FEDERAL UNIVERSITY OF TECHNOLOGY MINNA

KNOWING THE MOLECULAR HETEROGENEITY OF HUMAN PATHOGENIC VIRUSES: MY CONCERN AND YOUR HOPE

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PREAMBLE

Mr. Vice-Chancellor and other members of the University management team, I want to start the lecture by appreciating the creator and the sustainer of all lives for His favour and making it possible for me to stand before this special assembly that has come to listen to my inaugural lecture. Today is special to me because this event has strengthened my conviction that I belong to the academic community. The focus of the lecture is on the uniqueness of particles created by Almighty Allah popularly called viruses. In the past, diseases (such as Cancers, Hepatitis and Acquired Immune Deficiency Syndrome) associated with viruses were attributed to either spiritual attack or witchcraft due to difficulty associated with the diagnosis and even treatment of such diseases. This belief attracted accusations and counter accusations among family members and between one community and the other. Currently, science has made us understand that some of the diseases that were hitherto attributed to spiritual attacks or witchcraft were actually caused by viruses and we are also aware now that treatment of such diseases (viral diseases) are not easy due to their parasitic nature at molecular level. Therefore, the only viable option for the control of viral diseases in Nigeria and the world at large is identifying the genotypes/serotypes of pathogenic viruses in circulation for the development of indigenous vaccines now and in the future.

Introduction

Viruses are the smallest infectious agents (ranging from 20 to 300nm in diameter) and contain only one kind of nucleic acid (RNA or DNA) as their genome (Fig. 1). The nucleic acid is enclosed in a protein shell known as capsid (Fig. 1), which may be

surrounded by a lipid containing envelope (Carroll *et al*., 2015).

Unlike bacteria, fungi and protozoa, viruses do not have cell wall or membrane, cytoplasmic chamber and ribosome, so cannot produce proteins on their own. This makes them totally dependent on their host for survival (Carroll *et al.,* 2015).

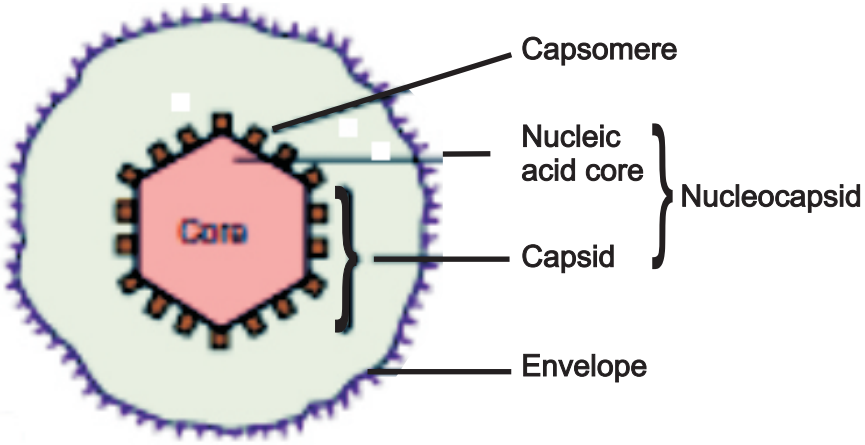

Fig. 1: Structure of a viral particle
Source: (Karen *et al*., 2016).

Properties of viruses

(i) Virus cannot be seen under light microscopes except electron microscope
(ii) A viral particle is not viable outside the body of a host (plant or animal)
(iii) Viruses can infect all kinds of life forms (i.e., animals or plants, and even microorganisms).

Origin of viruses

Life scientists have accumulated significant amount of

knowledge about how present-day viruses evolve, much less is known about how viruses originated. When exploring the evolutionary history of most organisms, scientists can look at the fossil records and historic evidence. Viruses do not fossilize, so researchers can only hypothesize about the origin of viruses by investigating how todays viruses evolve and by using biochemical and genetic information to create speculative virus histories (Forterre, 2006; Forterre & Prangishvili, 2009; Wessner, 2010).

There are three hypotheses formulated that tends to provide information on the origin of viruses. The hypotheses include:

(i). Regressive hypothesis: This explains the origin of viruses by suggesting that viruses evolved from free living cells. However, other components of the virus and how the components were formed are a mystery (Forterre, 2006; Forterre & Prangishvili, 2009; Wessner, 2010).

(ii). Progressive hypothesis: The hypothesis accounts for viruses having either an RNA or a DNA genome and suggests that viruses originated from RNA and DNA molecules that escaped from a host cell. However, this hypothesis does not explain the complex capsid and other structures on virus particles (Forterre, 2006; Forterre & Prangishvili, 2009; Wessner, 2010).

(iii). Self-replication hypothesis: This hypothesis lay emphasis on a system of self-replication similar to that of other self-replicating molecules, likely evolving alongside the cells they rely on as hosts; studies of some plant pathogens support this hypothesis (Forterre, 2006; Forterre & Prangishvili, 2009; Wessner, 2010).

Another challenge confronting scientists studying viral origin and evolution is their high rate of mutation, particularly the case

in RNA viruses such as HIV, Ebola and SAR-COV-2 (Basler, 2019; Howley & Knipe, 2020).

As knowledge in biotechnology advances, virologists will develop and refine further hypothesis to explain the origin of viruses. The emerging field called virus molecular systematics attempts to do that through comparisons of sequenced genetic material. This will help virologist to determine the treatment for the ailments produced by human pathogenic viruses (Basler, 2019).

Classification of Medically Important Viruses

The scheme for the classification of viruses as prescribed by International Committee on the Taxonomy of Viruses (ICTV) depends upon their structure, antigenic composition and other properties. Viral families and genera have been designated, though differentiation into species is still not complete (Ochei & Kolhatkar, 2007; Elliott *et al*., 2012). Viruses are classified into two major divisions depending on the type of nucleic acid (Elliott *et al*., 2012; Fenner *et al*., 2013; Drews, 2016; Howley & Knipe, 2020).

(i). Deoxyriboviruses, which contain DNA
(ii). Riboviruses, which contain RNA.

Each of the group mentioned above is further subdivided mainly on the basis of size and shape of the virion, symmetry of the nucleocapsid and strandedness of the nucleic acid. Major families of viruses are briefly discussed below.

A. DNA viruses

a. Family: Papovaviridae

(i) Papilloma virus which causes cutaneous, genital and laryngeal warts (Ochei & Kolhatkar, 2007).

(ii) Polyomavirus which produces neurological diseases (Elliott *et al*., 2012).

b. Family: Hepadnaviridae

(i) Hepatitis B virus is responsible for inflammation of the liver. The virus may be transmitted from person to person by infusion with infected blood, for instance, from a contaminated hypodermic syringes and needle. Procedures like tattooing and acupuncture can also be sources of infection (Elliott *et al*., 2012).

c. Family: Parvoviridae

Parvovirus causes gastroenteritis while others are responsible for haemolytic diseases (Fenner *et al*., 2013).

d. Family: Adenoviridae

There are at least 41 types of adenoviruses that can infect humans e.g., Adenovirus: They attack the lymphoid tissue and mucous membranes. Some adenoviruses can cause acute respiratory disease and conjunctivitis (Ochei & Kolhatkar, 2007; Fenner *et al*., 2013).

e. Family: Herpesviridae

(i) Herpes simplex virus: Herpes simplex virus type 1 may cause oral infection (gingivostomatitis or keratitis) (Elliott *et al*., 2012). Herpes simplex virus type 2 causes genital lesions (Ochei & Kolhatkar, 2007). (ii) Varicella/Zoster: Varicella (chicken pox) is the primary infection. The virus remains latent in the nerve ganglia for several years and may be reactivated when the immunity is lowered, resulting in an attack of Zoster (shingles) (Fenner *et al*., 2013). (iii) Cytomegalovirus (CMV): Usually CMV infections are symptomless. It may cause severe generalized neonatal infection or an infection similar to glandular fever in adults. Generalized infection may occur in immunosuppressed patients, especially in AIDS (Fenner *et al*., 2013). (iv) Epstein Barr

virus: This virus causes infectious mononucleosis (glandular fever). It is also associated with Burkitt's lymphoma although its exact role in the development of this malignancy is not certain. These viruses often cause asymptomatic and latent infections (Ochei & Kolhatkar, 2007).

f. Poxviridae

All poxviruses tend to produce skin lesions. The human pathogens include variola (smallpox), vaccinia (used for small pox vaccine) and Molluseum contagiosum virus. Some animal pathogens can also infect human e.g., cowpox and monkey pox (Ochei & Kolhatkar, 2007; Elliott, 2012). Variola (small pox) is a severe disease with high mortality rate in non-immunized persons. The virus causes skin lesions through the blood stream which later pustulate. Pustules break down and discharge the virus into the environment. The main route of transmission is respiratory. Small pox vaccine is prepared from the closely related, but much less virulent, vaccinia virus. In 1980, the World Health Organization announced that small pox had been eradicated worldwide (Ochei & Kolhatkar, 2007; Fenner *et al*., 2013; Drews, 2016).

B. Riboviruses (RNA Viruses)

a. Picornaviridae e.g. Rhinoviruses

There are more than 100 serotypes that are responsible for common cold. Enteroviruses: Poliovirus, Echovirus and Coxsackie virus belong to this genus. These viruses are ingested and multiply in the alimentary tract. They spread to the tissues and organs to which they have affinity, via the blood stream. The viruses are excreted in the faeces (Ochei & Kolhatkar, 2007; Fenner *et al*., 2013; Drews, 2016).

Poliovirus cause poliomyelitis. It is an acute infectious disease and in its serious form affects the central nervous system. It destroys the motor neurons in the spinal cord resulting in

paralysis. However, most poliovirus infections are subclinical. There are three serological types (1, 2, and 3) of the virus. An oral vaccine prepared from attenuated strains of the three serotypes provides effective immunization (Ochei & Kolhatkar, 2007; Fenner *et al*., 2013; Drews, 2016).

Coxsackievirus is a large subgroup of the enteroviruses, and is subdivided into groups A and B, they produce a variety of illnesses in humans. Herpangina, hand, foot and mouth diseases and acute haemorrhagic conjunctivitis are caused by some group A Coxsackie viruses. Group B serotypes are associated with myocarditis, pericarditis and meningoencephalitis. In addition, viruses in both groups can be responsible for aseptic meningitis, respiratory and undifferentiated febrile illness, hepatitis and paralysis. The paralysis is usually incomplete and reversible (Ochei & Kolhatkar, 2007; Fenner *et al*., 2013; Drews, 2016).

Echoviruses (enteric cytopathogenic human orphan viruses) have 30 serotypes some of them cause aseptic meningitis, febrile illness with or without rash, and common cold (Drews, 2016).

New enteroviruses: These are newly recognized enteroviruses which are given numbers instead of names. Enterovirus type 70 is known to cause acute haemorrhagic conjunctivitis (Fenner *et al*., 2013). Enterovirus type 71 can cause meningitis, encephalitis and a respiratory infection. Hepatitis A virus is now renamed as enterovirus type 72 (Elliott *et al*., 2012).

b. Family: Reoviridae

They include rotaviruses and other insect and plant viruses. Reoviruses cause minor febrile illness, diarrhea or enteritis and are not known to cause any severe illness. Rotaviruses are a major cause of diarrhea in infants and children. Typical symptoms include diarrhea, fever, abdominal pain and vomiting,

leading to dehydration. The name rotavirus is based on the wheel like appearance of the virus in electron microscopy. The margin of the capsid appears as the rim of a wheel surrounding radiating spokes from the inner hub like core (Ochei & Kolhatkar, 2007; Fenner *et al.*, 2013; Drews, 2016).

c. Family: Orthomyxoviridae

Examples of orthomyxoviruses are influenza viruses (types A, B and C). They have, as a part of their surface, projections that exhibit hemagglutinin and neuraminidase activity. Influenza is an acute respiratory tract infection which usually occurs in epidemics. Antigenic variation is observed very frequently in group A serotypes and less frequently in group B serotypes. Type C is antigenically stable (Ochei & Kolhatkar, 2007; Fenner *et al.*, 2013; Drews, 2016).

d. Family: Paramyxoviridae

Examples of paramyxoviruses are mumps virus, measle virus, parainfluenza viruses and respiratory syncytial virus (RSV) (Fenner *et al.*, 2013).

Mumps viruses: They are responsible for acute contagious disease characterized by a non-supportive enlargement of one or both of the parotid glands. Other organs may also be involved (Elliott *et al.*, 2012).

Measles (Rubeola) virus: It causes an acute, highly infectious disease characterized by a maculopapular rash and fever. It is associated with respiratory tract (Fenner *et al.*, 2013).

Parainfluenza viruses: Parainfluenza group of viruses can cause serious illness each as laryngotracheitis and croup bronchitis and pneumonitis, especially in immunocompromised individual (Elliott *et al.*, 2012).

Respiratory syncytial virus (RSV): This paramyxovirus causes the most serious bronchitis. RSV produces characteristic fusion of cells, syncytia, in human cell cultures (Ochei & Kolhatkar, 2007).

e. Family: Rhabdoviridae

Example of rhabdoviridae is the Rabies virus: Causes an acute infection of the central nervous system that is almost always fatal. The transmission of the virus is usually through the bite of rabid animals like dog (Fenner *et al*., 2013).

f. Family: Coronaviridae

Human coronaviruses (SARS-CoV-2, SARS-CoV and MERS-CoV) are responsible for acute lung injury and acute respiratory distress syndrome which can lead to pulmonary failure. The subgroups of coronaviruses family include; alpha, beta, gamma and delta. The transmission of the disease (COVID-19) is through body contact with an infected person, sharing of clothes with an infected person, contact with contaminated inanimate objects (Elliott *et al*., 2012; Fenner *et al*., 2013; NCDC, 2020).

g. Family: Togaviridae

Examples are rubella virus and arboviruses (arthropod-borne-viruses). Rubella virus: Causes an acute febrile illness with rash and lymphadenopathy. It affects children and young adults. Infections in the early pregnancy may result in abnormalities of the foetus. Arboviruses (arthropod-borne viruses): many Arboviruses are from the family Togaviridae. For example, yellow fever virus which causes acute, febrile mosquito borne illness. Severe cases may show jaundice, proteinuria and haemorrhage. Other examples of arbovirus in the family include chikungunya s, semilki forest and sindbis viruses (Elliott *et al*., 2012; Fenner *et al*., 2013).

h. Family: Arenaviridae

Examples: members of this family are rodent parasites which occasionally infect man, causing haemorrhagic illness e.g. Lassa virus (Ochei & Kolhatkar, 2007; Elliott *et al*., 2012).

i. Family: Retroviridae

The members of this family contain a unique enzyme, reverse transcriptase, which is an RNA directed DNA polymerase. The family has many tumor producing viruses such as the sarcoma viruses of birds and mice, and the leukemia viruses of mice, the causative agent of acquired immunodeficiency syndrome (AIDS), is also included in this family (Elliott *et al*., 2012; Fenner *et al*., 2013).

Human Immunodeficiency Virus (HIV)

Human immunodeficiency virus (HIV) is the causative agent of Acquired Immunodeficiency Syndrome (AIDS). HIV has a cylindrical core with nucleic acid cloned and sequenced. It is a retrovirus, but differs from other retroviruses such as human T lymphotrophic virus (HTLV) 1 and 2 (Drews, 2016). Cells bearing CD4 antigen (a major component of the viral receptor required of cell entry) are susceptible to HIV infections, but HIV has a particular affinity for T4 helper lymphocytes. An envelope glycoprotein of the virus (Fenner *et al*., 2013). Gp 120, specifically binds to the CD4 molecule receptor site on the surface of the T4 lymphocytes. Once the virus binds to cell receptor it can enter the cell. The viral reverse transcriptase enzyme on entering into the infected cell, makes DNA copy of the RNA genome (pro-viral DNA) (Fenner *et al*., 2013). The pro-viral DNA can thereby bring about the destruction of the cell/ the T4 lymphocyte has a central role in many immunological functions, and an infected cell can cause severe damage to the cellular immune system. Reduced immunity results in infections with many tumors such as Kaposi's sarcoma (Fenner *et al*., 2013).

HIV is transmitted sexually in blood or blood products and prenatally. Those most at risk of acquiring HIV infection are homosexuals, injecting drug users (IDU) and those with bisexual orientation. Others include individuals receiving unscreened blood or blood products and infants born of infected women (Artika *et al.,* 2020). AIDS is an illness characterized by one or more indicator diseases. Certain diseases, when definitively diagnosed in immunocompromised individuals without the symptoms of any other causes of immunodeficiency, are indicatives of AIDS. Irrespective of the presence of any other cause of immune deficiency, if there is a laboratory evidence of HIV infection, certain indicator diseases that require presumptive and definitive diagnosis are diagnostics of AIDS (Elliott *et al*., 2012; Fenner *et al*., 2013).

Acute HIV infection is usually accompanied by transient non-specific illness characterized by fever, malaise myalgia, lymphadenopathy, pharyngitis and rash. Most of these conditions are, however, subclinical. In two to six weeks, antibodies to the core and surface proteins are usually detected by enzyme immunoassay (EIA) and confirmed by immunofluorescence or Western blot technique (Drews, 2016; Howley & Knipe, 2020). A chronic infection of AIDS that follows is asymptomatic in early stages. In some patients, a persistent generalized lymphadenopathy in the form of nodes of 1 cm or more in diameter in two or more non-contagious extra-inguinal sites, commonly in the cervical and the auxiliary lymph nodes, usually develops. In the later stages of the illness there may develop symptoms such as fever, night sweats, diarrhoea and weight loss (Fenner *et al*., 2013; Drews, 2016; Howley & Knipe, 2020).

Patients may also suffer from 'minor' opportunistic infections such as oral candidiasis, oral hairy leucoplakia, herpes simplex,

folliculitis, seborrheic dermatitis, impetigo and tinea infections. These conditions which may be signs of major opportunistic infections to come are now collectively known as symptomatic non-AIDS; they were previously referred to as AIDS- related complex (ARC). The incubation period of HIV infection is long lasting up to 10 years before the symptoms develop. Classical complication of AIDS is very severe (Fenner *et al*., 2013; Drews, 2016; Howley & Knipe, 2020).

Pathogenic Viruses

The term pathogen (Greek words: Pathos – suffering and Genes – producers of) refers to a biological agent that causes disease or illness to its host. It is most often used to describe agents that are capable of disrupting the normal physiology of a host. Pathogenic viruses therefore, are viruses that cause diseases to either

Table 1: Some Human pathogenic viruses and the diseases associated with the viruses

Some Pathogenic viruses	Disease
Rotaviruses	Gastroenteritis/diarrhea
Hepatitis A, B and C viruses	Hepatitis
Rubivirus	Rubella
Measles virus	Measles
Mumps virus	Mumps
Rhabdovirus	Rabies
Polivirus	Polimyelitis
Varicella-zoster viruses	Chicken pox, shingles
Epstein-Bar virus	Infectious mononucleosis
Human papilloma Viruses	Cervical, breast and penal cancers
Flavivirus	Yellow fever, dengue fever
Human immunodeficiency Viruses	Acquired immunodeficiency syndrome
Ebola Viruses	Ebola fever/hemorrhagic fever
Lassa Viruses	Lassa fever/hemorrhagic fever
Corona Viruses (SAR-COV-2)	Corona virus disease 2019 (COVID-19)

Source: (Parvez and Parveen, 2017; Artika *et al*., 2020)

human host, animals or plants (Table 1). For the purpose of this lecture, our interest will be on pathogenic viruses (Rotaviruses, Hepatitis C Viruses and Human papilloma viruses) that are associated with human diseases.

Principles of Viral Diseases (Pathogenesis)

To cause disease, the virus must find its way into the body of a susceptible host, come in contact with susceptible cells or tissues, replicate and produce cell injury. While doing so, it must overcome the host defenses. Understanding mechanisms of viral pathogenesis at the molecular level is necessary in order to design effective and specific control strategies. However, much of our knowledge of viral pathogenesis is based on animal models because such systems can be readily manipulated and studied (Carroll *et al*., 2015).

Viruses enter the host through various portals such as the respiratory or alimentary tract, through skin or by sexual contact. Some viruses replicate and produce disease at the site of entry (Fig. 2) Many viruses migrate from the site of entry via the blood stream, lymphatics or nervous tissue to reach the organ or tissues, the viruses find susceptible cells with specific receptors on the surfaces (cell tropism) (Carroll *et al*., 2015).

After entering the host cell, the virus may remain latent without multiplication or cause widespread tissue damage. When the damage results in the death of the cell, it is called cytolytic (Fig. 2). The damage can also manifest as malignant transformation (Carroll *et al.*, 2015).

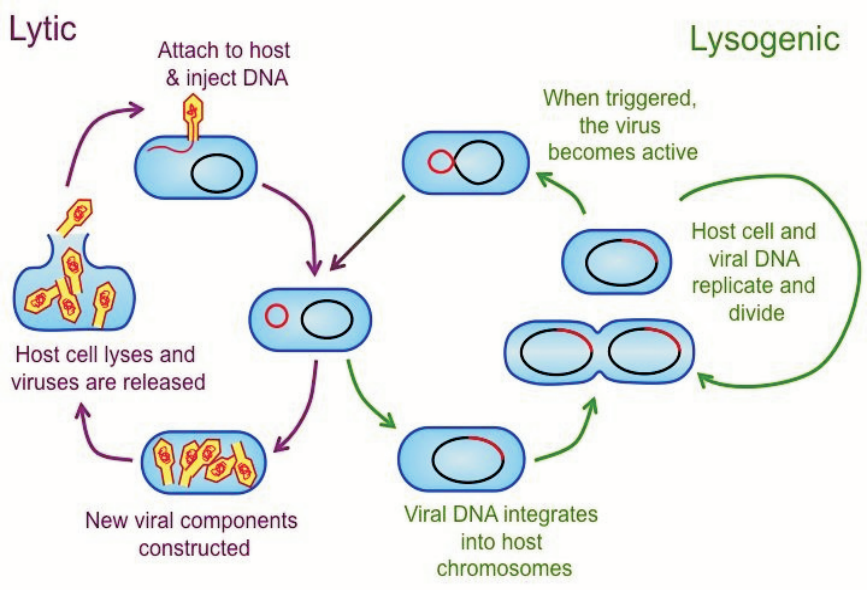

Fig. 2: Viral Replication Cycle

Source: (Carroll *et al.*, 2015).

The cellular damage or destruction can be due to:

a. Viral nucleic acids which often inhibit protein and DNA synthesis of the host cell.
b. Large amounts of viral proteins are accumulated in the host cell, exert its toxic effects and distort its structure.
c. There may be a change in permeability of plasma membrane that may lead to autolysis.
d. Viral antigens may appear on the cell surface e.g., hemagglutinin spikes of influenza virus appear on the host cell surface which make red cells adhere to them (Haemadsorption).
e. Changes in the cytoplasmic membrane by the respiratory syncytial virus bring about fusion of adjacent cell membranes resulting in the formation of big clumps or syncytia.

f. Some viruses e.g., measles, mumps, varicella cause damage to the chromosome of the host cell.

Immune response to viral infection

There are three ways the human immune system respond to viral infection. They include:
(i). Response via cytotoxic cells (ii). Response via interferon and (iii). Response via antibodies (Laing, 2013). When virus infects an individual (host), it invades the human cells (host) and replicate. Once inside the cells of the host, it becomes difficult for the immune system of the host to recognize the presence of the virus. To overcome this challenge, the host makes use of molecules called class I major histocompatibility complex proteins (MHC class 1). The MHC class 1 molecules help to expose the infected cells (Laing, 2013; Carroll *et al*., 2015).

A special cell of the immune system called T cells circulates looking for infections (Immunological Surveillance). One type of T cell is called the cytotoxic T cell because it kills cells that are infected with viruses with toxic mediators. Cytotoxic T cells have specialized proteins on their surface that help them to recognize virally-infected cells. These proteins are called T cell receptors (TCRs) (Laing, 2013). Each cytotoxic T cell has a TCR that can specifically recognize a particular antigenic peptide bound to an MHC1 molecule. If the T cell receptor detects a peptide from a virus, it warns its T cell of an infection. The T cell releases cytotoxic factors to kill the infected cell and, therefore, prevent survival of the invading virus (Laing, 2013; Carroll *et al*., 2015).

Viruses are highly adaptable, and have developed ways to avoid detection by T cells. Some viruses stop MHC molecules from getting to the cell surface to display viral peptides. If this happens the host cells do not know there is a virus inside the infected cell (Laing, 2013; Carroll *et al*., 2015).

However, another immune cell specializes in killing cells that have a reduced number of MHC class I molecules on their surfaces which is called natural killer cell. When the NK cell finds a cell displaying fewer than normal MHC molecules it releases toxic substances, in a similar way to cytotoxic T cells, which kill the virally-infected cell (Laing, 2013).

Cytotoxic cells are armed with preformed mediators. Cytotoxic factors are stored inside a compartment called granules, in both cytotoxic T cell and NK cells, until contact with an infected cell triggers their release. One of these mediators is **perforin**, a protein that can make pores in a cell. Enzymes called **granzymes** are also stored in, and released from the granules. Granzymes enter target cells through the holes made by perforin (Laing, 2013).

Once inside the target cell, the granzyme initiate a process known as programmed cell death or apoptosis causing the target cell to die. Another cytotoxic factor is granulysin, which directly attacks the outer membrane of the target cell, destroying it by lysis. Cytotoxic cells also synthesise and release other proteins, called cytokines, after making contact with infected cells. Cytokines include interferon-γ and tumor necrosis factor-α which transfer signal from the T cell to the infected, or other neighbouring cells, to enhance the killing mechanisms (Laing, 2013).

Via Interferons

Virally infected cells produce and release small proteins called interferons, which play very important role in protection against viruses. Interferons prevent replication of viruses, by directly interfering with their ability to replicate within an infected cell. They also act as signaling molecules that allow infected cell to warn nearby cells of a viral presence. This signal makes neighbouring cells increase the number of MHC class I molecules

upon their surfaces, so that T cells surveying the area can identify and eliminate the viral infection (Laing, 2013; Carroll *et al*., 2015).

Via antibodies

Viruses can also be removed from the body by antibodies before they get the chance to infect a cell. Antibodies are proteins that specifically recognize invading pathogens and bind (stick) to them (Laing, 2013). This binding serves many purposes in the eradication of the virus: First, the antibodies neutralize the virus, meaning that, it is no longer capable of infecting the host cell (Laing, 2013; Carroll *et al*., 2015). Second, many antibodies can work together, causing virus particle to sticks together in a process called agglutination. Agglutinated viruses make an easier target for immune cells than single viral particles (Laing, 2013; Carroll *et al*., 2015). A third mechanism used by antibodies to eradicate viruses, is the activation of phagocytes. A virus-bound antibody binds to receptors, called Fc receptors, on the surface of phagocytic cells and triggers a mechanism known as phagocytosis, by which the cell engulfs and destroys the virus (Laing, 2013; Carroll *et al*., 2015).

Finally, antibodies can also activate the complement system, which opsonizes and promotes phagocytosis of viruses. Complement can also damage the envelope (phospholipid bilayer) that is present on some types of virus (Laing, 2013).

Diagnosis of Viral Infections by Gross Evaluation and Histopathology

The great benefit of histopathology is that it can provide confirmation of specific viral diseases, especially when done in conjunction with appropriate laboratory virological testing such as immunohistochemistical staining for viral antigens or nucleic acid detection.

METHODS OF DETECTION OF VIRUSES

There are several methods of detecting viruses in clinical samples. The methods include:

Detection of Viruses by Electron Microscopy

This method of virus detection involves direct visualization of the virus itself. The morphology of most viruses is sufficient to identify the image as a virus and to assign an unknown virus to the correct family. Noncultivable viruses may also be detectable by electron microscopy (MacLachlan *et al*., 2017).

Two general procedures can be applied to virus detection by electron microscopy: negative-stain electron microscopy and thin-section electron microscopy. For the negative stain procedure, virus particles in a fluid matrix are applied directly to a solid support designed for the procedure. Contrast stains are applied and the virus particles are directly visualized by electron microscope (Goldsmith & Miller, 2009). Thin-section electron microscopy can be used directly on fixed tissue samples, usually containing "viral" inclusions from the affected tissue or on cell cultures growing an unidentified virus. Routine electron microscopy procedures have been largely replaced with more sensitive and less expensive procedures such as antigen-capture tests, immunostaining techniques or PCR tests, but because electron microscopy is an agent independent test, it still has use in specialized cases and in facilities with the necessary equipment and expertise (Goldsmith & Miller, 2009).

Detection of Viruses by Isolation

Despite the explosion of new techniques for "same-day diagnosis" of viral disease by demonstration of viral antigen or viral nucleic acid in specimens, virus isolation in cell culture remains an important procedure. Virus isolation remains the "gold standard" against which newer methods must be compared even though nucleic acid detection approaches,

particularly real-time PCR are now challenging that paradigm (Goldsmith & Miller, 2009; MacLachlan & Dubovi, 2017).

The choice of cell culture strategy for the primary isolation of an unknown virus from clinical specimens is largely empirical. Primary cells derived from fetal tissues of the same species usually provide the most sensitive cell culture substrates for virus isolation (Goldsmith & Miller, 2009). Continuous cell lines derived from the homologous species are, in many cases, an acceptable alternative (Goldsmith & Miller, 2009; MacLachlan & Dubovi, 2017).

Some specialized laboratories still have the capability to inoculate suckling mice, a system that has been valuable for isolating arboviruses that resist cultivation in cell cultures. Embryonated hens' eggs are still used for the isolation of influenza A viruses, even though cell cultures (Madin Darby Canine Kidney (MDCK) cells are now more commonly used. Many avian viruses also replicate more readily in eggs than in cell cultures derived from chick embryo tissues, and there are lack avian cell lines for routine virus isolation procedures. According to the virus of interest, the diagnostic specimen is inoculated into the amniotic cavity, or the allantoic cavity, the yolk sac, onto the chorioallantoic membrane or, in rare instances, intravenously into the vessels of the shell membrane and embryo (Hematian *et al.,* 2016; MacLachlan & Dubovi, 2017). Evidence of viral growth may be seen on the chorioallantoic membrane (e.g., characteristic pocks caused by poxviruses), but otherwise other means are used to detect viral growth (e.g. death of the embryo, hemagglutination, immunofluorescence or immunohistochemical staining of viral antigens, PCR, or antigen-capture ELISA) (Jerome, 2016).

There is no such thing as an emergency (“stat”) virus isolation;

each virus has its own biological clock and no amount of concern will speed up the replication cycle. For viruses such as the alphaherpesviruses, a successful isolation can be evident as cytopathic effect in the inoculated cell cultures within 23 days, whereas others are considerably slower and require repeated serial passage (Hematia *et al.,* 2016 ; MacLachlan & Dubovi, 2017). In general, the time for detection will depend on the laboratory procedures for identifying viruses in the culture system. For instance, noncytopathic bovine viral diarrhea virus can be detected by virus isolation as early as 3 days post inoculation or as late as 3 weeks, depending on laboratory procedures (Hematia *et al.,* 2016; MacLachlan & Dubovi, 2017). Procedures for routinely detecting and identifying virus in inoculated cell cultures include immunofluorescence or immunehistochemical staining of the infected monolayer, antigen-capture ELISA, nucleic acid detection tests such as PCR, hemadsorption, or even negative-stain electron microscopy for unknown isolates.

Detection of Viral Antigens

The direct detection of viral antigens in a clinical sample can be achieved in as little as 15 minutes with some immunoassays, or the procedure can take several days if extensive sample preparation and staining is involved. Viable virus is generally not required in the specimen for a positive antigen detection test result, but the timing of sample collection is as important with these assays as it is for virus isolation. Analytical sensitivity varies across the various test modalities, ranging from detection of a single infected cell to assays that require as much as 10^5 antigen units. The advance that revolutionized this type of testing was the development of monoclonal antibodies. These reagents are highly specific in their binding to antigen and, once developed, provide a virtually inexhaustible supply of the same material for test consistency (Hematia *et al.,* 2016; MacLachlan & Dubovi, 2017).

Immunofluorescence Staining

Immunofluorescence or fluorescent antibody staining is an antigen-detection test that is used primarily on frozen tissue sections, cell "smears," or cultured cells; formalin-fixed tissue samples are generally not useful with this procedure (MacLachlan & Dubovi, 2017). Antigen is detected through the binding to the sample matrix of specially modified, agent-specific antibodies. The modification is the "tagging" of the antibody with a fluorochrome that absorbs ultraviolet light of a defined wavelength, but emits light at a higher wavelength (MacLachlan & Dubovi, 2017). The emitted light is detected optically with a special microscope equipped with filters specific for the emission wavelength of the fluorochrome. The fluorochrome can be bound directly to the agent-specific antibody (direct immunofluorescence) or it can be attached to an anti-immunoglobulin molecule that recognizes the agent-specific antibody (indirect method. immunofluorescence). The indirect method enhances the sensitivity of the test, but may also increase background (MacLachlan & Dubovi, 2017; Hematian *et al*., 2016). Immunofluorescence staining does require specialized equipment, including a cryostat for sectioning frozen tissue along with a fluorescent microscope for detecting the bound antibody.

Immunohistochemical (Immunoperoxidase) Staining

In principle, immunohistochemical staining is very similar to immunofluorescence staining of viral antigens, but with several key differences (MacLachlan & Dubovi, 2017). The "tag" used in immunohistochemical staining is an enzyme, generally horseradish peroxidase. The enzyme reacts with a substrate to produce a colored product that can be visualized in the infected cells with a standard light microscope. The tissue sample will often be formalin-fixed, which permits testing of the specimen days to weeks after sampling, without the need for low temperature storage (MacLachlan & Dubovi, 2017).

Immunochromatography

Immunochromatography simply refers to the migration of antigen or antigen antibody complexes through a filter matrix or in a lateral flow format - for example, using nitrocellulose strips. In most formats, a labeled antibody binds to the antigen of interest (Jerome, 2016). The antigen antibody complexes are then immobilized in the support matrix by an unlabeled antibody bound to the matrix. All controls are included in the membrane as well, and results are seen as colored spots or bands, as one of the test reagents is conjugated to colloidal gold or a chromogenic substance (MacLachlan & Dubovi, 2017). This test format is especially convenient for point-of-care testing, as the test process is simple and each test unit contains both positive and negative controls to assess test validity (Hematian *et al*., 2016).

Detection of Viral Nucleic Acids

Viral nucleic acids can be detected in a wide range of clinical specimens, using hybridization and amplification techniques as follows:

Polymerase Chain Reaction

The PCR assay is an in vitro method for the enzymatic synthesis of specific DNA sequences using two oligonucleotide primers, usually of about 20 residues (20 - mers), that hybridize to opposite strands and flank the region of interest in the target DNA; the primer pairs are sometimes referred to as forward and reverse primers. Primers are necessary to provide the DNA polymerase with a substrate upon which to add new nucleotides, and to direct the reaction to the specific region of the DNA for amplification. Primers can also be designed to provide "tags" or "barcodes" on the amplified products for purposes of detection and sorting in complex reactions (MacLachlan & Dubovi, 2017).

In order to increase the sensitivity of the test, a "nested" PCR procedure is used. In this procedure, one set of primers is used to

do an initial amplification of a target area and the product of the first reaction becomes the template for a second PCR test in which new primers targeted a region internal to the first set of primers. This amplification of amplified product greatly increases the sensitivity of the test (MacLachlan & Dubovi, 2017).

The development of reverse transcriptase polymerase chain reaction (RT-PCR) methods to detect RNA sequences is a major advance in cell biology and viral diagnostics. For RT-PCR, the RNA is first transcribed into cDNA using a DNA polymerase capable of using RNA as a template, such as reverse trancriptase. Newer reverse transcriptase enzymes have been developed that permit synthesis of the cDNA strand at higher temperatures, which increases the analytical sensitivity and specificity of the reaction. In single-tube RT-PCR tests, all components for both reactions are placed in the reaction tube at the onset of the testing (MacLachlan & Dubovi, 2017). The cDNA synthesis step is followed immediately by the PCR reaction. In this test format, there is no opportunity for products of one reaction to cross contaminate another, because the reaction tube is never opened until the end of the testing protocol. Advances such as the single-tube test greatly increased the reliability of PCR test results by virtually eliminating laboratory contamination problems (Hematian *et al*., 2016).

Methods for Detection of Amplified Products

In the initial era of PCR testing, the amplified products were detected by analyzing the reaction products by gel filtration to visualize the amplified product. Amplified products of a defined size can be visualized by using fluorescent dyes that bound to the oligonucleotides separated in agarose gels. A "band" at the appropriate size can be taken as a positive test for the presence of an agent in a sample (MacLachlan & Dubovi, 2017).

Real-time PCR testing offers fluorimeter that could accurately measure (quantify) the accumulation of PCR product (amplicons) in the reaction tube as it was being made - that is, in real time. Product is measured by increases in fluorescence intensity generated by several different fluorescent reporter molecules, including nonspecific DNA binding dyes (SYBR Green I), TaqMan probes, and molecular beacons as examples (MacLachlan & Dubovi, 2017).

A further variation in PCR testing that is becoming more commonly used is multiplex PCR. In this method, two or more primer pairs specific for different target sequences are included in the same amplification reaction. In this manner, testing can be done for several agents at the same time and in the same assay tube, thereby saving time and costs. With real-time, multiplex PCR assays, several probes with different fluorescent molecules can be detected simultaneously. This type of application is useful in evaluation of samples from disease complexes, such as acute respiratory disease in dogs. Issues of test sensitivity must be addressed in this format, because several reactions must compete for common reagents in the reaction, thus an agent in high copy number might mask the presence of one at low copy number (Hematian *et al*., 2016).

Microarray (Microchip) Techniques

Another technological advance that is impacting the field of diagnostics is the advent of microarrays or microchips. The microchip for nucleic acid detection is a solid support matrix onto which have been "printed" spots, each containing one of several hundred to several thousand oligonucleotides. Increasingly, these oligonucleotides can represent conserved sequences from virtually all viruses represented in the various genetic databases, or can be customized to represent only viruses from a given species involved in a specific disease

syndrome, such as acute respiratory disease in cattle. The basis of the test is the capture by these oligonucleotides of randomly amplified labeled nucleic acid sequences from clinical specimens (Jerome, 2016). The binding of a labeled sequence is detected by laser scanning of the chip and software programs assess the strength of the binding. From the map position of the reacting oligonucleotides, the software identifies the species of virus in the clinical sample. This type of test was used to determine that the virus responsible for Severe Acute Respiratory Syndrome (SARS) was a coronavirus. With knowledge of the oligonucleotide sequences that bound the unknown agent, primers can be made to eventually determine the entire nucleotide sequence of a new species of virus (MacLachlan & Dubovi, 2017).

In Situ Hybridization

With the explosion in the identification of "new" viruses in virtually any animal species examined, the diagnostic dilemma becomes linking the presence of a virus in a clinical specimen with having caused the clinical disease under investigation. As previously noted this can be done using either immunofluorescence or immunohistochemistry. An issue with these techniques particularly with a newly discovered agent is having a validated antibody reagent available. The alternative to the antibody detection systems is the use of nucleic acid probes (FISH - fluorescence in situ hybridization). Small (2550 nucleotides) DNA probes corresponding to conserved regions of the genome are synthesized with a fluorescent tag at the 5^0 end (6-carboxyfluorescein as an example) (MacLachlan & Dubovi, 2017).

Detection and Quantitation of Virus-specific Antibodies (Serologic Diagnosis)

The detection of an immune response to an infectious agent has, for the most part, relied on determining the antibody response of

the host to the agent of interest (MacLachlan & Dubovi, 2017). This approach measures only one limb of the adaptive immune response (humoral immunity); techniques for reliably measuring the cell-mediated responses have not been routinely available or cost-effective. For many situations, measurement of antibody responses remains a valuable technique for defining the infection status of animals. Serological tests can be used to: (1) define whether an animal has ever been infected by a particular virus; (2) determine if a specific virus (or other pathogen) is linked to a clinical event; (3) determine if an animal has responded to a vaccination. For the serologic diagnosis of an acute viral disease in an individual animal, the classic approach has been to test paired sera - that is, an acute and a convalescent serum from the same animal, for a change in titer (fourfold or greater) of virus-specific antibody. The acute -phase serum sample is taken as early as possible in the illness; the convalescent-phase sample usually at least 2 weeks later. Given this time line, diagnosis based on this approach is said to be "retrospective." In recent years this approach has been complemented by serologic methods for detecting virus-specific IgM antibodies - in many viral diseases a presumptive diagnosis may be made on the basis of detecting IgM antibody in a single acute-phase serum specimen - for example, West Nile virus infection of horses (MacLachlan & Dubovi, 2017).

Use of serological tests to assess vaccine efficacy can be an important aspect of an infectious disease management programme. In many countries, purchase of vaccine can be done by the animal owner. Antibody testing of selected animals can provide the practitioner with valuable insight as to whether the immunization program of the producer is being performed correctly. As eradication programs expand for diseases of production animals, marker vaccines are more frequently being used and so-called DIVA serological assays can distinguish whether a given antibody response is caused by vaccine or

natural infection. For herpesvirus infections such as bovine herpesvirus 1, it is essential to determine whether an antibody response is the result of infection, because infection invariably leads to latency. Movement of a latently infected animal into a negative herd can result in an outbreak of disease, thus gene deletion "marker" vaccines were developed to facilitate differentiation of vaccinated and naturally infected cattle(MacLachlan & Dubovi, 2017; Hematian *et al*., 2016).

Enzyme Immunoassay - Enzyme-Linked Immunosorbent Assay (ELISA)

Enzyme immunoassays (EIAs, ELISA) are the serologic assays of choice for the qualitative (positive or negative) or quantitative determination of viral antibodies because they are rapid, relatively cost-effective, and may not require the production of infectious virus for antigen if recombinant antigens are used (Hematian *et al*., 2016). In the EIA test format for antibody detection, viral antigen is bound to a solid matrix. Serum is added and, if antibodies to the antigen are present in the sample, they bind to it. In direct EIA tests, the bound antibody is detected by an anti-species antibody tagged with an enzyme. With addition of the enzyme substrate, a color reaction develops that can be assessed either visually or with a spectrophotometer. Controls run with the sample define whether the test is acceptable and which samples in the test are positive. Kinetics-based EIAs offer the advantage that quantitative assays can be based on a single dilution of serum (Jerome, 2016; Hematian *et al*., 2016).

Serum (Virus) Neutralization Assay

As virus isolation is considered the gold standard for the detection of virus against which other assays must be compared, the serum (virus) neutralization test has historically been the gold standard, when available, for the detection and quantitation of virus-specific antibodies. For the assay of neutralizing antibody, two general procedures are available: the constant-

serum variable-virus method and the constant virus variable-serum method. Although the constant serum variable-virus method may be a more sensitive assay, it is rarely used because it utilizes relatively large amounts of serum, which may not be readily available (MacLachlan & Dubovi, 2017). The basis of the neutralization assay is the binding of antibody to infectious virus, thus preventing the virus from initiating an infection in a susceptible cell. The growth of the virus is detected by its ability to kill the cell (cytopathic effect) or by its ability to produce antigen in the infected cells that is detected by immunofluorescence or immunohistochemistry. The amount of antibody in a sample is determined by serial dilution of the sample and "challenging" each of these dilutions with a standard amount of virus (constant-virus variable-serum method). The last dilution that shows neutralization of the virus is defined as the endpoint and the titer of the serum is the reciprocal of the endpoint dilution; for example, an endpoint of 1:160 equates to a titer of 160 (MacLachlan & Dubovi, 2017).

Immunoblotting (Western Blotting)

Western blotting tests simultaneously but independently measure antibodies against several proteins of the agent of interest. There are four key steps to western blotting. First, concentrated virus is solubilized and the constituent proteins are separated into discrete bands according to their molecular mass (M_r), by sodium dodecyl sulfatepolyacrylamide gel electrophoresis (SDS-PAGE) (MacLachlan & Dubovi, 2017). Secondly, the separated proteins are transferred electrophoretically ("blotted") onto nitrocellulose to immobilize them. Thirdly, the test serum is allowed to bind to the viral proteins on the membrane. Fourthly, their presence is demonstrated using a radio-labeled or, most commonly, an enzyme-labeled antispecies antibody. Thus immunoblotting permits demonstration of antibodies to some or all of the proteins of any given virus, and can be used to monitor the

presence of antibodies to different antigens at different stages of infection. Although this procedure is not routinely used in a diagnostic setting with viruses, western blots were central to the identification of immunogenic proteins in a variety of viruses. Similarly, the assay is used in the analysis of samples for the presence of prion proteins in ruminant tissues (MacLachlan & Dubovi, 2017).

Indirect Immunofluorescence Assay

Indirect immunofluorescence assays are used for the detection and quantitation of antibody; specifically, these are tests that use virus-infected cells (usually on glass microscope slides) as a matrix to capture antibodies specific for that virus. Serial dilutions of test serum are applied to individual wells of the cell substrate and usually an antispecies antibody with a fluorescent tag is then added as the detector of antibody binding. Slides are read with a fluorescent microscope and scored as positive if the infected cell shows a fluorescent pattern consistent with the antigen distribution of the virus used. This test is rapid (less than 2 hours) and can be used to determine the isotype of the reacting antibody if one uses an antiisotype-specific serum such as an anticanine IgM (MacLachlan & Dubovi, 2017).

Hemagglutination-Inhibition Assay

For those viruses that hemagglutinate red blood cells of one or another species, such as many of the arthropod borne viruses, influenza viruses, and parainfluenza viruses, hemagglutination-inhibition assays have been widely used (MacLachlan & Dubovi, 2017). For detecting and quantitating antibodies in the serum of animals, the methods are sensitive, specific, simple, reliable, and quite inexpensive. In spite of all of the technological advances, hemagglutination inhibition assays remain the mainstay for determining antibody responses to specific influenza A viruses. The principle of the assay is simple - virus binds to red blood cells through receptors on their surface (MacLachlan & Dubovi,

2017). Antiviral antibodies bind to these receptors and block hemagglutination. Serum is diluted serially in the wells of the microtiter plate, usually in twofold steps, and to each well a constant amount of virus, usually four or eight hemagglutinating units, is added. The reciprocal of the highest dilution of serum that inhibits the agglutination of the red blood cells by the standardized amount of virus represents the hemagglutination-inhibition titer of the serum (Jerome, 2016; MacLachlan & Dubovi, 2017).

Immunodiffusion

Historically, agar gel immunodiffusion (AGID) assays were used for the specific diagnosis of a number of viral infections and diseases, including bluetongue, hog cholera, influenza, equine infectious anemia (the so-called "Coggins test" after its inventor, LeRoy Coggins), and bovine leukemia (MacLachlan & Dubovi, 2017). These assays are very simple to perform, they utilize inexpensive materials, and they do not require production of infectious material by the testing laboratory. Often crude cell extracts or even tissue extracts from infected animals can be used as the test antigen (MacLachlan & Dubovi, 2017).

IgM Class-Specific Antibody Assay

A rapid antibody-based diagnosis of a viral infection or disease can be made on the basis of a single acute-phase serum by demonstrating virus-specific antibody of the IgM class. Because IgM antibodies appear early after infection but drop to low levels within 12 months and generally disappear altogether within 3 months, they are usually indicative of recent (or chronic) infection (MacLachlan & Dubovi, 2017).

The most common method used is the IgM antibody capture assay, in which the viral antigen is bound on a solid-phase substrate such as a microtiter well. The test serum is allowed to react with this substrate and the IgM antibodies "captured" by

the antigen are then detected with labeled anti-IgM antibody matched to the species from which the specimen was obtained. A downside to the IgM assays is that they are generally not suitable for use in animals that have been vaccinated as the IgM responses to that antigen has already occurred in response to the vaccine (Hematian *et al*., 2016; MacLachlan & Dubovi, 2017).

New Generation Technologies

Flow Cytometry Platform

As with nucleic acid technologies, technological developments for analyte detection are rapidly evolving, and a substantial number of potentially novel platforms for serological assays have been developed that have not yet been fully validated for routine diagnostic use (Jerome, 2016). It is beyond the scope of this text to provide an exhaustive listing of these technologies, many of which will never find their way into routine diagnostic use.

However, one technology that has demonstrated particular promise in both the clinical and research arena is Multi Analyte Profiling (xMAP) developed by Luminex. The success of this testing platform probably reflects the maturity of existing technologies that were combined to provide a versatile analyte detection system. XMAP combines a flow cytometry platform, uniquely labeled microspheres, digital signal processing, and standard chemical coupling reactions to provide a system that can be used to detect either proteins or nucleic acids (MacLachlan & Dubovi, 2017).

The microspheres carry unique dyes (up to 100 different ones) that emit fluorescent signals that identify the individual beads coupled with a specific ligand. For antibody detection tests, the antigen of interest is coupled to a specific bead. The beads are exposed to the test serum and the bound antibody is detected with an antispecies antibody tagged with a reported dye. The

microspheres are analyzed in a flow cytometer in which lasers excite both the bead dyes and the reporter dyes. Multiple beads for each antigen are analyzed in each test, providing independent readings of the reaction (MacLachlan & Dubovi, 2017).

One distinct advantage of this system is its multiplex capability. Theoretically, 100 or more different antigens can be assessed for antibody reactivity in a single assay. For maximum sensitivity and specificity, recombinant antigens are needed to eliminate extraneous proteins that would reduce specific antigen density on the beads and increase nonspecific background reactivity that can confuse test interpretation.

Protein Microarrays

Another potential solution to the issue of simultaneous multiple epitope screening is the protein microarray. This type of test has become feasible as technology is now permitting production of high quality antigens or peptides in unlimited quantities (MacLachlan & Dubovi, 2017). Protein microarrays of virtually any size can be used to interrogate serum samples for the presence of antibodies to the range of peptides on the array. The output can simply provide a positive versus negative answer, or can be a quantitative output with serial dilution of the test samples. A practical example of the use of this technology is the screening of serum samples for reactivity to any influenza A virus. Typically this is challenging in that there are now 18 HA types. For example, to answer the question of which influenza A viruses are capable of infecting a given species (e.g. bats) entails an 18-HA antigen screen with μL quantities of test serum (MacLachlan & Dubovi, 2017).

Recombinant-generated HA1 antigens are spotted onto nitrocellulose coated slides at multiple locations within a defined array well. Dilutions of test sera are applied to the protein arrays

and the binding of antibody is detected with a fluorescent-tagged antispecies antibody. Slides are scanned for the intensity of the fluorescent signal and the positive signals are mapped to the particular antigen in the array. This type of antibody detection system can define the presence of antigen-specific antibodies in serum that represent exposure to any number of viruses (MacLachlan & Dubovi, 2017).

Chemotherapy of viral diseases

In the chemotherapy of viral infections, a drug should inhibit the growth and eliminate the virus when used at concentrations not detrimental to the host (Littler & Oberg, 2005). A number of antiviral drugs have been produced and formally licensed and are widely used for the treatment of specific viral diseases. The drugs in used fall primarily in the category of antiviral (Littler & Oberg, 2005).

For effective rational drug design, the molecular targets (i.e., proteins and enzyme specific to the virus) should be identified first and then the drugs should be tailored on the basis of the molecular configuration and action of the target proteins (selective toxicity). None of the antiviral drugs in circulation today have been developed by rational drug design instead, their antiviral activity was found first, often by chance and their molecular target determined later (Littler & Oberg, 2005). This explains the basis for the severe side effects usually observed with most antiviral drugs administered to patients.

Challenges of treatment of viral diseases

Viral diseases, especially the diseases caused by RNA viruses have become a leading cause of morbidity and mortality globally (Table 2). The global burden of viral infections has continued to grow. New infections caused by newly evolved serotypes as a result of genetic recombination and/or reassortment have

continued to emerge at a very rapid pace with attendant socio-economic consequences (Stanaway *et al.,* 2016).

In Nigeria, viral diseases such as Rotavirus Gastroenteritis, Hepatitis C, Human papilloma (cancer), Lassa Fever, Corona Virus Disease 2019 (COVID-19) and Hepatitis B have continued to be a major challenge to public health management (Table 2). At the moment, the prevalence of these diseases with the attendant treatment failure has made the diseases to be among the major killer infectious diseases in Nigeria and the world at large (Fasina *et al.,* 2016; Muhammad *et al*., 2017; NCDC, 2020).

Table 2: Viral diseases, prevalence and the case fatality (CFR)

Viral Diseases	Prevalence of the Diseases (%)	CFR (%)
Lassa fever (hemorrhagic fever)	23	15
HIV/AIDS	1.4	80-90
Ebola fever (hemorrhagic fever))	–	90
Hepatitis B (Liver cancer)	15	63-93
Rotavirus gastroenteritis	–	9.5
Human papilloma virus (cancer)	37	85
Hepatitis C (Liver cancer)	2	23
Measles	-	0.44 – 1.43
Coronavirus disease 2019 (COVID-19)	–	2 - 3.4

Key: CFR (Case Fatality Rate)

Source: (Alkali *et al.,* 2015; Olayinka *et al.,* 2016; Omatola *et al.,* 2016; Okunade *et al.,* 2017; Okunade *et al.,* 2017; Itelima *et al.,* 2017; Okonkwo *et al.,* 2017; Orah and Banjo., 2018; Oshun and Odeghe, 2019; WHO Africa, 2018; Magaji *et al.,* 2019; NCDC, 2020; NACA, 2020; UAIDS, 2018; WHO, 2020).

Currently, there are no definite cures of proven efficacy available for most viral diseases and treatment usually consists primarily of syndromic management and supportive care. The absence of cure for viral diseases, such as Rotavirus gastroenteritis, Hepatitis C, Human papilloma (cancer), HIV/AIDS, Lassa Fever,

Ebola fever, Coronavirus disease 2019 (CoVID-19) particularly in Nigeria have contributed to high morbidity and mortality, leading to huge health care cost (*Stanaway et al., 2016*). The ugly situation is further complicated by lack of infrastructural capacity to diagnose viral diseases, using advanced techniques coupled with non-availability of indigenous vaccines that can be used for the effective control of the diseases that are prevalent in Nigeria (Siddiqui *et al*., 2017).

There is the need for the development of a viable indigenous prophylactic strategy (Vaccine) for the control and elimination of viral diseases that have posed severe threat to human lives particularly in developing nations like Nigeria. This cannot be achieved without identifying the circulating serotypes/genotypes in the country (Siddiqui *et al*., 2017).

The main treatment for viral diseases is the use of class of drugs called antiviral. These drugs do not cure, but they can reduce the viral load in the body of an infected person, to enable the host defenses fight the viruses, for example, Human Immunodeficiency virus (HIV) (Branson, 2019).

Today, more than 40 antiretroviral drugs have been approved to treat HIV. Most people who treat their HIV will take two or more of these drugs each day for the rest of their lives (Branson, 2019). The drugs must be taken at the right time and in the right way for them to work properly. Taking these medications, the way a healthcare provider has prescribed is called adherence (Branson, 2019).

Adherence to treatment plan is not easy. Antiretroviral drugs can cause side effects (such as anaemia, hair loss and hallucination) that can be severe. Skipping doses of the drugs can cause the virus to become resistant to the drugs and the victim is helpless (Branson, 2019).

The use of herbs (alternative) has not yielded the desired results in the quest for treatment of viral diseases. Although many researchers have claimed to have treatment for some viral disease such as HIV, Hepatitis, Human papilloma virus but many of these claims have proven to be false (Siddiqui *et al.,* 2017).

It is important to note that judging from the replicative nature of viruses, particularly in the body of its host, where there is integration of the host genome and that of the viral genome, and the transcription and translation processes which are dependent on the host. It is difficult to admit the use of alternative drugs in the treatment of viral diseases (*Siddiqui et al.,* 2017; Samani & Kopaei, 2018).

My Contributions

Considering the difficulties associated with the treatment of diseases caused by viruses, the mortality and socioeconomic burden on the victims and their family members, it becomes very necessary for more attention to be given to researches that are focused on identifying the circulating serotypes/genotypes of pathogenic viruses responsible for high morbidity and mortality. Identifying the circulating serotypes/genotypes of the human pathogenic viruses will help in developing a robust data base for the development of indigenous vaccines for the control of viral diseases particularly in developing countries such as Nigeria.

Therefore, the need to know the molecular heterogeneity of the pathogenic viruses that are prevalent in Nigeria and the world at large has propelled me to conduct researches on identifying the serotypes/genotypes of Rotaviruses, Hepatitis C viruses and Human papilloma viruses.

(A) Rotaviruses

Rotaviruses are responsible for gastroenteritis in children (<1 to

5 years). Globally, over 500,000 - 870,000 children within <1 to 5 years die annually due to Rotavirus gastroenteritis. In Nigeria, an estimated 33,000 children die annually due to Rotavirus gastroenteritis (Aminu *et al*., 2008). Efforts to find cure by pharmaceutical companies have yielded no desired results due to genetic reassortment/recombination. The only viable option for the control of Rotavirus gastroenteritis is the use of vaccine. It is in the light of this that six hundred (600) stool samples from children in three North Central States and Abuja were collected and screened using ELISA technique. Forty-three (43) stool samples were found positive, representing 7.2% prevalence (Table 3).

Table 3: Prevalence of rotaviruses infection among children (< 1-5 years) in three North Central States and Abuja, Nigeria

State	NSS	NPS	Prevalence (%)
Niger	150	8	1.3
Nasarawa	150	10	1.7
Kwara	150	9	1.5
Abuja	150	16	2.7
Total	**600**	**43**	**7.2**

Key: NSS (Number of Sample Screened), NPS (Number of Positive Sample)

The nucleic acids (RNA) of the Rotaviruses were extracted from the 43 positive stool samples. The nucleic acids extracted were reverse transcribed to cDNA. To identify the serotypes of the rotaviruses involved in gastroenteritis, second round amplification was conducted on the reverse transcribed (cDNA) in order to generate VP4 and VP7 cDNAs. The identified serotypes are indicated in Table 4.

Table 4: Distribution of Rotavirus Serotypes/Genotypes in three North Central States and Abuja, Nigeria

State	G1	G2	G8	P4	P6	P8
Niger	2	3	2	–	2	–
Nasarawa	8	–	–	–	–	2
Kwara	1	–	2	3	3	–
Abuja	3	5	5	2	2	4
Total	**14**	**8**	**7**	**5**	**7**	**6**

Key: G1, G2, G8, P4, P6, P8 are the genotypes/serotypes

(B) Hepatitis C Viruses

Hepatitis C viruses are responsible for the inflammation of liver cells also known as hepatocytes. In chronic infections, patients may go on to develop liver cirrhosis and hepatocellular carcinoma (Eze *et al*., 2014). Globally, an estimated 71 million people have chronic hepatitis C virus infection. Approximately 399,000 people die from hepatitis C annually. Africa has a major share of the burden, accounting for 31.9 million (Eze *et al*., 2014). The use of chemotherapies for effective treatment of hepatitis C has failed due to genetic recombination or reassortment. Vaccine remains the most viable strategy for the control of hepatitis C, but this cannot be achieved without identifying the circulating serotypes of the virus. It is against this background that five hundred and sixty-five (565) blood samples were collected from both in and out patients in five hospitals in Niger State (Iduh *et al.,*

Table 5: Distribution of HCV Infection among Patients attending five General Hospitals in Niger State

Sample site	NSS	NPS	Prevalence (%)
GHM	113	5	0.9
GHS	113	2	0.4
GHK	113	14	2.5
GHW	113	15	2.7
USNHB	113	8	1.4
Total	**565**	**44**	**7.9**

KEY:
GHM = General Hospital, Minna
GHS = General Hospital, Suleja
GHK = General Hospital, Kontagora
GHW = General Hospital, Wushishi
HCV = Hepatitis C virus
NSS = Number of samples screened
NPS = Number of positive samples
USNHB = Umaru Sanda Ndayako Hospital, Bida

2018). The blood samples were screened for Hepatitis C virus using Enzyme Linked Immunosorbent Assay (ELISA). Forty-four were found positive, representing 7.9% (Iduh *et al.,* 2018). The distribution of hepatitis C virus infection according to the hospitals investigated is as indicated in Table 5.

The blood samples that tested positive for HCV were subjected to RNA extraction. The extracted RNAs of the virus were reverse transcribed to DNAs. The DNA were amplified, sequenced and BLAST (Iduh *et al.,* 2019). The results of the sequence and the BLAST were compared with the reference strains on the website of the National Centre for Biotechnology Information (NCBI). See details in Table 6.

Table 6: BLAST N Pairwise Alignment of Nine Amplicon Sequenced

Sample	Source	Length	Score	E-Value	Identities	Reference Strains	*Inference
1	HCV subtype 1b 5'UTR	202	366	1e-97	100	EU256066.1	Subtype 1b
7	HCV subtype 1b 5'UTR	185	311	5e-81	97	EU256066.1	Subtype 1b
14	HCV subtype 1b 5'UTR	201	339	3e-89	97	EU256078.1	Subtype 1b
19	HCV subtype 1b 5'UTR	201	355	3e-94	99	EU256066.1	Subtype 1b
21	HCV subtype 1b 5'UTR	202	364	4e-97	99	EU256066.1	Subtype 1b
30	HCV subtype 1b 5'UTR	200	361	5e-96	99	KY780123.1	Subtype 1b
36	HCV subtype 1b 5'UTR	200	364	4e-97	99	EU155279.2	Subtype 1b
****78**	HCV subtype 1b 5'UTR	201	357	7e-97	99	EU482877.1	Subtype 1b
121	HCV subtype 1b 5'UTR	201	359	2e-95	99	AB691953.1	Subtype 1b

* The query sequences covers 100%

(C) Human Papilloma Virus

Human papilloma viruses (HPV) are the main aetiology of cervical, breast and penal cancers. In 2018, approximately 311,000 women died from cervical cancers; more than 85% of these deaths occurred in low income countries (WHO, 2019). In Nigeria, about 14,943 women have been diagnosed of cervical cancer, out of which 10,403 die from the disease (Bruni *et al.*, 2019). Conventional methods such as chemotherapy and radical surgery used for the management of cancer patients have failed. Vaccine remains the credible option for the control of human papilloma virus induced cancers. In the light of the above; 501 blood samples and vagina swabs were collected from blood donors and pregnant women respectively from six hospitals in Abuja, Nigeria (Aondona *et al.,* 2020a). The blood and vagina swabs were screened for Human papilloma viruses using ELISA technique and the results are presented in Table 7.

Table 7: Prevalence of human papilloma virus among blood donors and pregnant women in Abuja, Nigeria

Sample Site	NSS	NPS	Prevalence (%)
Abaji	80	3	0.6
Asokoro	101	21	4.2
Bwari	80	2	0.4
Kuje	80	19	3.8
Kwali	80	5	1.0
Nyanya	50	5	1.0
Total	**501**	**55**	**11.0**

Key: NSS (Number of samples screened), NPS (Number of positive samples)

Blood and vagina swab samples that tested positive were subjected to DNA extraction. The extracted DNAs were amplified, sequenced and BLAST (Aondona *et al.,* 2020b). The results of the sequence and the BLAST were compared with the information on the website of NCBI. Details are indicated in Table 8.

Table 8: BLAST Pairwise Alignment of 15 Amplicon Sequenced

Sample	genotype	Length	Score	E-Value	Identities (%)	Reference strains
1	HPV 18	99	172	2E-39	98	MG195999.1
12.	HPV 70	108	102	3e-18	98.28	JN383600.1
24	HPV 18	103	174	5e-40	97.12	KU050127.1
37	HPV 6	91	261	6e-66	100	LC155236.1
47	HPV 72	95	377	8e-101	100	JN6178890.1
48	HPV 31	89	178	3e-41	100	HQ834585.1
63	HPV 70	102	113	1e-21	91.76	AB601048.1
67	HPV 81	88	738	0.0	100	EU911303.1
100	HPV 16	96	143	1e-30	95.60	KU961847.1
293	HPV 16	84	484	6e-133	100	KR674075.1
332	HPV 70	98	111	4e-21	91.67	AB601047.1
351	HPV 58	74	261	6e-66	100	LC155254.1
365	HPV 58	70	270	1e-68	100	EF140819.1
381	HPV 70	88	266	3e-64	100	DQ448184.1
394	HPV 66	73	486	2e-133	100	KR674072.1

Summary of the Findings

1. Three human pathogenic viruses were investigated. The pathogenic viruses include Rotaviruses, Hepatitis C viruses and Human Papilloma viruses.

2. The identified genotypes/serotypes of the three pathogenic viruses investigated at the different study areas include:

(a) Rotaviruses - G1, G2, G8, P4, P6, and P8
(b) Hepatitis C viruses - 1b
(c) Human papilloma viruses - HPV6, HPV16, HPV18, HPV31, HPV58, HPV66, HPV70 and HPV81

These findings suggest that these viruses are real and they are in our community. The earlier we identify their genetic diversity for prophylactic measures, the better for us.

Conclusion

Viral diseases (Rotaviruses gastroenteritis, Liver cirrhosis/Hepatocellular carcinoma, Cervical, Breast and penal cancers) can best be controlled through prophylactic measures rather than curative measures. The need to identify the circulating genotypes/serotypes of Human pathogenic viruses (Rotaviruses, Hepatitis C viruses and Human papilloma viruses) for the development of indigenous vaccine for the control of the viral diseases cannot be over emphasized, as there is no universally acceptable curative protocol in place for now. This is synonymous with the saying "prevention is better than cure".

Recommendations

1. Viral diseases have brought about socioeconomic distress among developing nations and have hampered effective service delivery. Hence, the need for synergy between government and non-governmental organisations to fund researches that will target production of indigenous vaccines to be used for the control of viral diseases.

2. There should be enabling laws to bring about strong collaborations between government, non-governmental organizations and universities in the area of funding researches targeted at identifying circulating genotypes/serotypes of most pathogenic viruses. The results of such researches will serve as a data for the development of indigenous vaccines, rather than importation of vaccines that may not serve the purpose it is meant.

3. Government should direct its attention towards establishment of regional laboratories equipped with state-of-the-art facilities that will be used to address problems of diagnosis of viral diseases particularly during epidemics (See the case of Coronavirus Disease, 2019).

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REFERENCES

Alkali, B. R., Daneji, A. I., Magaji, A. A., & Bilbis, L. S. (2015). Clinical symptoms of human rotavirus infection observed in children in Sokoto, Nigeria. Advances in virology, 2015.

Aminu, M., Ahmad, A. A., Umoh, J. U., Dewar, J., Esona, M. D., & Steele, A. D. (2008). Epidemiology of rotavirus infection in north-western Nigeria. *Journal of Tropical Pediatrics,* 54(5), 340-342.

Aondona, P. Y., **Kuta, F. A.,** Abalaka, M. E., & Adabara, N. U. (2020a). Prevalence of Human Papilloma virus infection from cervix of women attending selected hospitals in Abuja, Nigeria. *Asian Journal of Pharmaceutical and Health Sciences,* 10 (4), 2373 - 2378.

Aondona, P. Y., **Kuta, F. A.,** Abalaka, M. E., & Adabara, N. U. (2020b). Molecular identification Human Papilloma virus infection from cervix of women attending selected hospitals in Abuja, Nigeria. *Asian Journal of Pharmaceutical and Health Sciences,* 10 (4), 2538 - 2552.

Artika, I. M., Wiyatno, A., and Ma'roef, C. N. (2020). Pathogenic viruses: Molecular detection and characterization. Infection, *Genetics and Evolution,* 104215.

Basler, C. F. (2017, July). Molecular pathogenesis of viral hemorrhagic fever. In *Seminars in immunopathology,* 39 (5), 551-561.

Branson, B. M. (2019). HIV Diagnostics: Current

recommendations and opportunities for improvement. *Infectious Disease Clinics,* 33(3), 611-628.

Bruni, L., Barrionuevo-Rosas, L., & Albero, G. (posted on 17 June 2019). Catalan Institute of Oncology/International Agency for Research on Cancer (ICO/IARC) Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in Nigeria. Retrieved April 23, 2020, from www.hpvcentre.net.

Burrell, C. J., Howard, C. R., & Murphy, F. A. (2016). *Fenner and White's Medical Virology*. India: Academic Press.

Carroll, K. C., Butel, J., & Morse, S. (2015). *Jawetz Melnick and Adelbergs Medical Microbiology 27 E.* China: McGraw-Hill Education.

Drews, S. J. (2016). The taxonomy, classification, and characterization of medically important viruses. *Clinical Virology Manual*, 1-25.

Elliott, T., Casey, A., Lambert, P. A., & Sandoe, J. (2012). *Lecture Notes: Medical Microbiology and Infection*. Chichester, United Kingdom: John Wiley and Sons.

Eze, J. C., Ibeziako, N. S., Ikefuna, A. N., Nwokoye, I. C., Uleanya, N. D., & Ilechukwu, G. C. (2014). Prevalence and risk factors for hepatitis C and human immunodeficiency virus coinfection among children in Enugu, Nigeria. *African Journal of Infectious Diseases,* 8(1), 5-8.

Fasina, F. O., Shittu, A., Lazarus, D., Tomori, O., Simonsen, L., Viboud, C., & Chowell, G. (2014). Transmission dynamics

and control of Ebola virus disease outbreak in Nigeria, July to September 2014. *Eurosurveillance,* 19(40), 20920.

Forterre, P., & Prangishvili, D. (2009). The origin of viruses. *Research in Microbiology,* 160(7), 466-472.

Forterre, P. (2006). The origin of viruses and their possible roles in major evolutionary transitions. *Virus Research,* 117(1), 5-16.

Goldsmith, C. S., & Miller, S. E. (2009). Modern uses of electron microscopy for detection of viruses. *Clinical Microbiology Reviews*, *22*(4), 552-563.

Hematian, A., Sadeghifard, N., Mohebi, R., Taherikalani, M., Nasrolahi, A., Amraei, M., & Ghafourian, S. (2016). Traditional and modern cell culture in virus diagnosis. *Osong Public Health and Research Perspectives*, *7*(2), 77-82.

Howley, P. M., & Knipe, D. M. (2020). *Fields Virology: Emerging Viruses*. Lippincott Williams and Wilkins.

Iduh, M. U., **Kuta, F. A.**, Abalaka, M. E, Shitu, K. O. (2018). Seroprevalence of Hepatitis C Virus amongst patients attending five selected hospitals in Niger State, Nigeria. *Journal of Biomedical Research and Clinical Practice,* 1(3), 211-219.

Iduh, M. U., **Kuta, F. A.**, Abalaka, M. E., & Shitu, K. O. (2019). Molecular detection of Hepatitis C Virus amongst patients in five selected hospitals in Niger State, Nigeria. *Journal of Biomedical Research and Clinical Practice,* 2(1), 60-69.

Isa, I., Aminu, M., Abdullahi, S. A., Sani, M. A., Usman, M. A., Esona,

M. D., & Ella, E. E. (2017). Seroprevalence of hepatitis B virus and human immunodeficiency virus infection among students in Ahmadu Bello University, Zaria, Nigeria. *Archives of Medical and Biomedical Research,* 3(2), 77-90.

Itelima, J. U. (2017). Prevalence of Hepatitis B and C in Jos, Plateau State, Nigeria. 12th World Congress on Virology. October 16-17, 2017 Baltimore, USA.

Jerome, K. R. (Ed.). (2016). *Lennette's laboratory diagnosis of viral infections*. New York: CRC Press. Pp. 98-197.

Knipe, D. M., & Howley, P. (2013). *Fields virology*. United States: Lippincott Williams and Wilkins.

Kuta, **F. A.**, Uba, A. Nimzing, L. & Oyawoye, O. M. (2015). Molecular Identification of human rotavirus strains involved in gastroenteritis among children in Federal Capital Territory Abuja, Nigeria. *Elixir Biosciences Journal*, 78(2015), 29825 – 29828.

Kuta, **F. A.**, Damisa, D., Uba, A. Nimzing, L. & Adabara, N. U. (2013). Epidemiology and Molecular Identification of Rotavirus strains associated with gastroenteritis among children in Niger State. *Nigeria Journal of Technological Research*, 8(2), 68-71.

Kuta, **F. A.**, Damisa, D., Nimzing, L., Uba, A. and Yusuf, I. Z. (2014). Genetic variation of Human Rotavirus Strains involved in gastroenteritis among children in Nasarawa State. Development *Journal of science and Technology Research,* 3(1), 60-66.

Kuta F. A., Damisa, D. & Molokwu, O. (2013). Epidemiological study of Hepatitis C virus surface antigen among students of Federal University of Technology, Minna, Niger State, Nigeria. *Biological and Environmental Sciences Journal for the Tropics,* 10(1), 68-70.

Laing, K. (2013). Immune responses to viruses. Pathogens and disease. Retrieved April 23, 2020, from https://www.immunology.org/public-information/bitesized-immunology/pathogens-and-disease/immune-responses-viruses.

Littler, E., & Oberg, B. (2005). Achievements and challenges in antiviral drug discovery. *Antiviral Chemistry and Chemotherapy,* 16(3), 155-168.

MacLachlan, N. J. & Dubovi, E. J. (Ed.). (2017). Laboratory Diagnosis of Viral Infections: In *Fenner's Veterinary Virology (Fifth Edition).* Academic Press*,* pp.105-129.

Magaji, S. J., Aminu, M., Inabo, H. I., & Oguntayo, A. O. (2019). Spectrum of high risk human papillomavirus types in women in Kaduna State, Nigeria. *Annals of African Medicine,* 18(1), 30-35.

Muhammad, F., Abdulkareem, J. H., & Chowdhury, A. A. (2017). Major public health problems in Nigeria: a Review. *South East Asia Journal of Public Health,* 7(1), 6-11.

National Agency for the Control of AIDS (NACA), (2020). Nigeria Prevalence Rate. Available at https://naca.gov.ng/nigeria-prevalence-rate/ (Accessed: 19 February, 2020).

Nigeria Centre for Disease Control (NCDC) (2020). (Published: 2016-2020). Lassa Virus situation Report December, 2016 to 23 February, 2020). Available at https://ncdc.gov.ng/diseases/sireps/?cat=5andname=an%20updateof%20Lassa%20fever%20outbreakin%20Nigeria.

Ochei, J. & Kolhatkar, A. (2007). *Medical laboratory science theory and practice.* 5th Ed., McGraw-Hill, New Delhi, India, pp: 788-812.

Okonkwo, U. C., Okpara, H., Otu, A., Ameh, S., Ogarekpe, Y., Osim, H., & Inyama, M. (2017). Prevalence of Hepatitis B, Hepatitis C and human immunodeficiency viruses, and evaluation of risk factors for transmission: Report of a population screening in Nigeria. *South African Medical Journal,* 107(4), 346-351.

Okunade, K. S., Nwogu, C. M., Oluwole, A. A., & Anorlu, R. I. (2017). Prevalence and risk factors for genital high-risk human papillomavirus infection among women attending the outpatient clinics of a university teaching hospital in Lagos, Nigeria. *Pan African Medical Journal,* 28(1), 1-7.

Olayinka, A. T., Oyemakinde, A., Balogun, M. S., Ajudua, A., Nguku, P., Aderinola, M., Egwuenu-Oladejo, A., Ajisegiri, S. W., Sha'aibu, S., Musa, B. O., Gidado, S., & Nasidi, A. (2016). Seroprevalence of Hepatitis B Infection in Nigeria: A National Survey. *The American Journal of Tropical Medicine and Hygiene,* 95(4), 902–907.

Omotola, C. A., Olusola, B. A., & Odiabo, G. N. N. (2016). Rotavirus infection among under five children presenting with gastroenteritis in Ibadan, Nigeria. *Archives of Basic and Applied Medicine,* 4(1), 44-49.

Orah, N. O., & Banjo, A. A. (2018). Prevalence and distribution of high risk human papillomavirus subtypes in invasive cervical cancer in South-West Nigeria. *Annals of Tropical Pathology,* 9(2), 106-110.

Oshun, P. O., & Odeghe, E. (2019). Prevalence of Hepatitis C virus and HIV among adults presenting for health screening in Lagos. *African Journal of Clinical and Experimental Microbiology,* 20(2), 143-149.

Parvez, M. K., & Parveen, S. (2017). Evolution and emergence of pathogenic viruses: past, present, and future. *Intervirology,* 60(1-2), 1-7.

Samani, Z. N., & Kopaei, M. R. (2018). Effective medicinal plants in treating Hepatitis B. *International Journal of Pharmaceutical Sciences and Research,* 9(9), 3589-3596.

Siddiqui, M. H., Alamri, S. A., Al-Whaibi, M. H., Hussain, Z., Ali, H. M., & El-Zaidy, M. E. (2017). A mini-review of anti-hepatitis B virus activity of medicinal plants. *Biotechnology and Biotechnological Equipment,* 31(1), 9-15.

Stanaway, J. D., Flaxman, A. D., Naghavi, M., Fitzmaurice, C., Vos, T., Abubakar, I., & Forouzanfour, M. H. (2016). The global burden of viral hepatitis from 1990 to 2013: Findings from the Global Burden of Disease Study 2013. *The Lancet,* 388(10049), 1081-1088.

UNAIDS/AIDS estimates (2018). Summary of the global HIV epidemics (2018). Available at https://www.who.int/gho/hiv/en/. (Accessed: 19 February, 2020).

Wessner, D. R. (2010). The origins of viruses. *Nature Education*, *3*(9), 37.

WHO Africa (Published 1 August 2018). World Hepatitis Day: Ministry of Health Launches National Health Facility Directory for Viral Hepatitis. https://reliefweb.int/report/nigeria/world-hepatitis-day-ministry-health-launches-national-health-facility-directory-viral

WHO. (10 February 2020). Ebola virus disease. https://www.who.int/news-room/fact-sheets/detail/ebola-virus-disease. (Accessed: 19 February, 2020).

A BRIEF PROFILE OF THE INAUGURAL LECTURER

Professor Faruk Adamu Kuta was born on 26th October 1972 in Kuta (Niger State, Nigeria) to the family of Mall. Abdullahi Masu and Mallama Hauwa Abdullahi. He attended Central Primary School (now Dr. Idris Ibrahim Primary School), Kuta from 1976 to 1981. He gained admission into Government Science Teachers College, Wushishi where he had his post-primary education from 1981 to 1986. He proceeded to Usmanu Danfodiyo University, Sokoto in 1994 and graduated with a Bachelor of Science (B.Sc.) degree in Microbiology in 1998. Faruk Kuta was deployed to Borno State for his National Service during 1999/2000 service year and he served at School of Health Technology, Maiduguri.

He enrolled for his Master's degree in the year 2001 at Federal University of Technology, Minna and obtained his master's degree (MTech) in Pharmaceutical Microbiology in the year 2004.

Prof. Faruk Kuta joined the services of the Federal University of Technology, Minna on 27th July 2005 as Lecturer II in the Department of Microbiology.

He gained admission for his PhD programme at Abubakar Tafawa Balewa University (ATBU), Bauchi in 2007 and graduated with a Doctor of Philosophy in Medical Microbiology with research interest in Virology in the year 2012.

Professor Faruk Adamu Kuta rose through the academic ranks as

follows: Lecturer II (2005 - 2008), Lecturer I (2008 - 2012), Senior Lecturer (2012 - 2015), Associate Professor (2015 - 2018) and Professor (2018).

Professor Faruk Adamu Kuta has held many positions in the University such as Departmental examination officer (2007 - 2008), Deputy Dean, School of Natural and Applied Sciences (2012-2014), Deputy Dean, School of Life Sciences (2014 - 2017), Deputy Director, Academic Planning Unit (2017), Head of Microbiology Department (2017 - 2020), Director Academic Planning Unit (2020) and was a member of the University Governing Council (2016 - 2020).

He is a member of many professional bodies including the Nigerian Society for Microbiology, American Society of Microbiology, Biotechnology Society of Nigeria and European Society of Virology.

Professor Faruk Adamu Kuta has supervised over fifty undergraduate projects, more than ten Master's theses and four PhD students.

He is an external examiner to many Universities and Polytechnics at both undergraduate and post graduate levels.

He has attended many local and international conferences. He has over fifty scholarly publications in reputable Journals. Professor Faruk Adamu Kuta is married with two children.

Note

Note