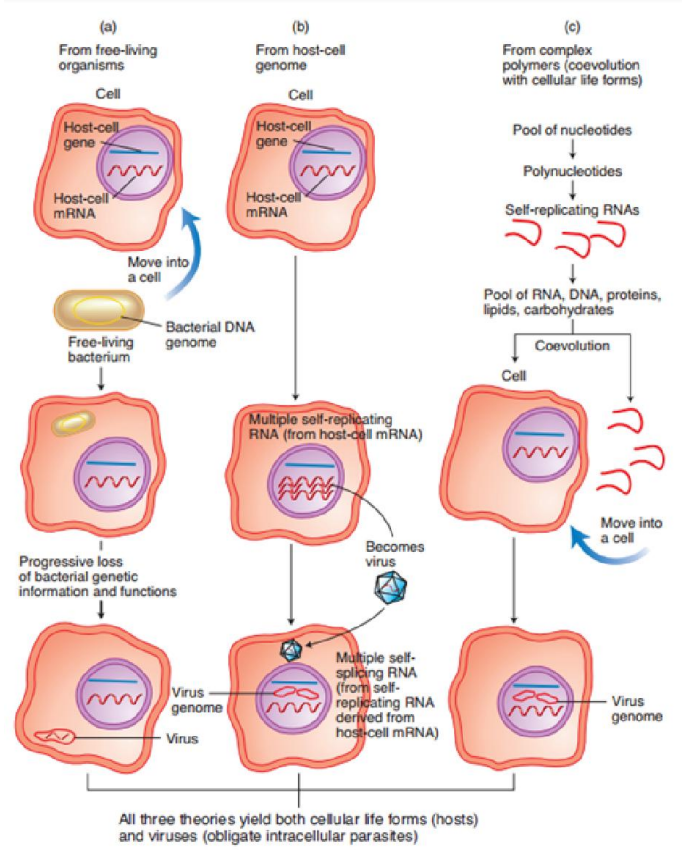


Figure 2.Theories of viral origin. Adapted from Levine, Arnold J. Viruses. Scientific American Library, 1991

The new viral Theory - Muton

Every "body" in the universe is subjected to a vanishing power but the vanishing power is not able to fade some things because any "body" has internal bearing, so if this bearing power is equal or greater than the vanishing power, the body will not fade but if the vanishing power is greater than the internal bearing power of body, the body will turn into Muton. To know the Muton properly, we have to know the vanishing power. vanishing power is the power that works on fading the atomic system inside the substance and the bio-system inside

the organism. It threatens everything because it turns it from the existence to non-existence. It is the nature of its work. It is a form that the substance or the living cell turns into when they are subjected to the vanishing power that is greater than their internal bearing power (Figure 1), in order to resist the vanishing power and reduce the impact of the vanishing power on them not to fade them permanently. Because Muton gathers the bearing power of the body and this is what gives Muton the ability to resist vanishing.

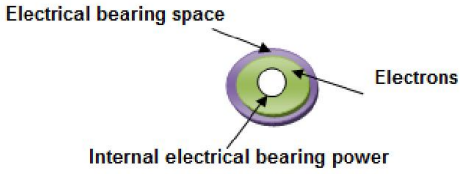


Figure 1. Electron Structure

If we display the electron is subjected to vanishing power (fh) and this power is greater than the internal bearing power of the electron, so the electron should fade but because of the resist of the fading, it turns into an electronic Muton. This Muton is the bearing power of the electron.

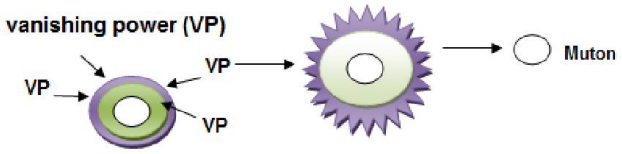


Figure 2. Vanishing Power and Muton

The Muton Properties

Muton gathers all the probability power of the electron "for example" single which increases the ability to resist the fading because the outcome of the probability power of the electron when turns into Muton is greater than the outcome of the bearing power of the electron naturally before exposing to fading, due to existing the electronic units and bearing electronic wall because their existence in the pooled form of the electron causing the strengthen of bearing power within the electron, but in the Muton, the internal bearing power is concentrated to resist fading. If there are probabilistic conditions for Muton, it will return to the first form, for example, if we have electronic Muton and there are certain probabilistic conditions" if the internal electronic power of the Muton becomes greater than vanishing power which caused fading the electron and turning it into electronic Muton, the electronic Muton will return to electron again.If the vanishing power overcame the internal bearing power of the Muton, it will expose to vanishing. Virus is a living cell exposing, in exceptional conditions, to the impact of vanishing power, then it turns from a living cell into Muton (Figure 3). This cellulous Muton is known with us as virus. The cell consists of several elements or components. When the cell exposes to the vanishing power, most components sometimes vanish leaving only core and sheath protein. This nucleus isa viral cellulous Muton caused by vanishing the living cell and the core which is usually called (DNA) of the transformed cell.

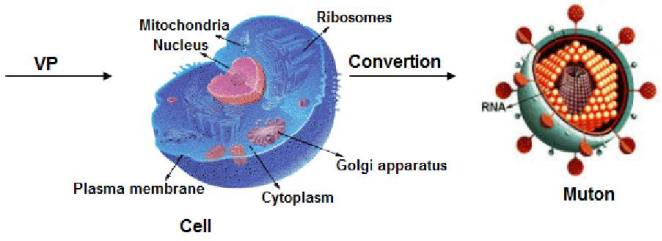


Figure 3. Conversion of Cell into Muton

Virus work inside and outside cells

And from here we can understand the working way of the Virus outside the organism and also inside. when the Virus is outside the organism, it is closer to the inanimate object because the bearing power of viral Muton is very great for resisting the influence of the vanishing power because the vanishing power is very great on the Virus when it is outside the organism body, then the internal bearing power of Virus is forming it in the stalemate to resist the vanishing because when the virus is outside the organism body, it is on high alert to resist the impact of the vanishing power because when the Virus is outside the organism body, it is more exposing to the vanishing. The body of the organism is a safe environment for the Virus because the impact of vanishing power on the organism is small because the bearing power inside the organism is very great in order to maintain the vital system of the organism from vanishing. There is inside the Muton what we may call as high dynamic units which press on viral Muton to make it return to the first condition, before the exposing to the vanishing, because the first condition is better and safer than the Muton‘s condition.

Pathogenicity of the Virus

The Virus infects the organism body in hiding to flee from the anti-bodies which the immune system secretes inside the organism body. Then the Virus starts to unit with the cell, meaning that it works in the same way of the cell, and this way is called the period of the Virus incubation. After that, the Virus separates (DNA) of the original cell from it and the Virus installs it‘s (DNAC) inside the cell. The Virus exploits the components of the original cell to produce new cells of it‘s first form, before exposing to the vanishing and turning to Muton, because the rest of the cell components provide the viral Muton with the reproductive capacity and production of cells because the viral Muton is not able to reproduce outside the cell because the mechanisms of the reproduction and natural division of the cells vanished because of the impact of vanishing power on it because DNA is unable to reproduce or divide but it needs biomaterial which exists inside the cell and provided by the rest of the cell components to achieve reproduction and division. The actual power of the Virus lies in its ability to separate DNA of the original cell and install its DNA. This process is the most important one for the settlement of the Virus inside the organism body. The same process has the ability to kill the Virus if we can prevent it from installing its (DNA) and separating (DNA) of the original cell to DNAC (Figure 4). The body refuses the viral cells because DNA of the viral cells does not correspond with DNA of the organism body.

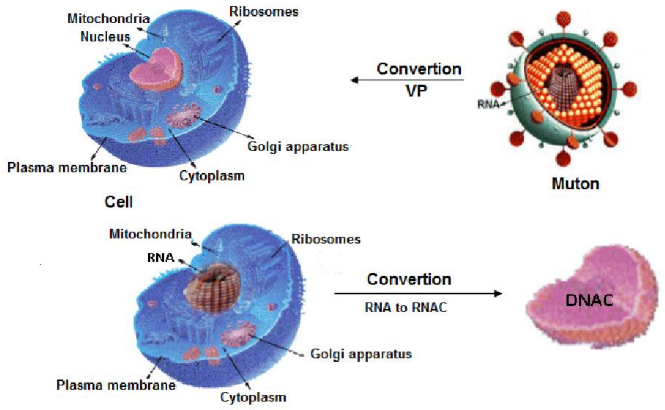


Figure 4. Conversion of RNA to DNAC

Cellular Death

When the Virus infects the organism body, resettles inside it, and starts to produce viral cells, it works as a vanishing power which threatens the original cells of the organism body. When the virus reaches to advanced stages in producing viral cells, it succeeds in converting the original cells, in the place of the infection inside the organism body, into viral Mutons that can attack other cells of another organism and this causes a bug in the vital functions of the infectious organism which leads to the death.

Types and Sizes of Viruses

The amount and arrangement of the proteins and nucleic acid of viruses determine their size and shape (Figure 3). The nucleic acid and proteins of each class of viruses assemble themselves into a structure called a nucleoprotein, or nucleocapsid. Some viruses have more than one layer of protein surrounding the nucleic acid; still others have a lipoprotein membrane (called an envelope), derived from the membrane of the host cell, that surrounds the nucleocapsid core. Penetrating the membrane are additional proteins that determine the specificity of the virus to host cells. The protein and nucleic acid constituents have properties unique for each class of virus; when assembled, they determine the size and shape of the virus for that specific class. The genomes of Mimiviruses and Pandoraviruses, which are some of the largest known viruses, range from 1 to 2.5 Mb (1 Mb = 1,000,000 base pairs of DNA) (Flint, 2009 and Pevsner, 2015).

Visualizing Viruses: Electron Microscopy

Electron microscopes were originally invented in the early 1930s to overcome the limitations of light microscopes to visualize non-biological materials such as metals and small electronic parts. Light microscopes at that time could magnify specimens as high as 1000 times. Instead of light rays, electron

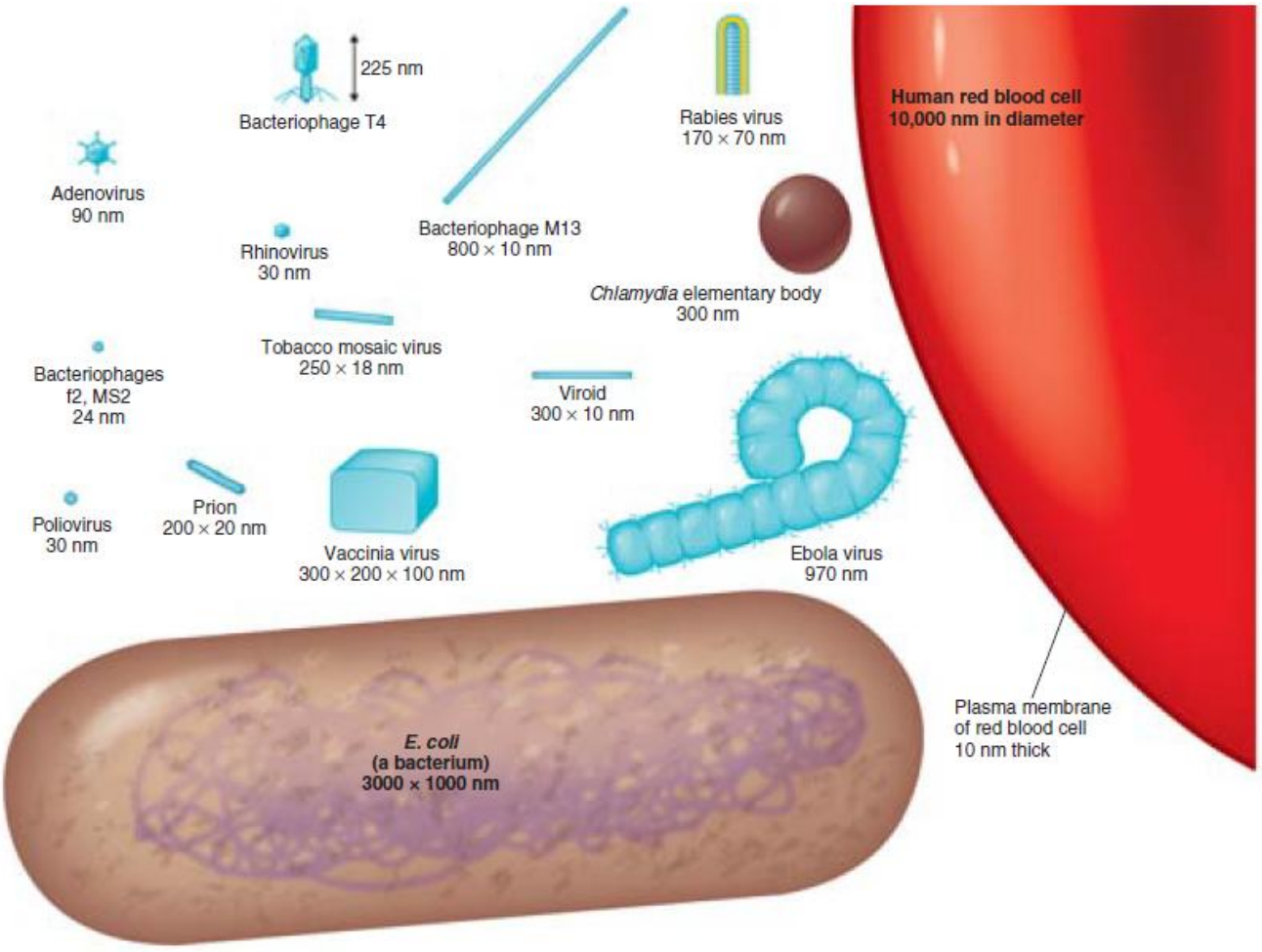
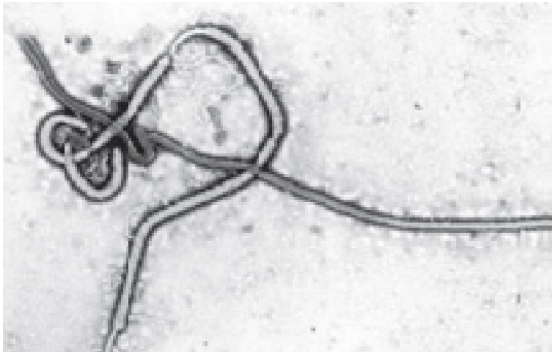


Figure 3. The sizes of several viruses (teal blue) and bacteria (brown) are compared with a human red blood cell, shown to the right of the microbes. Dimensions are given in nanometers (nm) and are either diameters or length by width (Milne, 2004)

microscopes use a beam of electrons focused by magnets to resolve minute structures. With electron microscopy, it is possible to magnify structures 100,000 times and resolve them at 0.5 nm. Virologists were quick to take advantage of this new, powerful tool. Kausche, Pfankuch, and Ruska published the first electron micrograph of TMV in 1939 (Shors, 2011).Today electron microscopes continue to be a powerful tool in studying how viruses are assembled within the cell, the structure of fragile viruses, and the rapid detection and diagnosis of viral infections (especially viruses that cannot be cultivated in the laboratory). The electron micrograph image in (Figure 4-a) represents the first isolation and visualization of Ebola virus in 1976. Some of the filamentous particles are fused together, end-to-end, giving the appearance of a "bowl of spaghetti." The electron microscope was instrumental in the initial identification of the new coronavirus, now known as SARS-CoV. Biologist Cynthia Goldsmith is observing a viral isolate via the electron microscope from the 2003 SARS outbreak in (Figure 4-b) (Starr, 2015).



(a)

(b)

Figure 4. (a) Transmission electron micrograph of Ebola virus particles that were isolated from a human diagnostic specimen and then cultured in vero cells. Magnification: 40,000. (b) Visualization of SARS-CoV via the electron microscope (McCarty, 2012**)**

Virus Mutation

Viruses mutation goes fast, each time a virus's genetic material is copied, there is potential for mutation. These "typos" in the copying process introduce variations in viral genes that may affect the virus's characteristics. Variations may enable a virus to enter a cell that it couldn't before; make a virus more disruptive, which is why some strains of viruses are deadlier than others; or help it evade the host's immune system. Once a cell is infected, it makes many, many copies of the virus. With so much copying going on, mutations happen frequently, quickly generating a lot of genetic variation (Figure 5).It's because of mutation that new influenza vaccines are recommended each year. Each flu season, mutation generates a slightly different assortment of viruses than we saw the year before (Barnes, 2009).

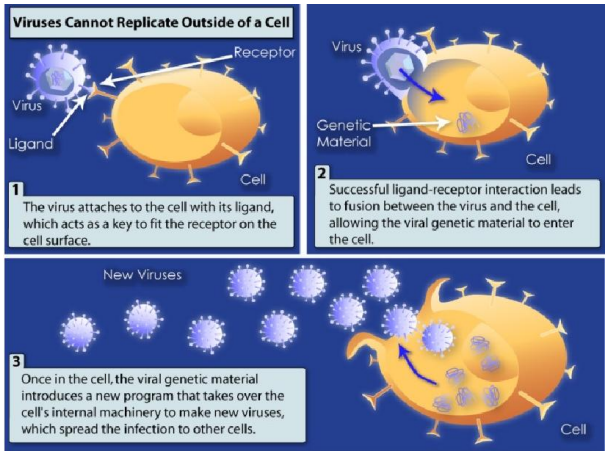


Figure 5. Stages of Virus Mutation and Replication inside of a Cell (Barnes, 2009)

Taxonomy of Viruses

Just as we need taxonomic categories of plants, animals, and bacteria, we need viral taxonomy to help us organize and understand newly discovered organisms. The oldest classification of viruses is based on symptomatology, such as for diseases that affect the respiratory system. This system was convenient but not scientifically acceptable because the same virus may cause more than one disease, depending on the tissue affected. In addition, this system artificially grouped viruses that do not infect humans (McGeoch, 2006; Mahy, 2010). New, fast DNA sequencing allows the International Committee on Taxonomy of Viruses to group viruses into families based on genomics and structure. The suffix -virus is used for genus names; family names end inviridae; and order names end in -ales. In formal usage, the family and genus names are used in the following manner: Family Herpes viridae, genus Simplex virus, human herpesvirus 2(Maniloff and Ackermann, 1998). A viral species is a group of viruses sharing the same genetic information and ecological niche (host range). Specific epithets for viruses are not used. Thus, viral species are designated by descriptive common names, such as human immunodeficiency virus (HIV), with subspecies (if any) designated by a number (HIV-1). Table 1, presents a summary of the classification of viruses that infect humans (Crowley, 2012; Pommerville, 2004; Alcamo, 2001; Levinson, 1996; Atlas, 2014; Nester, 2002 and Gerhardt *et al*., 1981).

Table 1. Families of Viruses That Affect Humans Viral Family Important Genera Clinical or Special Features

Double-Stranded DNaNonenveloped			
70–90 nm	Adenoviridae	*Mastadenovirus*	Medium-sized viruses that cause various respiratory infections in humans; some cause tumors in animals.
40–57 nm	Papovaviridae	*Papillomavirus* (human wart virus) *Polyomavirus*	Small viruses that cause warts and cervical and anal cancer in humans belong to this family.
Double-Stranded DNa enveloped			
200–350 nm	Poxviridae	*Orthopoxvirus*(vaccinia and smallpox viruses) *Molluscipoxvirus*	Very large, complex, brick-shaped viruses that cause smallpox (variola), molluscumcontagiosum (wartlike skin lesion), and cowpox.
150–200 nm	Herpesviridae	*Simplexvirus*(HHV-1 and -2) *Varicellovirus*(HHV-3) *Lymphocryptovirus*(HHV-4) *Cytomegalovirus* (HHV-5) *Roseolovirus*(HHV-6 and HHV-7) *Rhadinovirus*(HHV-8)	Medium-sized viruses that cause various human diseases: fever blisters, chickenpox, shingles, and infectious mononucleosis; cause a type of human cancer called Burkitt's lymphoma.
42 nm	Hepadnaviridae	*Hepadnavirus* (hepatitis B virus)	After protein synthesis, hepatitis B virus uses reverse transcriptase to produce its DNA from mRNA; causes hepatitis B and liver tumors.
Single-Stranded RNa, + Strand Nonenveloped			
28–30 nm	Picornaviridae	*Enterovirus* *Rhinovirus* (common cold virus) Hepatitis A virus	At least 70 human enteroviruses are known, including the polio-, coxsackie-, and echoviruses; more than 100 rhinoviruses exist and are the most common cause of colds.
35–40 nm	Caliciviridae	Hepatitis e virus *Norovirus*	Includes causes of gastroenteritis and one cause of human hepatitis.
Single-Stranded RNa, + Strand Enveloped			
60–70 nm	Togaviridae	*Alphavirus* *Rubivirus*(rubella virus)	Included are many viruses transmitted by arthropods (*Alphavirus*); diseases include eastern equine encephalitis (eee), western equine encephalitis (Wee), and chikungunya. Rubella virus is transmitted by the respiratory route.
40–50 nm	Flaviviridae	*Flavivirus* *Pestivirus* Hepatitis C virus	Can replicate in arthropods that transmit them; diseases include yellow fever, dengue and St. Louis and West Nile encephalitis.
80–160 nm	Coronaviridae	*Coronavirus*	Associated with upper respiratory tract infections and the common cold; SARS virus.
- Strand, One Strand of RNa			
70–180 nm	Rhabdoviridae	*Vesiculovirus*(vesicular stomatatis virus) *Lyssavirus* (rabies virus)	Bullet-shaped viruses with a spiked envelope; cause rabies and numerous animal diseases.
80–14,000 nm	Filoviridae	*Filovirus*	Enveloped, helical viruses; ebola and Marburg viruses are filoviruses.
150–300 nm	Paramyxoviridae	*Paramyxovirus* *Morbillivirus* (measles virus)	Paramyxoviruses cause parainfluenza, mumps, and Newcastle disease in chickens.
32 nm	Deltaviridae	Hepatitis D	Depend on coinfection with hepadnavirus.
- Strand, Multiple Strands of RNa			
80–200 nm	Orthomyxoviridae	Influenza virus A, B, and C	Envelope spikes can agglutinate red blood cells.
90–120 nm	Bunyaviridae	*Bunyavirus*(California encephalitis virus) *Hantavirus*	Hantaviruses cause hemorrhagic fevers such as Korean hemorrhagic fever and *Hantavirus* pulmonary syndrome; associated with rodents.
110–130 nm	Arenaviridae	*Arenavirus*	Helical capsids contain RNA-containing granules; cause lymphocytic choriomeningitis, Venezuelan hemorrhagic fever, and Lassa fever.
Produce DNa			
100–120 nm	Retroviridae	Oncoviruses *Lentivirus* (HIV)	Includes all RNA tumor viruses. Oncoviruses cause leukemia and tumors in animals; the *Lentivirus* HIV causes AIDS.
Double-Stranded RNaNonenveloped			
60–80 nm	Reoviridae	*Reovirus* *Rotavirus*	Generally mild respiratory infections transmitted by arthropods; Colorado tick fever is the best-known.

Management of Virus Infections

Viral diseases range from trivial infections to plagues that alter the course of history. Because of the enormous variations in viruses and in their epidemiology and pathogenesis, there is no single, magic-bullet approach to control. Each virus presents its own set of problems.

This chapter covers methods useful to various degrees in controlling selected viral diseases. The most spectacular progress so far has involved vaccines. Vector control and sanitation have contributed greatly. Also, a number of therapeutic antiviral agents are now available, including some for very serious infections such as human immunodeficiency

virus type 1 (HIV-1) infection. In addition, interferon alpha is now available for the therapy of several viral diseases (Zeng,)

Immunoprophylaxis

Immunoprophylaxis against viral illnesses includes the use of vaccines or antibody-containing preparations to provide a susceptible individual with immunologic protection against a specific disease. Immunization against viral illnesses can be either active or passive. With active immunity, protection is achieved by stimulating the body's immune system to produce its own antibodies by immunization with a virus preparation. Passive immunity is conferred by administering antibodies formed in another host. For example, an antibody-containing gamma globulin preparation may protect a susceptible individual exposed to a viral illness (Jung and Saif, 2015).

Active Prophylaxis (Vaccines)

The viral vaccines currently approved for use in the United States which are of three types:

(1) Attenuated live viral vaccines

Most live vaccines contain viruses that have been attenuated by laboratory manipulation. These attenuated viruses can infect and replicate in the recipient and produce a protective immune response without causing disease. Live attenuated viral vaccines can often confer lifelong immunity after one immunization series. However, because live viruses can multiply in the body, there is always the possibility that they may revert to a more pathogenic form. Adequate laboratory and animal testing and extensive clinical studies must be performed to assess this possibility. In addition, new recombinant technologies facilitate direct alteration of viral genetic structure, thus permitting scientists to produce attenuated viruses in which the genetic regions likely to lead to pathogenic reversion are modified or deleted (Bergeron *et al*., 2015).

(2) Killed (inactivated) viral vaccines

Killed viral vaccines contain either whole virus particles, inactivated by chemical or physical means, or some component(s) of the virus. Completely inactivated viral vaccines cannot cause infection. However, they do not generally produce lifelong immunity following one immunization series; additional doses are usually required. In addition, because killed virus does not multiply in the host, the inoculum itself must provide a sufficiently large concentration of viral antigens to induce the desired immune response (Zeng, 2015).

(3) Recombinant-produced antigens

Application of a recombinant DNA strategy to develop new vaccines is performed by identifying the specific component(s) that can elicit the production of protective antibodies, and then cloning and expressing the gene encoding that protein and assembly of a complex in some cases. This approach has made possible a safe and effective recombinant vaccine against hepatitis B virus, which has replaced the vaccine derived from the plasma of hepatitis B virus-infected individuals (Amador-Molina *et al*., 2016).

Immune Response to Vaccines

Vaccination evokes an antibody response which is, in turn, a measure of the effectiveness of the vaccine in stimulating B lymphocytes. Antiviral antibodies are classified as IgA, IgM, or IgG and can be measured by various techniques. Some antibody categories (IgA and IgM) are normally more abundant in respiratory and intestinal secretions; others (mainly IgG) are more abundant in the circulatory system (Klein *et al*., 2015). Vaccines also stimulate T lymphocytes, leading to cell-mediated responses that influence protection. Antibody assays are now routine laboratory procedures, but measuring cellular immunity in vitro usually requires the utilization of complex laboratory techniques. In general, despite the complexities of the immune system, resistance to the vaccine-preventable viral diseases often correlates well with the presence of circulating antiviral antibodies, which are easily measured (Bergeron *et al*., 2015; Amador-Molina *et al*., 2016; de Mendoza, 2015; Herrmann *et al*., 2015).

Vaccine Production

Because viruses are obligate intracellular parasites, all viral vaccines contain substances derived from the cells or living tissues used in virus production. Technical advances have improved production methods. One can think of generations of vaccines: those prepared in the tissues of an inoculated animal are the first generation (e.g., smallpox vaccine from the skin of a calf), products from the inoculation of embryonated eggs are the second generation (e.g., inactivated influenza virus vaccine), and tissue culture-propagated vaccines are the third generation (e.g., poliomyelitis, measles, mumps, and rubella vaccines). The vaccine generation indicates the production methodology, sophistication, and relative purity. Third generation vaccines usually contain the least host protein and other extraneous constituents, but they have been the most difficult to produce. Advances in biotechnology, i.e., recombinant DNA-derived subunit vaccines, now serve as the cornerstone for a fourth generation of vaccines and have led to the development and licensure of a recombinant hepatitis B vaccine. In addition, exciting new technologies such as polynucleotide vaccines are now being tested in animal studies for several viral diseases (Zeng, *et al*., 2015; Amador-Molina *et al*., 2016 and Volz and Sutter, 2016).

Developing new vaccines

The past success with developing highly effective viral vaccines has been considerable. To develop a new vaccine, researchers must first identify and then produce the virus (or virus components) in quantity under circumstances acceptable for vaccine preparation. Normally this means production of virus or virus components in cell cultures, embryonated eggs, or tissues of experimental animals or humans, or through nucleic acid recombinant technology. Finding an acceptable production system can be a problem, especially in developing inactivated viral vaccines, because a high concentration of

antigen is needed. As already mentioned, production of specific viral proteins by recombinant DNA procedures is providing a solution to many of these problems. A final consideration is the clinical importance of the virus. Normally, it must cause a disease of some severity and there must be an identifiable at-risk target population before consideration is given to developing a vaccine (Botting *et al*., 2015).

However, there are still important indications for which there is no effective vaccine. From a public health perspective an important example for which there is no effective vaccine available is human immunodeficiency virus type 1 (HIV-1). Some of the challenges for the development of an HIV-1 vaccine include the following: (1) the type of immune response required to prevent HIV-1 infection is unknown; (2) there is no animal model for AIDS caused by HIV-1; (3) there are multiple types or clades of HIV-1 which may require the development of a multivalent vaccine; (4) even within a clade, there is considerable viral antigen variation; (5) some successful traditional approaches to viral vaccines, such as live attenuated viruses, pose considerable potential safety risks to the vaccine (Botting, 2015; Wang *et al*., 2015 and Sheets *et al*., 2016).

Passive Prophylaxis

The use of immunoglobulin preparations remains a mainstay of passive prophylaxis (and occasionally of therapy) for viral illnesses. Passive immunoprophylaxis is most often recommended in one of these situations: (1) when exposure has occurred, or is expected to occur very soon, and time does not allow for vaccination and the development of an adequate post-vaccination immune response; (2) when no effective vaccine exists; (3) when an underlying illness precludes a satisfactory response to vaccination. Although once derived exclusively from animal sources, most immunoglobulins are now manufactured from human sources tandard immunoglobulin is produced by pooling plasma obtained from thousands of donors and contains antibodies to a number of common viruses. Specific immunoglobulins are produced from donors with high titers of antibodies to specific viruses, often selected following immunization with the relevant vaccine (Zeng, 2015Simmons, 2015 and Orange, 2015).

Sanitation and Vector Control

Several early approaches to virus control deserve recognition even though they are less dramatic than vaccination. One approach is the avoidance of viral exposure. This is an effective means of preventing the transmission of HIV-1, which is spread through sexual contact and exposure to blood of infected individuals. Blood bank testing, e.g., for hepatitis B surface antigen and for antibodies to HIV-1, HIV-2, HTLV-I, and hepatitis C, also avoids exposure by identifying and discarding blood units contaminated with these infectious agents (Orange, 2015). Control of nonhuman viral reservoirs is another early, worthwhile approach. Unfortunately, few opportunities exist for practical application. The most notable success was the control, and in some cases, the elimination of rabies in some countries through removal of stray dogs, quarantine of incoming pets, and vaccination of domestic animals (Suter, 2016). Another approach of enormous contemporary and historic importance is vector control. Transmission of viral disease by the bite of an arthropod vector was first demonstrated by Walter Reed and his associates, with their discovery that yellow fever was transmitted by mosquitoes. At the turn of the century, yellow fever was a disease of major consequence in the Americas and Africa. By immediately applying Reed's discovery, Gorgas mounted the anti-Aedesaegypti campaign in Havana that marked the beginning of the conquest of epidemic yellow fever. In dealing with the arthropod-borne diseases such as St. Louis encephalitis, any procedure that reduces vector populations or limits the access of the arthropod to humans has potential value. These procedures include draining swamps, applying insecticide, screening homes, and using insect repellant or protective clothing (Suter, 2016 and Pupo-Antúnez *et al*., 2015). The last of the older approaches is to improve sanitation. This method is applicable in a limited way to diseases whose epidemiology involves fecal-oral transmission. The well-known link between the discharge of raw sewage into tidal waters, contamination of shellfish, and type A hepatitis is an example of a situation readily reversible by improved sanitary practices (Pupo-Antúnez *et al*., 2015).

Antiviral Chemotherapy

Antiviral chemotherapeutic agents can be divided into three categories: virucidal agents, antiviral agents, and immunomodulators. Virucidal agents directly inactivate intact viruses. Although some of these agents have clinical usefulness (e.g., topical treatment of warts with podophyllin, which destroys both virus and host tissues), most virucides have no demonstrated therapeutic value. Antiviral agents inhibit viral replication at the cellular level, interrupting one or more steps in the life cycle of the virus. These agents have a limited spectrum of activity and, because most of them also interrupt host cell function, they are toxic to various degrees. The emergence of drug resistant viruses may occur during clinical use that further limits the effectiveness of various antivirals. Immunomodulators such as interferons that alter the host immune responses to infection could, in principle, be protective, and several are under investigation (Chong and Tan, 2016).

These antiviral agents improve the clinical course of disease, but typically have important limitations especially as therapeutics for chronic or latent infections. For example, the four nucleoside analog drugs now available for the therapy of HIV-1 do not prevent the ultimate worsening of disease. The concept of a targeted approach is now practical since information concerning the structure and replication of viruses and the spatial configuration and function of their proteins is available. Such data may be useful in identifying specific target sites for antiviral agents (Chong and Tan, 2016; Harnden, 2016 and Sullivan *et al*., 2015). Since the mid-1930s, scientists have recognized that under certain circumstances one virus can interfere with another. In 1957, Isaacs and Lindenman made a dramatic discovery that explained the mechanism of resistance. They found that virus-infected cells can elaborate a protein substance called interferon, which, when added to normal cells in culture, protects them from viral infection. Other microbial

agents (such as rickettsiae and bacteria) and natural and synthetic polypeptides were later shown to induce interferon. There are three types of interferon: alpha, beta and gamma. Interferon alpha is produced by leukocytes, interferon beta is produced predominantly by fibroblasts and interferon gamma is produced by activated lymphocytes. Interferons tend to exhibit species specificity (mouse cell interferon protects mouse cells to a much greater extent than human cells) and are inhibitory to numerous viruses (Katze, 2015).For many years it was not possible to obtain sufficient quantities of interferons to conduct major studies. However, recombinant DNA technology and cell culture technology led to the production of adequate supplies of interferons and the subsequent conduct of extensive clinical trials. Although broadly antiviral in some animal models, interferon alpha has proven effective in a limited number of viral illnesses of humans, including chronic hepatitis B and C and refractory condylomataacuminata. In addition, interferons have been effective in the treatment of other diseases. For instance interferon alpha is effective for hairy cell leukemia and AIDS-related Kaposi's sarcoma in a selected group of individuals; interferon beta for relapsing-remitting multiple sclerosis; and interferon gamma for reducing the frequency and severity of serious infections associated with chronic granulomatous disease (Banga, 2015 and Hussein *et al*., 2015).

Identifying New Effective Therapeutics

The improved basic science knowledge base of viruses combined with the urgent need for improved therapeutics, especially for HIV-1, has given considerable impetus to the search for new approaches. Some approaches under investigation that may lead to future approved therapies are described here:

Combination Therapy

The use of multiple drugs with different mechanisms of action is being studied as a method of improving clinical effectiveness. Such combinations may offer advantages over monodrug therapy such as improved antiviral activity, preventing or delaying the development of drug resistance, and use of lower, less toxic doses. Combinations of various antiviral agents have been extensively studied for HIV. In addition, approaches investigated for HIV have included combining a cytokine with one or more antiviral agents. Combination therapy has been effective in the treatment of diseases caused by other infectious agents (e.g., Mycobacterium tuberculosis and Pseudomonas aeruginosa) (Murray *et al*., 2015; Shen, 2015 and Ho, 2015).

Discovering New Drugs

New drugs with novel mechanisms of action are being sought and developed. Some of these have displayed considerable antiviral activity in human clinical trials, e.g., protease inhibitors for HIV-1 (Orange, 2015 and Katze *et al*., 2015).

Evaluating Available Drugs for New Indications

Interleukin-2, a cytokine currently approved for treating renal cell carcinoma, has shown considerable immunomodulatory activity in some HIV-1 infected patients in early human studies that may also face bioterrorism involving the intentional release or dissemination of biological agents like bacteria, viruses, or toxins (Lee *et al*., 2015).

Gene therapy is an experimental technique that uses genes to treat or prevent disease. Viruses have evolved to become highly efficient at nucleic acid delivery to specific cell types while avoiding immunosurveillance by an infected host. These properties make viruses attractive gene-delivery vehicles, or vectors, for gene therapy. Several types of viruses, including retrovirus, adenovirus, adeno-associated virus (AAV), and herpes simplex virus, have been modified in the laboratory for use in gene therapy applications. Because these vector systems have unique advantages and limitations, each has applications for which it is best suited. Retroviral vectors can permanently integrate into the genome of the infected cell, but require mitotic cell division for transduction. Adenoviral vectors can efficiently deliver genes to a wide variety of dividing and nondividing cell types, but immune elimination of infected cells often limits gene expression in vivo (Grieger, 2016 and Cox *et al*., 2015). On the other hand, virus used in Bacteriophage (phage) therapy involves using phages or their products as bioagents for the treatment or prophylaxis of bacterial infectious diseases. Much evidence in support of the effectiveness of phage therapy against bacterial infectious diseases has accumulated since 1980from animal model studies conducted in Western countries (Choińska-Pulit *et al*., 2015; Aznar and Reguera, 2016; Sungevie, 2015 and Yeroslavsky *et al*., 2015).

Conclusion

Viruses impact all forms of life. The origin of viruses remains a debatable topic. Early pioneers of virology studied bacteriophages, plant viruses such as TMV, and smallpox virus that caused large numbers of outbreaks and mortalities throughout recorded human history.

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