Salwa Akl



بسم الله الرحمن الرحيم

مركز الشبكات وتكنولوجيا المعلومات قسم التوثيق الإلكتروني



-Call +600-2

Salwa Akl



جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها على هذه الأقراص المدمجة قد أعدت دون أية تغيرات





Salwa Akl

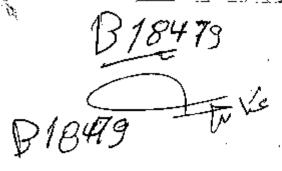




بعض الوثائق الأصلية تالفة وبالرسالة صفحات لم ترد بالأصل



Cairo University
Faculty of Veterinary Medicine
Department of Zoonoses



Epidemiological Studies on Some Animal Reservoirs Hosts of Influenza Virus

Thesis Presented By

Eman Aly El-Ghareeb Hamza

(B.V.Sc., Cairo University 1993) (M.V.Sc., Cairo University 1997)

For Ph.D. Vet. Sc. degree (Zoonoses)

Under Supervision of

Prof.Dr.Osman Mohamed Hamed

Professor of Zoonoses Faculty of Vet. Medicine Cairo University

Prof.Dr.Nahed Hamed Ghoneim

Professor of Zoonoses
Faculty of Vet. Medicine
Cairo university

Dr.Rifky Mohamed El Karamany

Consultant of Virology
Egyptian Organization for
Biological products and Vaccines

(2001)

<u>بسم الله الرحمن الرحيم</u>

قرار لجنة القحص والمناقشة

قامت اللجنة يفحص الرسالة ووجدت أن لها قيمة علمية حيث إشتملت على بحوث هادفة لها أهميتها البالغة في مجال الأمراض المشتركة وقد قامت اللجنة بمناقشة المنقدمة مناقشة مستفيضة ووجدت أن سيادتها ملمة إلماما تاما بكل ما جاء بها.

قررت اللجنة ترشيح السيدة طرب إيدان على الغريب حمزة للحصول على درجة الكتوراه الفلسفة في العلوم الطبية البيطرية (أقراض مشتركة).

أعضاء اللجنة

أ.د. إ ماجدة عبد المنعم أمين

أستاذ ورئيس قسم الأمراض المشتركة - كلية الطب البيطرى

جامعة الزقازيق.

أ.د./ وفاء وحيد محمد رضا

أستاذ الأمراض المشتركة كلية الطب البيطرى

جامعة القاهر مَ

أ.د./ عثمان محمد حامد

أستاذ الأمراض المشتركة- كلية الطب البيطرى

جامعة القاهرة والمشرف على الرسالة.

أ.د./ ناهد حامد غنيم

أستاذ ورنيس قسم الأمراض المشتركة- كلية الطب البيطرى جامعة القاهرة والمشرفة على الرسالة.

<u>ACKNOWLEDGEMENT</u>

I am glad to have this wonderful opportunity to express my greatly debt to my kind supervisor *Prof. Dr. Osman M. Hamed, Professor of Zoonoses, Faculty of Veterinary Medicine, Cairo University* for his guidance and continuous stimulus.

A special word of thanks is best owed to *Prof. Dr. Nahed H. Ghoneim, Chairman of Department of Zoonoses, Faculty of Veterinary Medicine, Cairo University* for her keen supervision, valuable suggestions and encouragement.

I would like to gratefully acknowledge *Dr. Rifky M. El*Karamany, Consultant of Virology, Egyptian Organization for

Biological Products and Vaccines for his great assistance.

It is great pleasure to forward my deepest appreciation to the intense kind efforts exerted by *Dr. Mostafa H. Orchan, Director of WHO National Influenza Center, Agouza, Egypt.* His expert technical advice help to accomplish the practical part of this work.

wish to extend my great thanks to the skilful laboratory members of the Influenza Research Unit, *Egyptian Organization* for *Biological Products and Vaccines*; supervised by *Dr. Nabila M. Sharaan and Dr. Nagwa F. El-Kholy* for their co-operation.

Best regards and thanks to *Dr. Wael Anwar*, lecturer of Hygiene and to all members of *Zoonoses Department*, *Faculty of Veterinary Medicine*, *Cairo University*.

Contents

Subject	Page
Introduction	1
Review of literature:	3
Materials and Methods	90
Results	99
Discussion	122
Conclusion	146
Summary	15 1
References	155



INTRODUCTION

Nowadays, the world confronts tremendous episodes of emerging and reemerging diseases. Nearly, all have involved zoonotic or species jumping infectious agents. These are a consequence of anthropogenic environmental changes, immigrations and globalization without improvement of the public health measures.

One of the most intriguing problems in the Centers of Disease Control and Prevention is *Influenza* and the next pandemic. The name influenza has its origin in early fifteenth century. It was adopted in Europe to explain the sudden and unexpected appearance of an epidemic thought to be under the influence of the stars.

Influenza viruses are part of the Orthomyxoviridae family and are grouped into types A, B and C plus subtypes of A. Type A influenza viruses are the only Orthomyxoviruses known to exhibit zoonotic potential under natural conditions. Humans, pigs, horses, sea mammals and birds are involved in interspecies transmission of influenza A viruses. (Slemons and Brugh, 1994).

Influenza is cited as a paradigm of emerging and reemerging disease. Indisputable pandemics of human influenza A viruses have been emerging for many centuries with three occurring in the 20th century: 1918 (H1N1), 1957 (H2N2) and 1968 (H3N2). Non human sources of influenza virus have been implicated in the origin of these pandemics (Monto,1997). During the inter-pandemic periods; influenza manage to change its immunogenic face producing epidemics almost every year. The earth is a unity for influenza A virus; epidemics appear to be

travelling to and fro across the world. Global influenza outbreaks have sickened large numbers of people, claimed many lives and dramatically disrupted social and economic relations.

Since 1996, recent emerging zoonoses caused by avian influenza A viruses "H7N7, H5N1 and H9N1" have been transmitted from birds to humans, crossing the species barrier. Everyone held his breath with the frightful 1997 Hong Kong avian outbreak, that with the "right mutation" might have started the next pandemic. This reminded us that we are continually at risk for unpredictable pandemic (Bucker, 2000).

Based on the genetic information of influenza viruses that have been isolated in this century, introduction of genes of the avian influenza virus reservoir is obviously required. Interspecies transmission, via another mammalian host and reassortment of avian and human influenza viruses are potential mechanisms for such introduction (Claas, 2000). This highlights that studying the inter-pandemic influenza is the key strategy for pandemic preparedness.

Therefore, the aim of the present study is concentrated on the following points:

- 1. Isolation and identification of influenza A virus circulated in Egypt during the 2000/2001 season in human population.
- 2. Monitoring of human influenza A viruses in pigs raised in Egypt to verify their possible role in the ecology of influenza A virus.
- 3. Following up migratory aquatic birds (visiting Egypt) for influenza to provide information on prevalent subtypes.
- 4. Clarifying the potential role of rodents in the epidemiological chain of influenza A virus.



REVIEW OF LITERATURE

Influenza is an infection of human beings and several animal species. Type A influenza viruses are the most important as they cause severe epidemics and pandemics. Type A influenza viruses are classified into different subtypes depending on the nature of their surface glycoproteins: haemagglutinin (HA) and neuraminidase (NA). The continuous appearance of point mutations in the genes coding for the HA and NA proteins, leads to the progressive emergence of new viral strains "antigenic drift" which occurs annually. The sudden changes which involve total replacement of the gene coding for one or both surface glycoproteins (HA, NA), leads to the emergence of a new viral subtype "antigenic shift", this is responsible for pandemics.

The available literature for influenza A virus will be reviewed under the following topics:

- I) Evolutionary history of influenza A viruses.
- II) Influenza pandemics and propensity for zoonotic potential.
- III) Laboratory diagnosis of influenza virus.
- IV) Preventive and control measures.

I)Evolutionary history of influenza A

<u>viruses:</u>

<u> 1. Human influenza :</u>

Hippocrates (412Bc) was the first who described influenza.

Webster (1800) stated that the first well recorded pandemic of influenza-like disease in humans occurred in 1580. In this pandemic,

mortality was frequently high. It was believed to have originated in Asia before spreading to Africa and Europe.

The first pandemic for which there is more than descriptive reports was that of 1889-1890. Since that time until 1918, the bacillus of Pfeiffer was generally regarded as the cause of influenza.

Smith et al.(1933)demonstrated that epidemic influenza is caused by a filterable virus. This was done by inoculating ferrets intranasally with filtrates of throat washings obtained from cases of the 1918 influenza epidemic early in the course of the disease. The virus was transmitted from ferret to ferret and subsequently to mice. It was readily propagated in the choric allantoic fluid of embryonated hens' eggs.

Blake (1948) denoted that the authentic history of influenza began with the European epidemic of 1510. Since that time, numerous epidemics have been recognized and recorded in all parts of the world. At least eight great pandemics with their preceding and succeeding epidemics have occurred: 1580: 1729-32; 1780-82; 1830-33; 1836-37; 1847-48; 1889-92 and 1918-20. He added that the history of influenza shows that great pandemics sweep the world at irregular intervals and that less severe, more circumscribed epidemics occur fairly frequently during interpandemic periods.

Burnett and Clark (1948) suggested that an early epidemic occurred in chunking, China during July1918, and this together with the movement of large numbers of Chinese laborers into Europe ,may account for a Chinese origin for this pandemic; however this is a tenuous association. They also reported that this pandemic appeared in three successive waves of quite different mortality. The virus appeared first in

a relatively mild form, acquired its increased lethality on passage in humans, and then settled down to a less lethal form.

Chu (1958) reported that the 1957 pandemic (Asian) virus was first detected in Hong Kong in April and was quickly recognized as a new influenza A subtype (H2N2). During May, the virus had already reached Japan and Southeast Asia, and the West Coast of the United States.

Mulder and Masurel (1958) carried out a retrospective seroepidemiologic study and interpretated that the influenza epidemic occurred in humans in 1889 and 1890 was caused by a virus antigenically similar to the more contemporary 1957 Asian strains (H2N2).

pandemic hit Taiwan in April and swept the island in 40days. An estimated 50 80% of the population was infected. The epidemic was of more than usual interest because of the paucity of influenza epidemics during 1958. One of the few epidemics of Asian influenza occurring in 1958 was reported from Taiwan. Sixteen viruses were isolated and additional cases were confirmed serologically. These cases occurred both in foreigners and in the native population. The majority of the cases studied were staff members and patients of the United States Naval Medical Research Unit No.2 located in Taipei. There was an attack rate of 18% in the Chinese members of the staff.

Crosby (1976) discussed that while influenza had killed untold millions throughout the centuries, the pandemic of 1918-1919 was particularly severe. Not only did Spanish influenza, as it was called, kill between 20 and 40 million people worldwide, it also altered the course of

history. The severity of the pandemic of 1918-1919 greatly accelerated the search for the causative agent of influenza.

Hemon et al. (1977) studied the possible consequences of influenza during pregnancy on the weight of the new born. They showed that the major 1969-1970 winter influenza epidemic in Alsace was followed by a decrease in the mean birth weight registered in Haguenau's maternity hospital.

Spira et al. (1977) carried out a study on 1940 pregnant women in the Haguenau Maternity Hospital (Bas-Rhin) when an epidemic of influenza occurred in 1972-1973. They found that the mean birth weight dropped in infants of mothers who had contracted influenza during pregnancy. The drop in weight of the placenta (37.3 g as a mean) was more obvious and can totally explain the drop in fetal weight. These results suggested that there is no direct passage of influenza virus across the placenta which, however, is itself modified by the infection.

Griffiths et al. (1980) sought for serological evidence of infection with influenza A and B viruses during three successive winters. Paired sera from 1595 pregnant women were studied and 79 infections occurred in 77 women (4.8%). A further 77 women who had no serological evidence of recent influenza infection were selected from the study population to serve as a control group. Although all the infections occurred in either the second or the third trimesters of pregnancy, the cases delivered more babies with congenital abnormalities than did the controls. The possibility was considered that the presence of an abnormal fetus made these women more susceptible to influenza infection.