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Review Article

REVIEW ON EBOLA VIRUS

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ABSTRACT

This review consist of what is Ebola virus and its origin. Its etiology, pathology, sign & symptoms and various aspects of Ebola virus. In this the life cycle of Ebola is also explain how it work. Management of Ebola virus patient.

Keywords: Ebola virus, Filoviridae, Viral hemorrhagic fever, Immune system, Immunofluorescent assay.

INTRODUCTION

Ebola virus, a member of the Filoviridae, burst from obscurity with spectacular outbreaks of severe, haemorrhagic fever. It was first associated with an outbreak of 318 cases and a case-fatality rate of 90% in Zaire and caused 150 deaths among 250 cases in Sudan. Smaller outbreaks continue to appear periodically, particularly in East, Central and southern Africa. In 1989, a haemorrhagic disease was recognized among cynomolgus macaques imported into the United States from the Philippines. Strains of Ebola virus were isolated from these monkeys. Serologic studies in the Philippines and elsewhere in Southeast Asia indicated that Ebola virus is a prevalent cause of infection among macaques (Manson 1989). The disease, also known as Ebola hemorrhagic fever or Ebola virus, kills up to 90% of people who are infected. As the virus spreads through the body, it damages the immune system and organs. Fatality rates are between 50% and 100%. This leads to severe, uncontrollable bleeding. In 2014, a major outbreak of Ebola Virus spread amongst several African countries, including Sierra Leone, Guinea, and Liberia.

The virus first appeared in the Democratic Republic of the Congo (formerly Zaire) in the summer of 1976. Ebola is a rare but deadly virus that causes bleeding inside and outside the body. Ebola belongs to a family of viruses entitled Filoviridae, and is commonly classified as a viral hemorrhagic fever (CDC, 2002). The known causes of viral hemorrhagic fever include arenaviruses, filoviruses, bunyaviruses, and flaviviruses. All virions classified as hemorrhagic are enveloped (covered) RNA viruses, whose survival is dependent on an animal reservoir. Viral hemorrhagic fever commonly describes a medical scenario in which multiple organ systems of the body are affected as well as extensive internal hemorrhaging (bleeding) (WHO,2000). Ebola along with the Marburg virus are the only viruses identified in the Filoviridae family (CDC, 2002). Filovirus virions are characterized by having one molecule of single stranded, negative-sense RNA, as well as their unique "U" shaped structures (CDC, 2002).

There are four known constituents of Ebola namely: Ebola-Zaire, Ebola-Sudan, and Ebola-Ivory Coast. The fourth, Ebola-Reston (CDC,2002). Only three of the four forms listed above are known to cause disease in humans. Ebola Reston is characterized as a non-human primate infections disease. Ebola itself has an average length 920 nm and a diameter of 80 nm

(WHO,2000). The virus is considered a level 4 biohazard and is only handled in the most sterile environments in full protective suiting. Ebola is spread through direct contact with blood or other bodily secretion of infected people (CDC, 2002) (WHO, 2000). This close proximity infection, makes outbreaks among small communities and families very common. Infection can also be caused through contact with contaminated medical equipment such as needles, glassware, no sterile equipment, or careless lab procedures. The Ebola virus is diagnosed by specific antigens detected in blood specimens, isolation of virus in cell cultures, or detection of IgM and IgG antibodies(WHO,2000) . ELISA tests are often used to diagnose the viruses. It should be noted that all tests are conducted in the most stringent laboratory conditions in order to protect scientists and other patients. There is no established treatment for Ebola. Infected patients are treated using antiviral drugs (ribavirin) as well as generally supportive therapy that replenishes intravenous fluids, maintains blood pressure, and other bodily functions (CDC, 2002). Below is a 3D image of Ribavirin, a drug commonly used in treatment of hemorrhagic fevers that acts as an RNA mutagen on the virion particles.

These threadlike polymorphic viruses are highly variable in length apparently owing to concatemerization. However, the average length of an infectious virion appears to be 920 nm. The virions are 80 nm in diameter with a helical nucleocapsid, a membrane made of 10 nm projections, and host cell membrane. They contain a unique single-stranded molecule of noninfectious (negative sense) RNA. The virus is composed of 7 polypeptides, a nucleoprotein, a glycoprotein, a polymerase and 4 other undesignated proteins. Proteins are produced from polyadenylated monocistronic mRNA species transcribed from virus RNA. The replication in and destruction of the host cell is rapid and produces a large number of viruses budding from the cell membrane.

Epidemics have resulted from person to person transmission, nosocomial spread or laboratory infections. The mode of primary infection and the natural ecology of these viruses are unknown. Association with bats has been implicated directly in at least 2 episodes when individuals entered the same bat-filled cave in Eastern Kenya. Ebola infections in Sudan in 1976 and 1979 occurred in workers of a cotton factory containing thousands of bats in the roof. However, in all instances, study of antibody in bats failed to detect evidence of infection, and no virus was isolated form bat tissue. The index case in 1976 was never identified, but this large outbreak resulted in 280 deaths of 318 infections. The outbreak was primarily the result of person to person spread and transmission by contaminated needles in outpatient and inpatient departments of a hospital and subsequent person to person spread in surrounding villages. In serosurveys in Zaire, antibody prevalence to Ebola virus has been 3 to 7%. The incubation period for needle- transmitted Ebola virus is 5 to 7 days and that for person to person transmitted disease is 6 to 12 days.

The virus spreads through the blood and is replicated in many organs. The histopathologic change is focal necrosis in these organs, including the liver, lymphatic organs, kidneys, ovaries and testes. The central lesions appear to be those affecting the vascular endothelium and the platelets. The resulting manifestations are bleeding, especially in the mucosa, abdomen, pericardium and vagina. Capillary leakage appears to lead to loss of intravascular volume, bleeding, shock and the acute respiratory disorder seen in fatal cases. Patients die of intractable shock. Those with severe illness often have sustained high fevers and are delirious, combative and difficult to control.

Ebola virus (EBOV) is considered one of the most aggressive infectious agents and is capable of causing death in humans and nonhuman primates (NHPs) within days of exposure. Recent strategies have succeeded in preventing acquisition of infection in NHPs after treatment; however, these strategies are only successful when administered before or minutes after infection. The present work shows that a combination of three neutralizing monoclonal antibodies (mAbs) directed against the Ebola

envelope glycoprotein (GP) resulted in complete survival (four of four cynomolgus macaques) with no apparent side effects when three doses were administered 3 days apart beginning at 24 hours after a lethal challenge with EBOV. The same treatment initiated 48 hours after lethal challenge with EBOV resulted in two of four cynomolgus macaques fully recovering. The survivors demonstrated an EBOV-GP–specific humoral and cell-mediated immune response. These data highlight the important role of antibodies to control EBOV replication in vivo, and support the use of mAbs against a severe filovirus.

EBOLA AND THE IMMUNE SYSTEM

Interaction of Ebola with the immune system is essential to understanding the pathogenesis of the virus. One of the characteristics of infection with the Ebola virus is the destruction of the immune system. The majority of patients infected with the virus are unable to develop sufficient immune responses. This is mainly attributed to the viruses infection of the fibroblastic reticular system, which plays a role in maximizing immune responses (Takada, 2001). Scientists speculate that disruption of cytokine production is affected by infection of both fibroblastic reticular system and mononuclear phagocytes, in addition to disruption of antigen trafficking (Takada, 2001). It is also thought that transmission of virions between tissues is partially due to infection from macrophages and circulating monocytes. One of the primary failures of the immune system in regards the Ebola virus, is the inability to activate T-cells early in the course of the infection resulting in an insufficient humoral response which include both antibody and cytokine responses(Takada, 2001). Another result of the failure to activated T-cells adequately is apoptosis of blood leukocytes (Takada, 2001). These characteristics of Ebola infection are commonly associated with fatality in patients. In both fatally infected patients and experimentally infected monkeys, the virus was found to cause extensive damage to lymph nodes, spleen, and bone marrow. Patients surviving infection by Ebola virions were found to develop stronger antibody responses in the early stages of infection than patients who eventually succumbed to the disease (Takada, 2001). The role of the innate immune response in the first few days of infection is considered very important in control of viral replication. Conversely up regulation of interluken 2, 10, tumor necrosis factor, and interferons are associated with infection of the Ebola virus (Takada, 2001) . Although their role is poorly understood, antibodies are thought to play an essential role in inhibiting infection of Ebola (Maruyama, 1999). Antibodies have been found that bind to the nucleoprotein, the envelope protein, and the secreted envelope glycoprotein (see Fig. 4 below). Studies have shown that neutralizing antibodies made in response to these glycoproteins are effective against the Ebola virus and show some promise in designing a vaccine (Maruyama, 1999). VP35 (see diagram above) is thought to play a pivotal role in the synthesis of viral RNA, serving as an interferon antagonist. The production of INF antagonist is thought to be an essential factor to increasing the pathogenicity of the Ebola Virus. There is a very strong possibility that the potency of VP35 could account for the varying degrees of virulence among different strains of the Ebola virus (Takada, 2001). Immunsupression of the Ebola virus is largely attributed to a section of the glycoprotein (see diagram above: G1 and G2), which shares a strking homology to another immunosuppressive protein found in oncogenic retroviruses (Takada, 2001). This particular sequence is thought to aid the Ebola virus in evading the human immune responses in addition to suppressing the major histocompatibility complex (MHC) (Takada, 2001).

SIGN AND SYMPTOMS

Symptoms characterizing Ebola are unspecific in the first few days of the infection, making the virus even more dangerous. Infection is marked by initial signs of fever, fatigue, exhaustion, muscle aches, and dizziness (WHO, 2000). As the disease progress bleeding under the skin, in internal organs, and from the eyes, ears, and mouth are seen. Patients with severe progressions

of the disease express symptoms of shock, delirium, coma, seizures, and nervous system malfunction (CDC, 2002). Incubation ranges from 2 to 21 days. High fever, Headache, Joint and muscle aches, Sore throat, Weakness, Stomach pain, Lack of appetite.

Stage I (Unspecific)

- Extreme asthenia (body weakness)
- Diarrhea, nausea and vomiting, anorexia abdominal pain
- Headaches
- Arthralgia (neuralgic pain in joints)
- Myalgia (muscular pain or tenderness), back pain
- Mucosal redness of the oral cavity, dysphagia (difficulty in swallowing)
- Conjunctivitis
- Rash all over body except in face

** If the patients don't recover gradually at this point, there is a high probability that the disease will progress to the second phase, resulting in complications which eventually lead to death (Mupapa et al., 1999**).**

Stage II (Specific)

- Hemorrhage
- Neuropsychiatric abnormalities
- Anuria (the absence of urine formation)
- Hiccups
- Tachypnea (rapid breathing).

** Patients who progressed to phase two EHF almost always die. (Ndambi et al., 1999)

Late Complications

- Arthralgia
- Ocular diseases (ocular pain, photophobia and hyperlacrimation)
- Hearing loss
- Unilateral orchitis (inflammation of one or both of the testes)

** These conditions are usually relieved with the treatment of 1% atropine and steroids

As the disease gets worse, it causes bleeding inside the body, as well as from the eyes, ears, and nose. Some people will vomit or cough up blood, have bloody diarrhea, and get a rash.

BOLA SEROLOGY

The serologic method used in the discovery of Ebola was the direct immunofluorescent assay. The test is performed on a monolayer of infected and uninfected cells fixed on a microscopic slide. IgG- or IgM-specific immunoglobulin assays are performed. These tests may then be confirmed by using western blot or radio immuno precipitation. Virus isolation is also a highly useful diagnostic method, and is performed on suitably preserved serum, blood or tissue specimens stored at -70oC or freshly collected.

TREATMENT OF EBOLA

RECENT RESEARCH ON EBOLA MEDICATIONS

As of Aug 14, 2014, the FDA has approved no medications or vaccines to treat or prevent Ebola and advises people to watch out for fraudulent products. The unavailability of experimental treatments in the most affected regions during the 2014 outbreak spurred controversy, with some calling for experimental drugs to be made more widely available in Africa on a humanitarian basis, and others warning that making unproven experimental drugs widely available would be unethical, especially in light of past experimentation conducted in developing countries by Western drug companies. On 12 August the WHO released a statement that the use of not yet proven treatments is ethical in certain situations in an effort to treat or prevent the disease. In July 2014, an experimental drug, Z Mapp, was first tested on humans. It was administered to two Americans who had been infected with Ebola. Both people appeared to have had positive results. Z Mapp was also administered to a third person with Ebola, a 75 year old Spanish priest, who died and three Liberian health workers who showed improvement. Favipiravir looks like it may be useful in a mouse model of the disease. Estrogen receptor drugs used to treat infertility and breast cancer (clomiphene and toremifene) inhibit the progress of Ebola virus in infected mice. Ninety percent of the mice treated with clomiphene and fifty percent of those treated with toremifene survived the tests. A 2014 study found that Amiodarone, an ion channel blocker used in the

treatment of heart arrhythmias, blocks the entry of ebola virus into cells *in vitro*. Given their oral availability and history of human use, these drugs would be candidates for treating Ebola virus infection in remote geographical locations, either on their own or together with other antiviral drugs.

Antibodies

Researchers looking at slides of cultures of cells that make monoclonal antibodies. These are grown in a lab and the researchers are analyzing the products to select the most promising of them. During an outbreak 1999 in the Democratic Republic of the Congo, seven of eight Ebola patients who received blood transfusions from individuals who had previously survived the infection survived themselves. However, this potential treatment is considered controversial. Intravenous antibodies appear to be protective in non-human primates who have been exposed to large doses of Ebola.

Other Treatments

Other promising treatments rely on antisense technology. Both small interfering RNAs (siRNAs) and phosphorodiamidate morpholino oligomers (PMOs) targeting the Zaire Ebola virus (ZEBOV) RNA polymerase L protein could prevent disease in nonhuman primates. TKM-Ebola is a small-interfering RNA compound, currently tested in a phase I clinical trial in people. No specific antiviral therapy presently exists against Ebola virus, nor does interferon have any effect. Supportive management of infected patients is the primary method of treatment, with particular attention to maintenance of hydration, circulatory volume, blood pressure, and the provision of supplemental oxygen. There is no specific treatment outside of supportive management and palliative care. As of the present, there are no licensed vaccines or specific antiviral treatments available for Ebola virus infections. Past recommendations for isolation of the patient in a plastic isolator have given way to the more moderate recommendation of strict barrier isolation with body fluid precautions. This presents no excess risk to the hospital personnel and allows substantially better patient care. The major factor in nosocomial transmission is the combination of the unawareness of the possibility of the disease by a worker who is also inattentive to the requirements of effective barrier nursing. After diagnosis, the risk of nosocomial transmission is small.

PREVENTION AND CONTROL OF EBOLA

The basic method of prevention and control is the interruption of person to person spread of the virus. However, in rural areas, this may be difficult because families are often reluctant to admit members to the hospital because of limited resources and the culturally unacceptable separation of sick or dying patients from the care of their family. Experience with human disease and primate infection suggests that a vaccine inducing a strong cell- mediated response will be necessary for virus clearance and adequate protection. Neutralizing antibodies are not observed in convalescent patients nor do they occur in primates inoculated with killed vaccine. A vaccine expressing the glycoprotein in vaccinia is being prepared for laboratory evaluation.

POSSIBILITIES FOR CURE

Recently a protein known as cyanovirin-N found in blue-green algae has become associated with both HIV and the Ebola Virus. Cyanovirin has been found to partially inhibit the ability of both Ebola and HIV to bind and infect cells, there-by extending the host's survival time (Barrientos, 2003). Cyanovirin has been found to bind to the outside of cells there by inhibiting their ability to cross the cellular membranes (Barrientos, 2003). Cyanovirin shows promise in its ability to attatch to sugar molecules found on the surface of both HIV and the Ebola virus (Barrientos, 2003). Research trials have been performed using animal models, in which test animals were infect with Ebola and given injections of cyanovirin once a day. This trial resulted in a delay in the onset of the disease, and longer survival in those animals injected with the protein than in those that were not injected (Barrientos, 2003). Below is a 3D chime image of the protein Cyanovirin.

ANTIBODIES TO CONTROL EBOV REPLICATION IN VIVO & SUPPORT THE USE OF MABS AGAINST A SEVERE FILOVIRUS INFECTION

Ebola virus (EBOV) is considered one of the most aggressive infectious agents and is capable of causing death in humans and nonhuman primates (NHPs) within days of exposure. Recent strategies have succeeded in preventing acquisition of infection in NHPs after treatment; however, these strategies are only successful when administered before or minutes after infection. The present work shows that a combination of three neutralizing monoclonal antibodies (mAbs) directed against the Ebola envelope glycoprotein (GP) resulted in complete survival (four of four cynomolgus macaques) with no apparent side effects when three doses were administered 3 days apart beginning at 24 hours after a lethal challenge with EBOV. The same treatment initiated 48 hours after lethal challenge with EBOV resulted in two of four cynomolgus macaques fully recovering. The survivors demonstrated an EBOV-GP–specific humoral and cell-mediated immune response. These data highlight the important role of antibodies to control EBOV replication in vivo, and support the use of mAbs against a severe filovirus infection. Ebola virus (EBOV) can cause a fulminant infection and rapid progression to death in up to 90% of infected humans. EBOV infection in humans or macaques results in the development of clinical sequelae with a high degree of similarity, justifying the use of macaques as the most relevant model of human infection. Pigs are the only other animal lethally infected by a non-adapted EBOV; however, the disease in pigs is more respiratory in nature, and therefore different from humans. African green monkeys, hamadryad baboons, cynomolgus macaques, and rhesus macaques have all been used as nonhuman primate (NHP) filovirus infection models Because African green monkeys and hamadryad baboons are somewhat resistant to some filoviruses, both cynomolgus and rhesus macaques have been routinely used for the study of EBOV, and both show the same disease profile for EBOV infections.

Although of relatively low consequence to public health worldwide, EBOV infections are a public health concern because of the high mortality rate and lack of prophylactic/therapeutic interventions. Recent advances in vaccine development against EBOV resulted in the identification of several successful immunization strategies to mount protective immune responses to macaques. The vesicular stomatitis virus (VSV)–based Ebola vaccine resulted in 50% protection in rhesus macaques when administered 20 to 30 min after a lethal challenge with EBOV. This finding demonstrated that fast-acting therapeutic interventions could be developed to protect macaques against a lethal EBOV exposure.

Indeed, other treatment protocols that provided partial survival in macaques have been identified. Continuous intravenous infusion for 7 days beginning 30 to 60 min after EBOV infection with recombinant human activated protein C (rhAPC), which inhibits blood coagulation and inflammation while promoting fibrinolysis, resulted in an 18% survival. Another inhibitor of coagulation, recombinant nematode anticoagulant protein c2 (rNAPc2), resulted in 33% survival if given subcutaneously 10 minutes or 24 hours after EBOV challenge and treated daily for 14 or 8 days, respectively. Another type of therapy, antisense therapy for RNA viruses such as EBOV, was tested using a positively charged phosphorodiamidate morpholino oligomers (PMOplus), which is a synthetic antisense oligonucleotide analog that interferes with translation by forming base-pair duplexes with specific RNA sequences. PMOplus delivered by a combination of intraperitoneal and subcutaneous doses initiated 30 to 60 min after infection for 10 to 14 days resulted in 62.5% surviving the EBOV challenge. More recently, daily intravenous administration of small interfering RNAs (siRNAs) targeting the EBOV genome showed a 66% survival rate with four intravenous doses and 100% with seven doses. Notably, all these

strategies required initiation within 20 to 60 min of virus challenge. All of the above studies for studying treatment protocols implemented after infection were conducted in rhesus macaques over cynomolgus macaques, largely because the average time to death in rhesus macaques is about 2 days longer thereby offering more time for successful clinical intervention. Passive antibody transfer has also been investigated for EBOV treatment, with inconsistent results. Initially, whole blood from convalescing survivors of the 1995 Kikwit outbreak was given to EBOV-positive patients displaying symptoms. A marked improvement was seen: Seven of eight patients survived. However, in later studies, cynomolgus macaques were not protected when treated with purified equine immunoglobulin G (IgG) from EBOV-hypervaccinated horses. The neutralizing monoclonal antibody (mAb) KZ52 provided complete protection in guinea pigs when given 1 hour before or after infection but failed to protect NHPs. Despite these inconsistent results, there is evidence that a strong early humoral immune response correlates with survival. Therefore, we optimized a treatment protocol with three of eight EBOV glycoprotein (GP)-specific mAbs (1H3, 2G4, and 4G7) that were previously generated from mice vaccinated with the VSVΔG/EBOV-GP vaccine. In enzyme-linked immunosorbent assays (ELISAs), mAb 2G4 bound to GP2, and 4G7 bound to epitopes in the C-terminal portion of GP1 of the EBOV-GP, whereas 1H3 bound to the soluble GP (sGP) portion (amino acids 1 to 295). None of these EBOV-GP–specific mAbs are cross-reactive with Marburg virus or other EBOV species but did react with other EBOV strains. Individually, these antibodies protected mice and were more efficacious when administered 24 or 48 hours after the infection than at 1 to 4 days before infection. Although individually the antibodies were less protective in guinea pigs, a combination of the three neutralizing antibodies (1H3 + 2G4 + 4G7: 15 mg/kg combined total) was fully protective when administered on day 2 after infection.

On the basis of the success of the combination therapy in guinea pigs, the next step was to test the mAb cocktail in the NHP model. The current study builds upon the optimized treatment protocol in rodent experiments presents a combination of three neutralizing mAbs (named ZMAb) to treat NHPs that have been infected with EBOV, and examines their survival, clinical manifestations, and immune response to the EBOV infection

SELECTIVE PRESSURES AND CONSTRAINTS

It is of interest to determine, what, if any, limits are placed on virus variation. Despite high mutation rates and opportunities for genetic reassortment, many factors act to minimize emergence of new influenza A epidemics (Morse and Schluederberg 1988), even though avian and human influenza viruses are widespread (in humans an estimated 100 million infections yearly), pandemic influenza viruses emerge infrequently (every 10-40 years). Powerful constraints appear to exist since pandemic human influenza strains vary in their H gene, whereas the neuraminidase and most other genes are conserved.

These constraints on viral evolution are not surprising when one considers the selective pressures imposed by the host at each stage of the virus life cycle. Tissue tropism determinants include site of entry, viral attachment proteins, host cell receptors, tissue- specific genetic elements (for example promoters), host cell enzymes (like proteinase), host transcription factors, and host resistance factors such as age, nutrition and immunity. Host factors contribute significantly: sequences such as hormonally responsive promoter elements and transcriptional regulatory factors can link viral expression to cell state.

The interaction of virus and host is thus complex but highly ordered, and can be altered by changing a variety of conditions. Unlike bacterial virulence, which is largely mediated by bacterial toxins and virulence factors, viral virulence often depends on host factors, such as cellular enzymes that cleave key viral molecules. Because virulence is multigenic, defects in almost any viral gene may attenuate a virus. For example,

some reassortments of avian influenza viruses are less virulent in primates than are either parental strain, indicating that virulence is multigenic (Treanor and Murphy 1990). Viral and host populations can exist in equilibrium until changes in environmental conditions shift the equilibrium and favour rapid evolution (Steinhauer and Holland 1987). It seems reasonable to expect that new viruses will emerge occasionally, but the stochastic and multifactorial nature of viral evolution makes it difficult to predict such events. According to Doolittle, retrovirus evolution is sporadic, with retroviruses evolving at different rates in different situations. For instance, the human endogenous retroviral element is shared with chimpanzees, indicating no change in over 8 million years, whereas strains of HIV have diverged in mere decades. Endogenous retroviruses carried in the germline evolve slowly compared with infective retroviruses. Generation of new viral pathogens is rare, and often possible only because of high mutation rates that permit many neutral mutations to accumulate before selective pressure forces a change. The seeming unpredictability of these events ensure that recognition of new pathogens must await their emergence.

CONCLUSION

The proposed American fiscal budget for 1995 allows allocations for the CDC which remain basically the same as those for past years and the $11.5 billion budget for the National Institutes of Health includes only a modest increase for non-AIDS infectious and immunological diseases research (Cassell 1994). In view of the magnitude of the problem, this budget is unacceptable. Currently, infectious diseases remain the leading cause of death worldwide. In the United States infectious diseases directly account for 3 and indirectly account for 5 of the 10 leading causes of death, AIDS is the ninth leading cause. Infectious diseases account for 25% of all visits to physicians in the United States. In total, the annual cost of AIDS and other infectious diseases reached $120 billion in 1992, about 15% of the nation's total health-care expenditure. The expanding pool of immunodeficient patients due to the AIDS epidemic, cancer treatment, transplant recipients, and hemodialysis has caused an explosion of opportunistic infections due to a number of fungal, parasitic, viral and bacterial agents. According to the Gail H. Cassel, president of the American Society of Microbiology, the public health system is not prepared to meet the challenges of new and re-emerging infections. Perhaps the most obvious defect is inadequate disease surveillance and reporting. In America, only one-quarter of the states have a professional position dedicated to surveillance of food-borne and waterborne diseases. In 1992, only $55000 was spent on federal, state and local levels tracking drug-resistant bacterial and viral infections. In addition, the public health laboratories are eroding. Overall, CDC's budget for infectious diseases unrelated to AIDS has declined approximately 20% in the last decade. This is the case in the developed world of the United States, and we in developing South Africa are certainly no better off in terms of disease surveillance and concomitant protection. It should be clear that a mixture of basic and applied research related to infectious disease is needed. Coupled with this, better diagnostic techniques, prevention strategies and risk factor analysis is needed. Finally, enhanced communication among health care professionals and the public is integral in coming to terms and dealing with this issue. The American National Institute of Allergy and Infectious Diseases (NIAID) plans to develop a research and training infrastructure to elucidate the mechanisms of molecular evolution and drug resistance and to learn more about actual disease transmission through molecular and environmental studies and to continue their emphasis on vaccine development. For example, NIAID-funded research has already led to the creation of a new Haemophilus influenzae type B vaccine which is expected to save nearly $400 million in health-care costs each year. Similarly, the NIH spent less than $27 million dollars to find the connection between *Helicobacter pylori* and chronic peptic ulcers, yet using antibacterial therapy for the disease will save $760 million dollars in health care costs annually. Given the

diverse nature of threats from infectious diseases, it is not adequate merely to face each crisis as it emerges, as this may provide a strategy which proves to be too little and too late. Instead, a more holistic approach is required. This must include a global perspective as well as the need to address the issue of infectious disease within the context of shared environmental responsibility. Improved health care derived from socioeconomic betterment is crucial, as are long term policies involving systems thinking as opposed to the limiting nature of long term over-specialization.

Figures 1 and 2: Scanning electron micrographs of Ebola, Figure 1 was the first photograph ever taken of Ebola in 1976

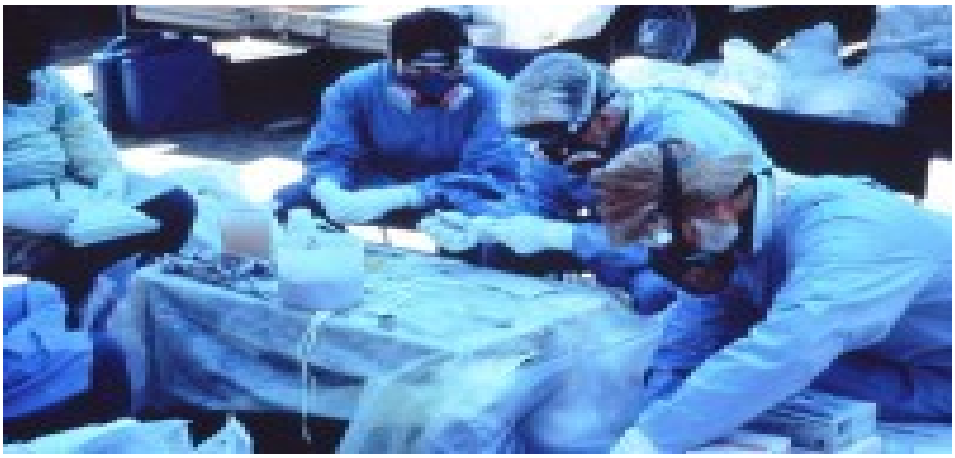

Figure 3: Scientists working with Ebola in protective clothing

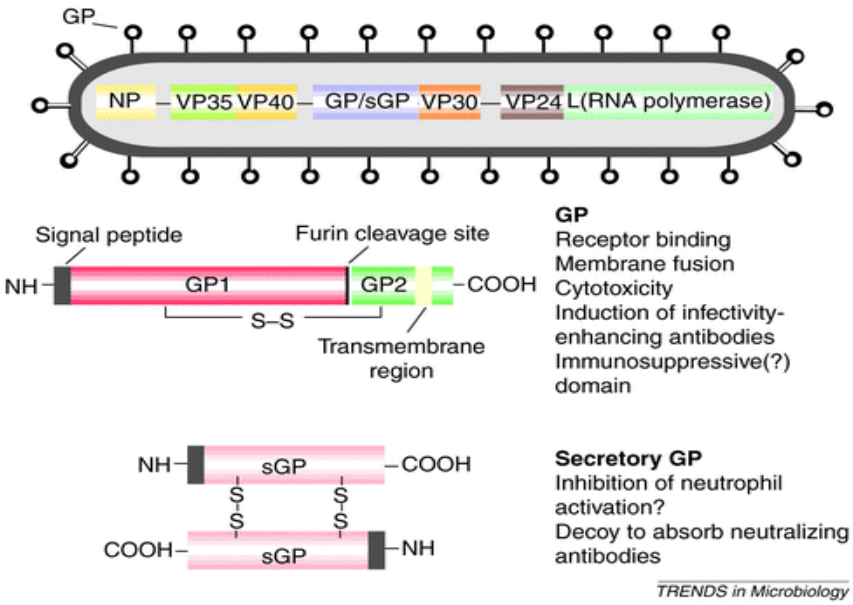

Figure 4: A protein map of Ebola viurs RNA, (Takata, 2001) permission pending. *www.bmn.com*

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