Rift Valley Fever
Human prevalence in Egypt

Thesis Submitted For Partial Fulfillment Of M.D. In Microbiology

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ABSTRACT

Rift Valley fever (RVF) is an acute, fever-causing viral disease that affects domestic animals (such as cattle, buffalo, sheep, goats, and camels) and humans. RVF is most commonly associated with mosquito-borne epidemics during years of heavy rainfall.

The disease is caused by the RVF virus, a member of the genus Phlebovirus in the family Bunyaviridae. The disease was first reported among livestock by veterinary officers in Kenya in the early 1900s.

This study was done to determine the prevalence of RVF virus in Egypt by screening IgM and IgG in a random sector of susceptible persons referred to the Central Public Health Laboratory of Ministry of Health (CPHL of MOH). The association of these antibodies to age, sex and occupation as well as regional prevalence is to be screened. This is to be compared to a control group of healthy individuals referred to (CPHL of MOH) for other check up reasons. In addition a group of other Arboviruses were IgG assayed , they are West Nile, Sandfly and Sindbis viruses, this was done to screen for the magnitude and endemicity of these viruses in relation to RVF virus.

The study revealed that there was a mild positive correlation between RVF IgM and "AGE", RVF IgG and Age, the percentage of positivity of RVF IgG for male and female was 2:1 possibly related to occupation as male jobs are mostly related to animals as there was a positive correlation between RVF IgG and "Occupation", there was a mild positive correlation between governorate and IgM, meaning that patients in certain governorate had more chances to catch infection.

There were 4 patients both RVF IgG +ve and IgM +ve, all from Dakahlia all are males all in middle age all related to animal jobs except one student who may be intimate to animals at home, there were also 3 patients RVF IgG –ve but IgM +ve, 2 from Dakahlia, males, one child of 3 years and one cattle rising of 9 years, the third was from Monofia, a 60 years old male farmer.

A mild correlation was also found between West Nile IgG and "Governorates", Sandfly IgG and "Governorate distribution”. And a moderate correlation was found between West Nile IgG and "AGE", Sandfly IgG and "AGE".

Key Words

Rift Valley Fever, Rift Valley Fever virus, Haemorrhagic Fevers, Arboviruses.

APPENDIX

EQUIPMENTS & SUPPLIES FOR IgM ASSAY:

1. ELISA Reader
2. ELISA Plate washer
3. Adjustable micropipettes (20, 200, 1000 µl)
4. Adjustable multichannel pipettor (50-200 µl)
5. Incubator
6. Microwell plates
7. Reservoir or troughs (any common plastic weigh boats work)
8. Dilution Tubes
9. Pipettor Tips (appropriate sizes).

- **REAGENTS:**

1. Anti-human IgM (gamma chain)(Affinity Purified Antibody Goat Anti-human IgM)
2. HIMAF anti-RVF (mouse)
3. Anti-mouse IgG (Affinity Purified Antibody to mouse IgG)H+L (Human Serum Adsorbed)
4. ABTS substrate
5. Skim milk (Bacto)
6. PBS (phosphate buffer saline)
7. RVF CS Ag (cell slurry)
8. Control CS Ag (cell slurry)
9. Positive serum control
10. Negative serum control
11. Normal human serum

- **EQUIPMENTS & SUPPLIES FOR IgG ASSAY:** ***(****As for IgM****).***

- **REAGENTS:**

1. Anti-human IgG (γ chain) HRP conjugate (Affinity Purified Antibody Peroxidase Labeled- Goat anti-human IgG γ).
2. ABTS substrate.

3. Skim milk (Bacto).
4. PBS (phosphate buffer saline).
5. RVF CS Ag (cell slurry) (RVF cell lysate Ag for IgG detection dissolved in 1ml PBS).
6. Control CS Ag (cell slurry).
7. Positive serum control.
8. Negative serum control.
9. Normal human serum.

INTRODUCTION AND AIM OF WORK

Historical background

The disease was first identified and reported among livestock by veterinary officers by Daubney and co-workers in Kenya in 1931, and it is endemic almost everywhere in subtropical Africa ***(Daubney et al., 1931& Peters, 1997).***

Geographic location & Geologic feature of RVF: Africa's Great Rift Valley is a 6,000 mile crack in the earth's crust, stretching from Lebanon to Mozambique. One of its most dramatic sections slices through east Africa dividing Kenya into 2 segments. Geologists know that Rift Valley was formed by violent subterranean forces that tore apart the earth's crust. These factors caused huge chunks of the crust to sink between parallel fault lines forcing up molten rock in volcanic eruptions. Kenya's Rift Valley has a geographic feature called dambos. These are shallow depressions located often near rivers filled with water during the rainy season. A dambo can be a kilometer in length and several hundreds of meters in width. Due to the frequent presence of water, tall papyrus and several other grasses grow around their edges. These dambos are breeding grounds for mosquitoes, even in the dry season as they remain greener than other areas ***(Sherine, 2000).***

As early as 1913, a disease fitting the description of RVF was blamed for the loss of sheep in the Rift Valley of Kenya. In July 1930, Kenya was hit with very heavy rains that substantially increased the wetlands where mosquitoes bred, at the same time, occurrence of the disease increased and one of the carriers for the disease was found to be the mosquito. Those studying the disease made the connection between increased rains, wetlands, mosquitoes, disease and were able to identify the associated virus. Since that time, major outbreaks have been noted throughout sub-Saharan Africa, with occasional outbreaks in other parts of the continent ***(Sherine, 2000).***

The potential of RVF as a disease emerging in new areas was documented in Egypt in 1977 ***(Laughlin et al., 1979),*** epidemics have occurred in Sudan in 1973 and 1976 ***(Eisa et al., 1977 and Eisa et al., 1980),*** Mauritania (1987 to 1988 and1998), Madagascar (1990 to 1991), Egypt (1993), and eastern Africa (in Kenya, Somalia, and Tanzania) in 1997 and 1998 ***(Sall et al., 1998 and Sall et al., 1999)***. Later on an outbreak on the Arabian Peninsula (in Yemen and Saudi Arabia) represented the first case of RVF outside Africa ***(Ahmad, 2000 and CDC, 2000).*** Then an outbreak of Rift Valley fever in humans in Egypt was reported in August of 2003 ***(OIE, 2003)***

Rift Valley fever (RVF) is an acute, fever causing viral disease that affects domestic animals (such as cattle, buffalo, sheep, goats, and camels) and humans ***(Meegan., 1979)***. RVF is most commonly associated with mosquito borne epidemics during years of heavy rainfall. ***(Linthicum. et al, 1999)*** The disease is caused by the RVF virus; a member of the genus PhIebovirus in the family Bunyaviridae ***(Sall et al, 1999)***.

In 1977, the Rift Valley Fever Virus (RVFV) was detected in Egypt (probably exported in infected domestic animals from Sudan) and caused a large number of outbreaks of RVF among animals and humans. The first epidemic of RVF in West Africa was reported in 1997 and was linked to construction of the Senegal River Project. The project caused flooding in the lower Senegal River area and altered interactions between animals and humans resulting in transmission of RVF to humans ***(Sharkawy et al, 1994)***.

Humans can get infected with the virus as a result of bites from mosquitoes and possibly other blood-sucking insects that serve as vectors. Humans can also get the disease if they are exposed to either the blood or other body fluids of infected animals. This exposure can result from the slaughtering or handling of infected animals or by touching contaminated meat during the preparation of food. Infection through aerosol transmission of RVF virus has resulted from contact with laboratory specimens containing the virus ***(Wilson, 1994)***.

RVF virus can cause several different diseases syndromes. People infected with RVFV typically have either no symptoms or mild illness associated with fever and liver abnormalities. However, in some patients the illness can progress to haemorrhagic fever (which can lead to shock & haemorrhage), encephalitis (which can lead to headaches, coma, or seizures) or ocular disease that may reach up to retinitis and loss of vision, which is the most common complication. Patients who become ill usually experience fever, generalized weakness, back pain, dizziness, and extreme weight loss at the onset of the illness. Typically, patients recover within two days to one week after onset of illness. There is no established course of treatment for patients infected with the Rural Northern virus. However, studies in monkeys and other animals have shown promise for ribavirin; an antiviral drug, for future use in humans. Additional studies suggest that interferon; immune modulators and convalescent phase plasma may also help in the treatment of patients with RVF ***(Wilson, 1994).***

A number of challenges need to work upon for the control and prevention of RVF. Knowledge regarding how the virus is transmitted among mosquitoes and the role of vertebrates in propagating the virus must be answered to predict and control future outbreaks of RVF. Vaccines for veterinary use are available, but they can cause birth defects and abortions in sheep and induce only low-level protection in cattle. The human live-attenuated vaccine, MP-1, has demonstrated promising results in laboratory trials in domestic animals, but more research will be needed before the vaccine can be used in the field. In addition, surveillance (close monitoring for RVF infection in animal and human populations) is essential to learning more about how RVF virus infection is transmitted and to formulate effective measures for reducing the number of infections ***(CDC, 2006).***

The aim of this work is to determine the prevalence of RVF in Egypt and its association to age, sex and occupation. Regional prevalence is to be assessed as well.

Rift Valley Fever Virus

RVFV was first isolated from sheep in E.Africa 1930. In man, it produces an acute, 'flu-like illness, transmitted by mosquitoes from animal reservoirs (e.g. sheep) to man leads to EPIZOOTICS. In the last decade, there have been massive outbreaks of RVF. In sub-Saharan Africa - millions of people were infected; and attack rates were of up to 35%. In January 16th, 1998, the United Nation (U.N.) Food and Agriculture Organization (FAO) warned that an outbreak of Rift Valley Fever in Kenya and Somalia thought to have killed at least 600 people risked spreading to other parts of Africa. FAO also reported that a serious outbreak of Rift Valley Fever in parts of northeastern Kenya and adjacent areas of Somalia constitutes an international emergency. Reports from the World Health Organization (WHO) recorded that, the disease has killed 300 people in Kenya and claimed another 300 lives in Somalia. Heavy flooding in parts of Kenya has brought people into closer contact than usual with animals (***AJC, 1998)***.

FAO stated that there was a high risk the disease could spread to other countries in the region. "As well as new areas of Kenya and Somalia, the countries most at risk are Sudan, Egypt, Ethiopia, Uganda, and Tanzania," The organization warned that because mosquitoes could be transported long distances on the wind there was even a risk the disease could cross the Red Sea to the Arabian Peninsula (***AJC, 1998)***. Epidemics have occurred in eastern Africa (in Kenya, Somalia, and Tanzania) in 1998 ***(Sall et al., 1998 and Sall et al., 1999)***. An outbreak on the Arabian Peninsula (in Yemen and Saudi Arabia) represented the first case of RVF outside Africa ***(Ahmad, 2000 and CDC, 2000).*** Then an outbreak of Rift Valley fever in humans in Egypt was reported in August of 2003 ***(OIE, 2003).***

The only effective means of protecting livestock was through preventative immunization, but vaccination once an epidemic has taken hold usually fails to prevent substantial livestock losses. There was no vaccine for humans until 1998 (***AJC, 1998)***, later on Phillip and his colleges concluded that the use of TSI-GSD-200 is safe and provides good long-term immunity in humans when the primary series and one boost are administered (Phillip et. al., 2000)

Classification:

Rift Valley fever (RVF) virus belongs to the genus *Phlebovirus,* family Bunyaviridae ***(Fontenille et al., 1998).***

It is one of the Arboviruses which are a large group (more than 400) of enveloped RNA viruses which are transmitted primarily (but not exclusively) by arthropod vectors (mosquitoes, sand flies, fleas, ticks, lice, etc) & which were previously grouped together under the name 'Arboviruses'. More recently, this disordered assemblage has been split into four bona fide virus families (**table 1).**

Mostly, these viruses are relatively fragile (e.g. not resistant to desiccation), therefore, many are reliant on vector for transmission. This dependency tends to limit them to tropical & sub-tropical regions with some exceptions e.g. rubella). They have complex life cycles & replicate in both the primary hosts, secondary hosts (which may often be dead-ends) & the arthropod vectors. Therefore, there may be several animal reservoirs for

each virus. Eradication would be practically impossible & the best approach is to block transmission by human vaccination and eradication of the vector (e.g. mosquitoes) ***(Midline Plus Medical Encyclopedia, 2007)***

Table 1: Classification of Arboviruses

Family:	Genus:	Type Species:	# Serotypes:
Togaviridae	Alphavirus	Sindbis	27 serotypes
	Rubivirus	Rubella	1 serotype
Flaviviridae	Flavivirus	Yellow fever, West Nile	69 serotypes
	Pestivirus	Bovine-viral-diarrhoea	3 serotypes
	Hepatitis-C-virus	HCV	Variable
Bunyaviridae	Bunyavirus	Bunyamwera	168 serotypes
	Hantavirus	Hantaan	32 serotypes
	Phlebovirus	Sandfly fever, Rift Valley fever	51serotypes,>200serotypes
	Nairovirus	Crimean-Congo haemorrhagic fever	35 serotypes
	Tospovirus	Tomato spotted wilt	2 serotypes
	Unassigned		42 serotypes
Arenaviridae	Arenavirus	Lymphocytic choriomeningitis	17 serotypes

(Midline plus Medical Encyclopedia, 2007).

The virion: Fig. (1&2)

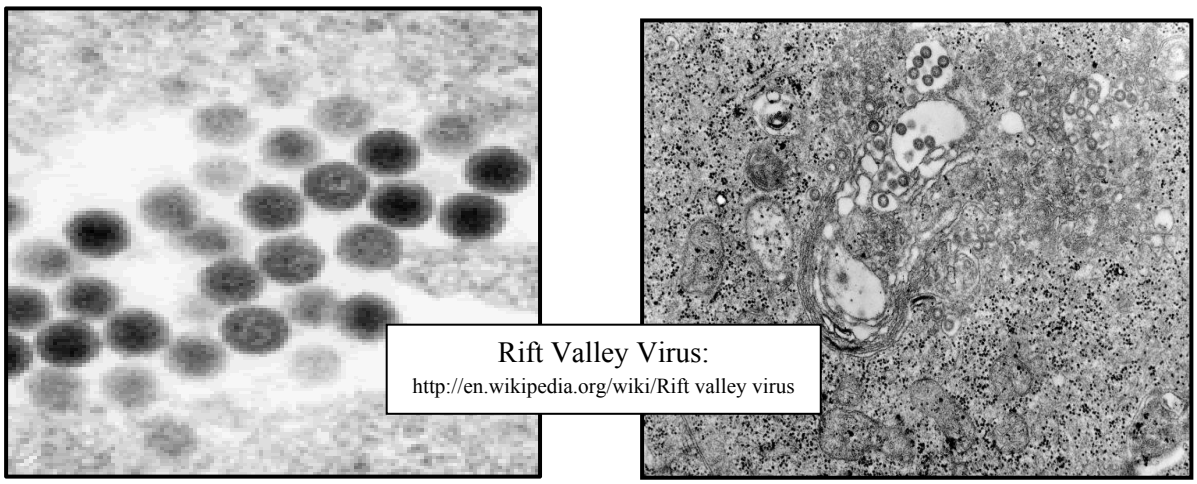

Fig. (1&2) E/M picture of Rift Valley Virus

RVFV belongs to the *Bunyaviridae* family (genus *Phlebovirus*), a family of spherical enveloped viruses with a tripartite RNA genome of negative or ambisense polarity ***(Schmaljohn, et al.,2001).***The RVF virus is a RNA lipid-enveloped spherical structure, 80 nm to 120 nm in diameter and contains 5-nm to 10-nm surface spikes (G1 and G2). The virus has a helical nucleocapsid and three single-stranded negative sense and ambisense (L, M, S) RNAs. The virus lipid envelope contains 20-30% lipids totally derived from the host cell membrane. The virion spikes mediate the attachment of the virus to the host cell receptors, serve as hemagglutinin and are the targets for the host's neutralizing antibodies ***(Sherine, 2000).***

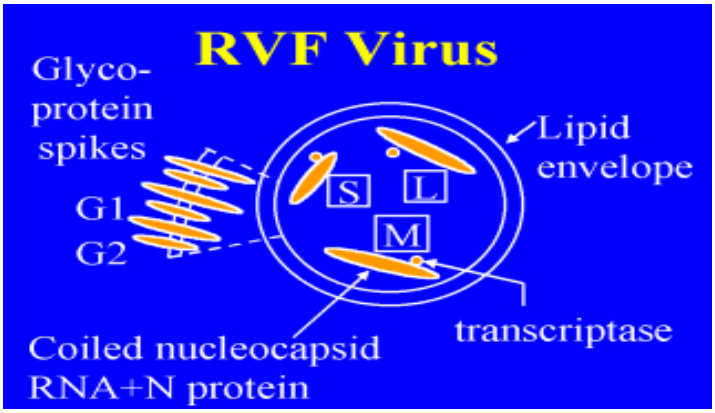

Fig. (3): Diagramatic Picture of RVF ***(Sherine, 2000).***

The largest segment, named L, codes for an RNA-dependent RNA polymerase (L protein). The M segment codes for a precursor to two virion glycoproteins (G1 and G2) and, in some cases, for a nonstructural protein (NSm) whose role is not yet understood. The S segment codes for the nucleoprotein N, and, in most genera, also for a nonstructural protein called NSs. The N protein associates with the genomic and antigenomic RNA segments to form helical nucleocapsids. Genome replication and transcription take place in the cytoplasm, while virus budding generally occurs at the Golgi apparatus **(Fig. 3),** ***(Elliott, 1996; Elliott, 1997).***

Human RVF previously had been described as a "dengue-like" disease in which complications occasionally were noted, but the patient was expected to recover. The human infections observed in Egypt differed in that complications which resulted in numerous deaths developed. Although the virus isolated in Egypt was serologically indistinguishable from other RVF virus (RVFV) isolates, health authorities were concerned that a new strain that was more virulent for humans may have emerged ***(Laughlin, 1979).***

While testing antisera to African viruses in an enzyme-linked immunosorbent assay using RVFV as antigen, the Yale Arbovirus Research Unit detected a cross-reaction between Zinga virus hyper immune antisera and RVFV. The relationship between RVF and Zinga viruses was determined using three monoclonal antibodies, each highly specific for different antigenic sites on three structural proteins found in all RVFV strains that have been examined. In indirect fluorescent antibody tests, each monoclonal antibody reacted to either RVFV or Zinga virus antigen with identical titers confirmed that the prototype strain of Zinga virus was serologically identical to RVFV ***(Digoutte, 1974)***. Zinga virus has been studied in many laboratories in North America, Europe, and Africa, and numerous Zinga infections have resulted from laboratory accidents ***(Digoutte, 1981)***. Any laboratory with Zinga virus in its collection should be aware that it is a strain of RVFV and represents a substantial biohazard to people and animals ***(Meegan, et al, 1983).***

RVFV Replication:

i) **Virus polymerase (L protein) copies genome** to form:

- mRNA encoding N protein, which is obtained by cannibalizing host cell mRNAs.
- (+) sense intermediate

ii) **(+) sense intermediate is copied by L protein** to form new genomic RNA

iii) **Virus buds into Golgi vacuoles - released when cell lyses** (***AJC, 1998)***.

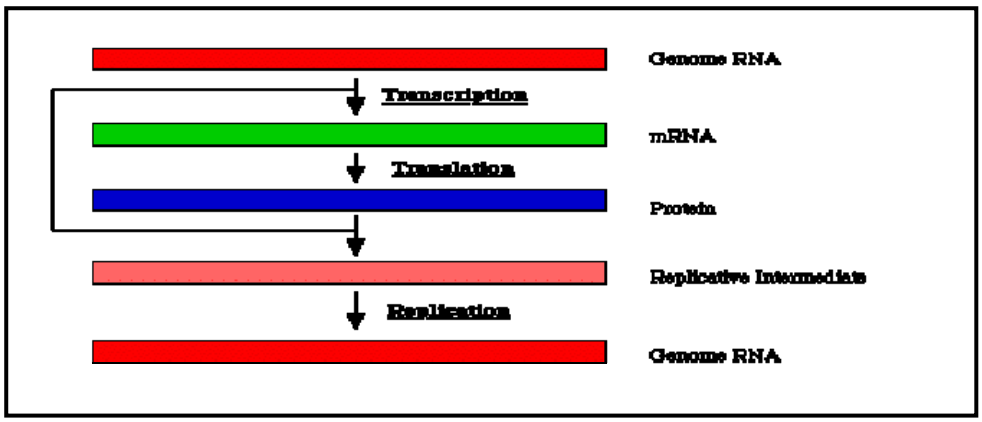

Fig. (4): RVFV Replication (***AJC, 1998)***

Replication occurs in the cytoplasm. In most bunyaviruses the genome is antisense. In some phleboviruses, the small RNA segment is ambisense (i.e., one portion is viral complementary in sense and the other portion is viral in sense). Genetic reassortment can occur during infection because the RNA is segmented **(Fig. 4).** Virus particles bud into the Golgi cisternae and are liberated from the cell by plasma membrane disruption and by fusion of intracellular vacuoles with the plasma membrane ***(Robert, 1991).***

Reassortment of RVFV occurs when a cell is infected simultaneously with two different but closely related bunyaviruses. Each of the three RNA segments is a gene. Parent viruses A and B each donate three genes. These replicate in the cytoplasm, are packaged in different combinations, and are released as eight kinds of progeny viruses, two of which are identical to the parent strains and six have reassorted genes **(Fig. 5)**,***(Robert, 1991).***

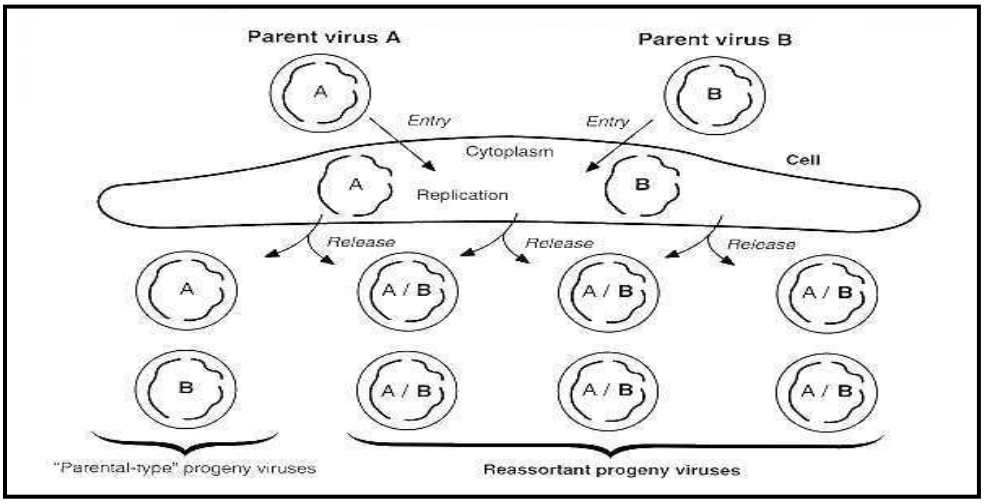

Fig.(5):Reassortment of RVFV (***AJC, 1998)***

Resistance to physical and chemical action:

- ***Temperature:*** RVFV survives several months at 4^0C. In serum, it is inactivated by 56^0C for 120 minutes.
- ***PH:*** The virion is resistant to alkaline pH but inactivated by pH<6.8.
- ***Chemicals:*** RVFV is inactivated by ether and chloroform.
- ***Disinfectants:*** RVFV is inactivated by strong solutions of sodium or calcium hypochlorite.
- ***Survival:*** It survives in dried discharges and multiplies in some arthropod vectors. It can survive contact with 0.5% phenol at ^{40}C for 6 months ***(OIE, 2007).***

The RVF virus is easily destroyed by disinfectants. However, some disinfectants are easily inactivated by organic material (manure, feed, animal tissues, etc.). Therefore, cleaning is the first important step when treating an area that has become contaminated with RVF virus. When cleaning and disinfecting, it is important to wear personal protective equipment (gloves, coveralls, boots, protective eyewear and a respirator) since the virus may become airborne. Cleaning begins by removing all organic material from the surface. Next, soap or a detergent with warm water should be used and the surface should be left to dry before applying the disinfectant. One part bleach diluted with 10 parts water or using the product Virkon-S® by DuPont will destroy the RVF virus ***(Center for Food Security and Public Health Iowa State University , 2007).***

EPIDEMIOLOGY

Occurrence

RVF has been recognized exclusively in African countries, with an underlying association with high rainfall and dense populations of vector mosquitoes. The only epizootic outbreaks of RVF outside sub – Saharan Africa were recorded in animals and humans in Egypt in 1977-78, Mauritania in 1987 and again in Egypt in 1993, then in humans only in Egypt in 2003 (**Fig. 6).** Laboratory infections have been recorded in other parts of the world ***(OIE, 2003& 2007).***

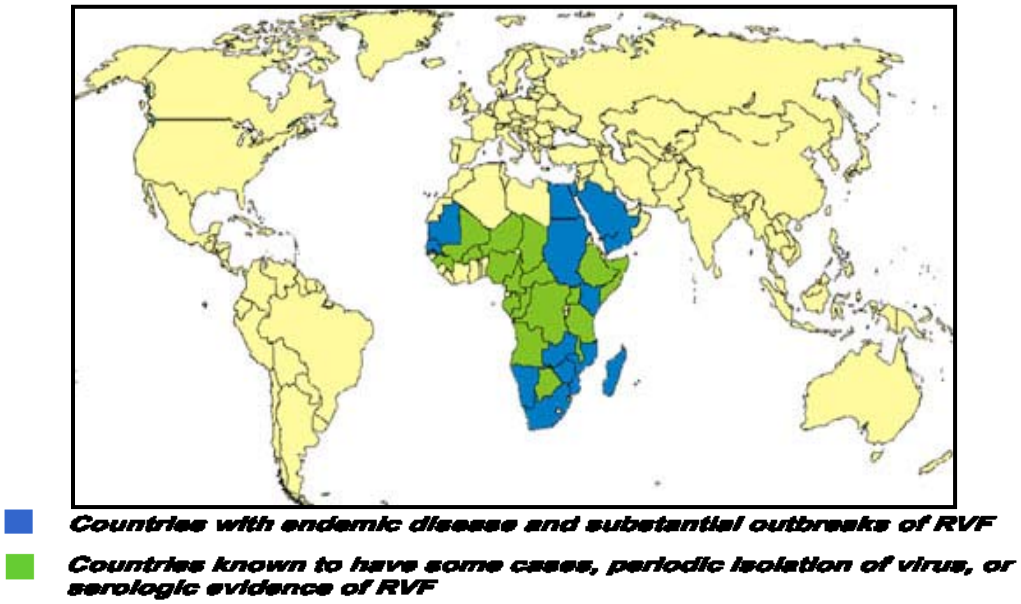

Fig. (6) Distribution of Rift Valley fever (http://en.wikipedia.org/wiki/Image: Rift_valley_fever_distribution.jpg- *Updated, December 2007)*

Normalized Difference Vegetation Index NDVI, a measure of vegetation greenness, is often highly climate dependent. Rainfall amount coupled with types of soils that have high capacity of retaining moisture create suitable conditions for high NDVI values. NDVI also increases in low-lying dambo areas when they are flooded for about 60 days ***(Davies et. al.1985)***. This fast growth of NDVI values in dambo areas due to the availability of water in these depressions provides suitable conditions for mosquito breeding. Animals are attracted to these areas for fodder and water sources making them highly exposed to mosquito bites that can result in RVF epizootics. So that NDVI can be predicted skillfully. Such forecasts of NDVI are thus a potential input to an RVF forecast model ***(Matayo, et.al, 2006).***

El Niño/Southern Oscillation related climate anomalies were analyzed by using a combination of satellite measurements of elevated sea-surface temperatures and subsequent elevated rainfall and satellite-derived normalized difference vegetation index data. A Rift Valley fever (RVF) risk mapping model using these climate data predicted areas where outbreaks of RVF in humans and animals were expected and occurred in the Horn of Africa from December 2006 to May 2007. The predictions were subsequently confirmed by entomological and epidemiological field investigations of virus activity in the areas identified as at risk. Accurate spatial and temporal predictions of disease activity, as it occurred first in southern Somalia and then through much of Kenya before affecting northern Tanzania, provided a 2 to 6 week period of warning for the Horn of Africa that facilitated disease outbreak response and mitigation activities. To our knowledge, this is the first prospective prediction of a RVF outbreak (***Anyamba et. al., 2009).***

The presence of vectors and their population dynamics are strongly linked to land cover patterns. For example, the annual rainfall at **Lake Nasser in Egypt** is very low, resulting in minimal amplification of the mosquito population. However, high densities of *Culex* spp. (consisting of 93% of *Cx. pipiens* and 4.5% *Cx. univittatus*) were observed during outbreaks of RVF in this area in 1977 and 1978, and were believed to be associated with local irrigation practices. Evidence supporting *Cx. pipiens* as the main vector in these outbreaks included:

- The bioecology of *Cx. pipens* (population dynamics, biting activity and host preference).
- A decrease in the number of RVF human cases corresponding with a decrease in the *Cx. pipiens* population, occurring at the beginning of the cold season.
- Isolation of the virus from non blood-fed field specimens ***(Hoogstraal et. al., 1979; Meegan et. al., 1980 and Sellers et. al., 1982).***

Conversely, a variety of mosquito species, some of which had previously been confirmed experimentally as vectors for RVF (i.e. *Cx. pipiens*, *Ae. caspius* and *Cx. perexiguus*)**,** were associated with an outbreak of disease in the same region in 1993 ***(Arthur, 1993; Turell, 1996).***

Vector presence and population dynamics are also strongly linked to climatic factors, so that the disease follows the rainy seasons in most countries in Africa, which has a bimodal character, the epizootics may follow either of the rainy seasons. **In West Africa** for example, this results in RVF virus activity being detected from August to December. **In Egypt**, most virus activity has occurred between May and October. Peak mosquito populations are seen in June, July and August. **In East Africa**, RVF virus activity follows the March/April rains, with most cases in between May and August, but it may also follow the short rains in October, with cases in November through to January ***(AGA, 2007)***.

In East Africa, the occurrence of outbreaks has been clearly correlated to unusually heavy rainfall associated with El Niño ***(Davies et. al., 1980; Swanepoel et. al., 1981 Davies et. al., 1985 and Linthicum et. al., 1999),*** such as the December 1997 outbreak in Kenya which occurred following a rainfall of 60 to 100 times the average level. The outbreak then rapidly spread to Somalia and Tanzania resulting in an estimated 89,000 human cases ***(Sall et. al., 1998)***. The primary vectors involved in this outbreak were floodwater mosquitoes belonging to the *Aedes* genus, (i.e. *Ae. cumminsii*, *Ae. circumluteolus, Ae. mcintoshi*), with *Cx. zombaensis* acting as secondary vectors ***(*Véronique *et. al., 2004).***

In West Africa, where climatic factors have not been implicated in outbreaks of RVF, other factors, such as herd immunity, may be important determinants in the temporal pattern of disease outbreaks. A cyclical pattern of disease emergence, with virus circulation recorded every five to six years during the past 20 years, has been observed in northern Senegal and southern Mauritania 1987 ***(Jouan et. al., 1990),*** Mauritania and Senegal 1993 ***(Zeller et. al., 1997)***, Mauritania 1998 ***(Nabeth et. al., 2001).*** More recently, in 2002-2003, RVF led to severe animal losses in Mauritania, Senegal, the Gambia, and Mali ***(Thiongane et. al., 2003).***

A similar periodicity has also been observed in Egypt. The interepizootic period coincides with the time when the herds are renewed ***(Thiongane et. al., 1996).*** Following an outbreak, it has been demonstrated that herd immunity may reach 80% ***(Thiongane et. al., 2003)*** with a subsequent decrease in immunity occurring over the following years. If additional exposure does not occur, the herd immunity will decrease over subsequent years resulting in an increasing susceptibility of the herds once again ***(*Véronique *et. al., 2004).***

There are several hypotheses explaining how the virus is maintained during the dry season:

- The presence of animal reservoir such as rodents, i.e. antibodies to RVF have been detected in the African grass rat (*Arvicanthis niloticus*) and the Guinea multimammate mouse (*Mastomys erythroleucus*) in Senegal (Gora et. al., 2000), while the Namaqua rock rat (*Aethomys namaquensis*) is believed to be a reservoir of RVF in South Africa ***(Pretorius et. al., 1997).***
- Vertical transmission: floodwater Aedes mosquitoes are capable of transovarian transmission to offspring via eggs, so new generations of infected mosquitoes may hatch from their eggs. This provides a durable mechanism for maintaining the virus in nature, as the eggs of these mosquitoes may survive for periods of up to several years in dry conditions ***(Sherine, 2000).***

Hypotheses regarding the processes involved in the transmission of RVF within the breeding habitats (referred to in Kenya as dambos) of these mosquitoes have been derived through studies of mosquito ecology. *Ae. mcintoshi*, female mosquitoes of the flood water *Aedes spp.* transmit the virus to their descendents by vertical transmission ***(Linthicum et. al.,1985)***. The eggs are laid in the wet soil of temporary ponds where they are capable of surviving for several years once the soil dries ***(O'Malley, 1990 and Trouillet et.al., 1995)***. Subsequent flooding of these areas results in a mass hatching of mosquito eggs ***(Harwood et. al., 1959; Mondet et.al., 2003)***, some of which are infective, this then leads to a new outbreak of disease. To a lesser extent, the transmission cycle also involves *Culex* mosquitoes; however, they require a semi-permanent body of water to persist ***(*Véronique*, et al; 2004).***

Humans, other primates, cattle, sheep, goats, camels, wild and domestic buffaloes have been shown experimentally to replicate RVF virus to a level where infection of other feeding mosquitoes would be likely

to occur. However, there is considerable variation in the response to infection with RVF virus in most animal species. Some breeds and strains are much more susceptible than others. Species such as horses, which develop lower levels of viraemia, are not present in sufficient numbers in epizootic areas to play any role in amplification of the virus. The same applies to dogs and cats, which play no role in epizootic situations, although they do develop viraemia and disease. Rodents and bats have been shown to become infected by RVF in serological investigations. There are higher proportions of positive RVF cases after periods of epizootic activity (2-15%). Most of the vector mosquitoes which have been studied do not show any preference to feed upon these hosts, when ruminants are available ***(AGA, 2007).***

RVF has been isolated from Culicoides, which do not replicate RVF virus biologically though they can transmit the virus mechanically. Other biting flies have also been shown to be capable of transmitting RVF mechanically. Culicoides feed in huge numbers, the abdomens of cattle and camels have been seen to be black with thousands of feeding mosquitoes in epizootic conditions. RVF virus transmission following interrupted feeds is very likely to occur, *Stomoxys, Tabanids, Glossina* (tsetse flies) may all play a role in epizootic situations **(*Turell, 1987)***.

Human development activities have also been implicated in outbreaks of Arboviruses, such as RVF. **The flooding of the Aswan dam in Egypt in 1971**, and the subsequent irrigation of vast areas used for cultivation provided local mosquitoes with ideal breeding habitats and resulted in high numbers of *Culex* mosquitoes during the following summer. In addition, increases in grassy areas attracted breeders from foreign regions leading to a very high density of ruminants in the region. Ruminants from infected southern areas may have introduced the virus into this new favourable ecosystem. This combination of events led to the first reported outbreak in this region in 1977 to 1978 ***(Hoogstraal,et. al.,1979; Sellers,et. al.,1982)***. At present this area is still considered endemic, with outbreaks or evidence of circulating virus recorded in 1993 ***(Arthur et. al., 1993),*** 1997 ***(Abd El-Rahim, et. al., 1999)*** and 2003 ***(WHO, 2003)***.An important observation from Egypt and elsewhere is that RVF is a rural and semi rural disease and does not cause problems in heavily populated towns and cities. This was notably the case in Egypt, where cases could be found in peri-urban situations but not urban. There was no evidence for the amplification of RVF virus in the urban situations ***(Abd El-Rahim, et. al., 1999).***

The extension of RVF, from the enzootic and epizootic areas in sub-Saharan Africa into Egypt, has posed problems for epidemiologists. The movement of insect vectors both within and beyond continental boundaries has been well documented for insect pests, for malarial mosquitoes and other insect-borne viruses. The appearance of RVF occurs when convection and low-level air currents could have transported infected insect vectors from active foci of RVF virus activity 500 km to the south. The prevailing air currents are generally in the opposite direction. A period 5-6 days, when this reversal occurred in 1993, was followed 14-21 days later by RVF cases in Aswan. The disease then spread up the Nile to the delta within 3 months; again, it is suggested, by insect movements. Egypt provides a very receptive area for RVF amplification in summer, as there are large populations of Culex spp. and other mosquitoes. The virus persists for 1-3 years and then it is not possible to show any residual foci of RVF virus activity ***(Ali, et. al., 1978; AGA, 2007).***

The dissemination of RVF virus has, in many cases, been attributed to livestock movements. In Saudi Arabia; ***(CDC, 2000 and CDC, 2000 update)*** six strains of RVF isolated from mosquitoes in the Jizan region