ARBOVIRAL AND RICKETTSIAL CAUSES OF UNDIFFERENTIATED FEVER IN EGYPT

THESIS
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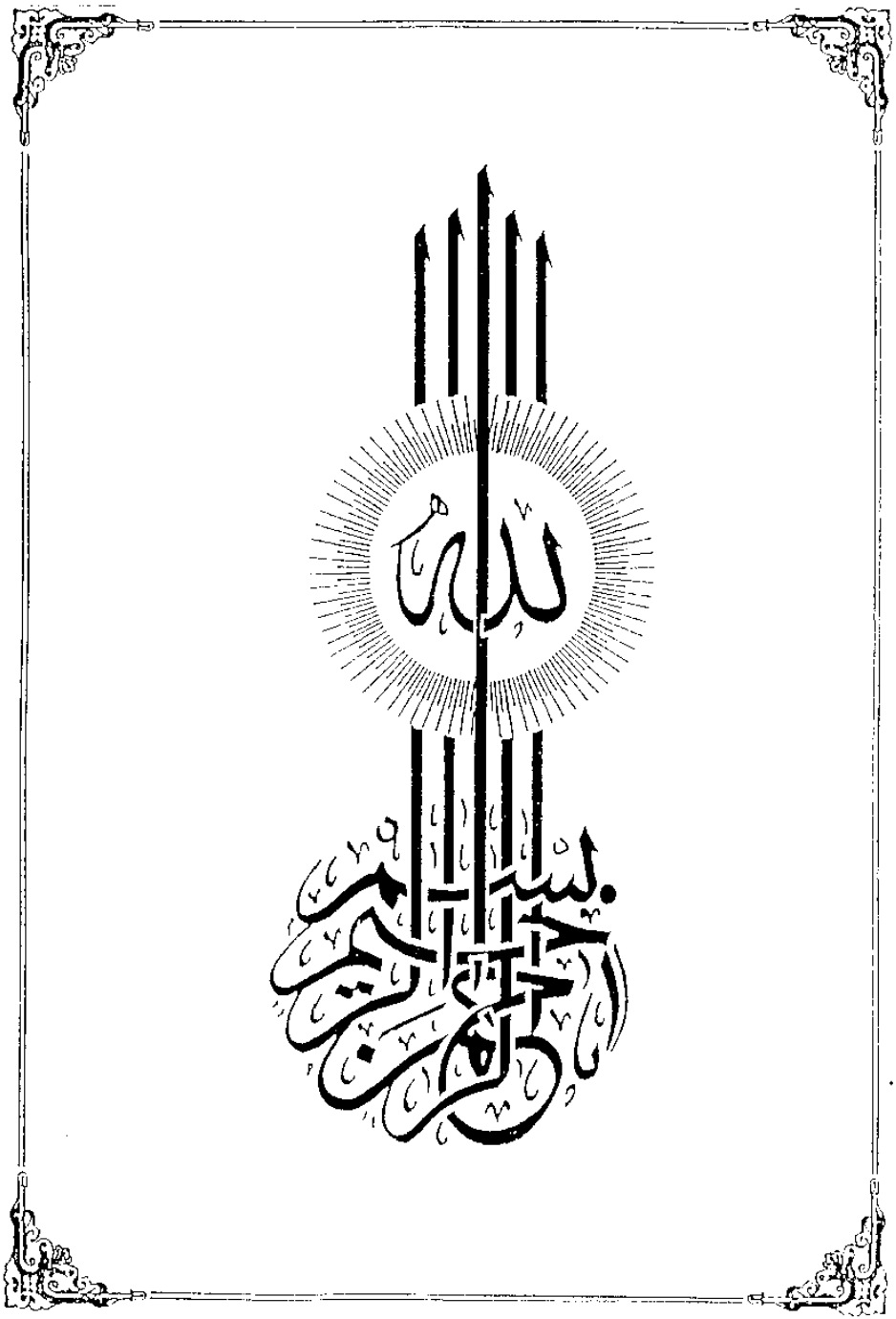

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Introduction & Aim Of Work

I- INTRODUCTION AND AIM OF WORK

Fever and myalgia are non-specific manifestations of illness. In hospitalized patients in Egypt, these symptoms are common and usually diagnosed as "influenza". Non-specific fevers with myalgia are often observed in patients with arboviral and rickettsial infections.

Arboviruses belong to a number of different taxonomic groups, some of which include viruses not transmitted by arthropods. A state of the art definition of arboviruses is given which do recognize the importance of vertical transmission in arthropods to the basic maintenance of some arboviruses. Most of the arboviruses which affect humans are included in the families Togaviridae, Flaviviridae, Bunyaviridae, Reoviridae and Rhabdoviridae. Many arbovirus infections are symptomless. Clinical manifestations range from mild febrile illness which may or may not be accompanied by skin rash and by arthralgia to severe and often fatal encephalitis or haemorrhagic fever with shock ***(Rehle, 1989)***.

Rickettsiae are small bacteria that are obligate intracellular parasites and except for Q-fever are transmitted to humans by arthropods. Rickettsiae are transmitted transovarially in the

arthropod, which serves as both vector and reservoir. Rickettsial diseases typically exhibit non specific fever, rashes and vasculitis *(Jawetz et al., 1991).*

AIM OF THE WORK :

The aim of this work is to study a relatively larger number of representative cases of undifferentiated fevers for the role of certain endemic arbovirous and rickettsial agents in the aetiology of the diseases.

Review Of Literature

II. REVIEW OF LITERATURE

A. ARBOVIRUSES

Arboviruses are viruses that are maintained in nature principally, or to an important extent, through biological transmission between susceptible vertebrate hosts by haematophagous arthropods or through transovarian and possible venereal transmission in arthropods; the viruses multiply in the tissues of arthropods, and are passed on to new vertebrates by the bites of arthropods after a period of extrinsic incubation *(WHO 1985).*

Arboviruses are world wide in distribution and include the causative agents of some of the most devastating and important epidemic and enzootic diseases *(Varma and Webb, 1985).* They form a biological rather than a natural taxonomic group and include members of different families, such as Togaviridae and Rhabdoviridae, some members of which may not be associated with arthropods at all.

Most of the 446 arbovirus species listed by the American Committee on Arthropod- borne Viruses (1988) are not true arboviruses and do not comply with the guidelines established by the subcommittee of Evaluation of Arthropod-borne status. In these

cases the viruses are classified with the arboviruses because of their relationship with known arboviruses or because morphological, epidemiological and biological arguments favour this classification *(Rehle, 1989).*

1- TAXONOMIC CLASSIFICATION :

The earliest formal classification was based on serological tests such as neutralization, complement-fixation and haemagglutination-inhibittion *(Casals and Brown, 1954)*. Additionally gel precipitation tests, radio-immunoassay and immuno-electro-osmophoresis have been applied succesfully.

Advanced techniques in biochemistry and electron microscopy allowed a more rational classification based on the structure and the physico-chemical properties of an arbovirus. According to their morphology, mode of viral replication and antigenic relationships, the viruses are subdivided into families, genera and groups. Most of the arboviruses which affect humans are included in the families Togaviridae, Flaviridae, Bunyaviridae, Reoviridae and Rhabdoviridae *(Rehle, 1989)*.

Arboviruses belong to a number of different taxonomic groups, some of whch include viruses not transmitted by arthropods. The taxoniomic classification of arboviruses by *Jawetz (1991)* is shown in table 1.

Table (1) : Taxonomic status of some arboviruses and roboviruses*

Taxonomic Classification	Important Arbovirus and Robovirus members
Togaviridae Genus Alphavirus	Chikungunya, eastern equine encephalitis, Mayaro, O'Nyong-nyong, Ross River, Semliki Forest, Sindbis, and Venezuelan and western equine encephalitis viruses.
Flavivirdae Genus Flavivirus	Brazilian encephalitis (Rocio Virus), dengue, Ilheus, Japanese B encephalitis, Kyasanur Forest disease, Murry Valley encephalitis, Omsk hemorrhagic fever, Powassan, St. Louis encephalitis, tick-borne encephalitis, US bat salivary gland, West Nile fever, yellow fever and Zika viruses.
Bunyaviridae Genus Bunyavirus	Anopheles A and B, California, Guama, Simbu (Oropouche), and Turlock viruses.
Genus Phlebovirus	Sandfly (Phlebotomus) fever viruses and Rift Valley fever viruses.
Genus Nairovirus	Crimean-Congo hemorrhagic fever, Nairobi sheep disease, and Sakhalin viruses.
Genus Hantavirus	Hantaan virus (Korean haemorrhagic fever, haemorrhagic fever with renal syndrome).
Reoviridae Genus Orbivirus	African horse sickness, bluetongue, and Colorado tick fever viruses.
Rhabdoviridae Genus Vesiculovirus	Junin, Lassa, Machupo, and Pichinde viruses.
Arenaviridae Genus Arenavirus	Marburg and Ebola viruses.
Filoviridae	

* Rodent-borne viruses *(Jawetz et al., 1991)*

a- Togaviridae :

The Togaviridae is a family of spherical, enveloped viruses (diameter 50- 70 mm) having genomes containing a single molecule of positive sense single-stranded RNA *(Matthews, 1982; Shope 1985)*. The family is now divided into three genera : The genus Alphavirus formerly known as the group A arboviruses; The genus Rubivirus, containing a single member, rubella virus; and the genus Pestivirus, which includes three viruses producing important diseases in domestic animals : bovine diarrhoea, hog cholera and border disease in sheep *(Simpson, 1984)* Rubella and Pestivirus are not arthropod-borne viruses.

b- Flaviviridae :

The family Flaviviridae comprises the genus Flavivirus which contains 65 related species and two possible members *(Westaway et al., 1985)*. The Flaviviruses, formerly known as group B arboviruses of Casals and Brown, are small enveloped viruses (diameter 45 mm) that contain a single strand of positive -sense RNA *(Monath, 1990)*. Untill 1984 they were considered to represent a genus of the family Togaviridae. Based on the unique structure, replication strategy and morphogenesis of the Flaviviruses, the Togaviridae Study Group proposed the creation of a new family, the Flaviviridae, and this way approved by the International Committee on Taxonomy of viruses in September 1984 *(Rehle, 1989)*.

c- Bunyaviridae :

The family Bunyaviridae is the largest taxonomic grouping and includes five genera. Of the 232 recognized members of the family Bunyaviridae, 147 are in the genus Bunyavirus which is subdivided into 16 serogroups *(Calisher, 1983)*.

The other genera are : Phlebovirus, Nairovirus, Unkuvirus and Hantavirus. Members of the only recently included genus Hantavirus differ from all other members of the family Bunyavridae in not being arthropod-borne. Hantaviruses resemble in their ecology more closely viruses in the family Arenaviridae with transmission directly from vertebrate to vertebrate through infected secretions. All Bunyaviridae are spherical and enveloped (90 - 100 nm in diameter) and contain a genome of single - stranded, negative - sense RNA, divided in three segments. The viruses are capable of genetic reassortment *(Calisher, 1983)*.

d- Reoviridae :

In the family Reoviridae only the genus Orbivirus includes arboviruses. The described orbiviruses are differentiated into 12 serological groups. Orbiviruses contain genomes consisting of 10 -12 segments of linear, double - stranded RNA. Gene reassortment occurs at least within serogroups *(Gorman and Taylor, 1985)*.