DIAGNOSTIC PROCEDURES OF VIRAL CAUSES OF LOWER RESPIRATORY TRACT INFECTIONS

THESIS
SUBMITTED IN PARTIAL FULFILMENT
OF THE MASTER DEGREE

IN CLINICAL AND CHEMICAL PATHOLOGY

BY

Eman Samir Sadek
(M.B.,B.Ch.)

SUPERVISORS

Prof. Dr. Ibrahim Khalil Aly
Professor of Clinical and Chemical Pathology
Faculty of Medicine
Ain Shams University

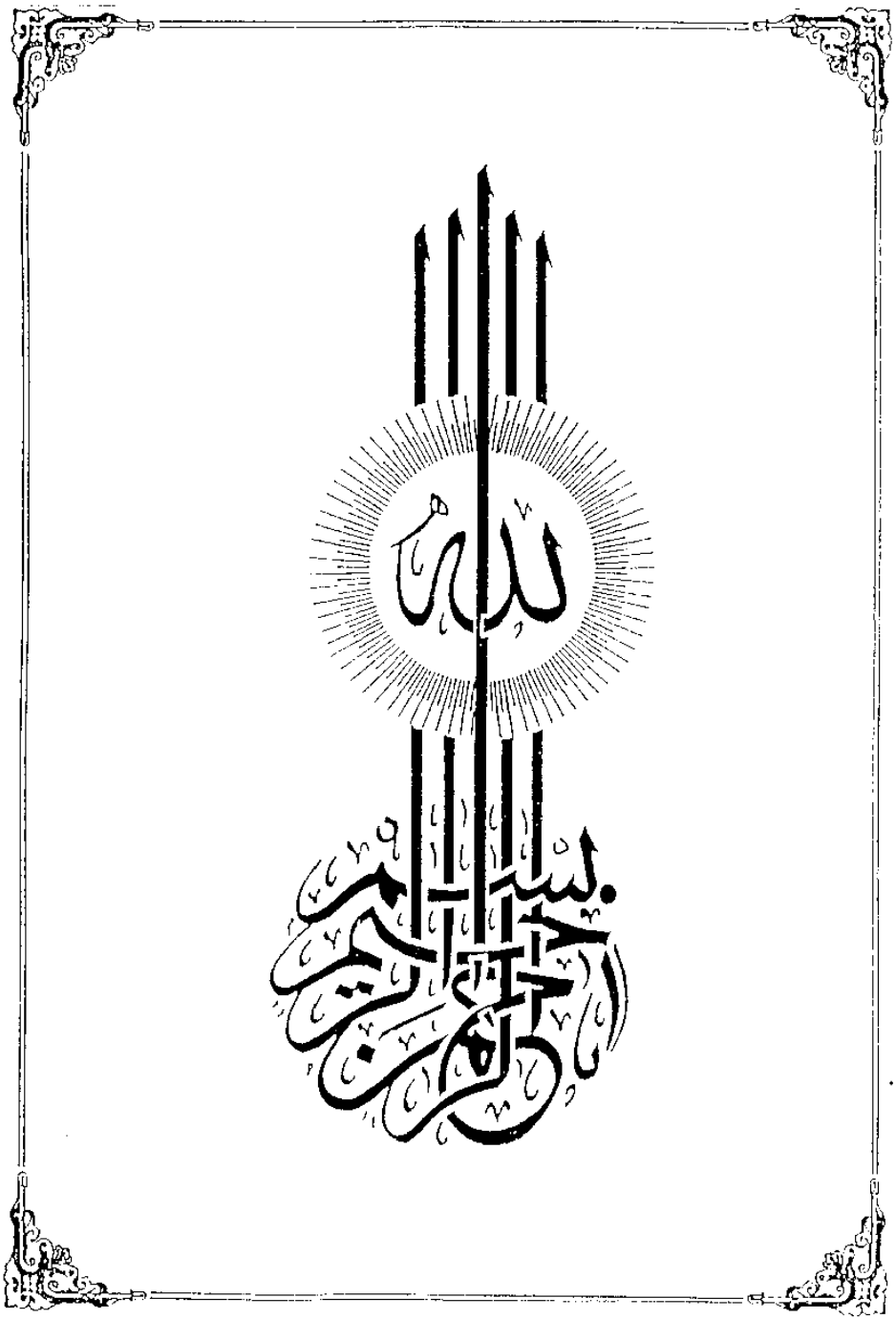
Dr. Nevine Nabil Kassem
Lecturer of Clinical and Chemical Pathology
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
1993

Acknowledgment :

I would like to express my deepest gratitude and cordinal appreciation to my *Prof. Dr. Ibrahim Khalil Aly, Prof. of Clinical Pathology, Faculty of Medicine, Ain Shams University*, for his support, valuable comments and advice throughout the work.

I am greatful to *Dr. Nevine Nabil Kassem, Lecturer of Clinical Pathology, Faculty of Medicine, Ain Shams University* for her advice and co-operation in this work.



List of abbreviations:

ARI:	Acute respiratory infections
CFT:	Complement fixation test
CLIA:	Chemiluminescence immunoassay
ELISA:	Enzyme linked immunosorbent assay
EM:	Electron microscope
FC:	Flow cytometry
HAI:	Haemagglutination inhibition test
IF:	Immunofluorescence
LRTI:	Lower respiratory tract infection
NT:	Neutralization test
PIV:	Parainfluenza virus
RIA:	Radioimmunoassay
RSV:	Respiratory syncytial virus
TC:	Tissue culture
WB:	Western blot technique

Contents:

INTRODUCTION AND AIM OF THE WORK

Introduction:

The lower respiratory system can be infected by many of the same bacteria and viruses that infect upper respiratory tract *(Tortara et al., 1988)*.

The mechanism by which viruses spread from upper to lower respiratory tract is not clear, but it is assumed that the route of spread is via the respiratory epithelium or through aspirated secretions *(Fields, 1990)D*.

The epidemiological studies of acute respiratory infections (ARI) in developed countries have provided evidence that the major number of LRTI is associated with non-bacterial infections which account for high mortality among infants and children and respiratory syncytial virus (RSV) was found to be the most important cause *(Mcintoch, 1990)*.

Adenovirus has been also reported to be a cause of pneumonia that are showing serious clinical manifestations. Other viruses as Myxoviruses (Rhino virus, influenza virus, parainfluenza virus, and mumps virus) have been associated with bronchiolitis *(Chanock, 1988)*.

Several laboratory tests are used in diagnosis of viral L.R.T.I. e.g., smears examined by electron microscopy, tissue cultures, shell vials technique, animal inoculation and western blot technique for detection of viral antigen *(Lennette et al., 1985)*.

Serological diagnosis including complement fixation test (CFT), neutralization test (NT), immunofluorescence test (IF), enzyme linked immunosorbent assay (ELISA) are commonly used *(Schmidt, 1979)*.

Recently, genotyping rather than serotyping, flow cytometry, chemiluminescence has been described in diagnosis of RSV and adenovirus *(Shapiro, 1991)*.

Aim of the Work:

The aim of this work is to throw light upon the common diagnostic procedures used in viral infections of lower respiratory tract emphasis on the methods that can be useful in developing countries in respect to the coast-benefits and reliability.

REVIEW OF LITERATURE

RESPIRATORY ANATOMY AND PHYSIOLOGY

Lung development and growth:

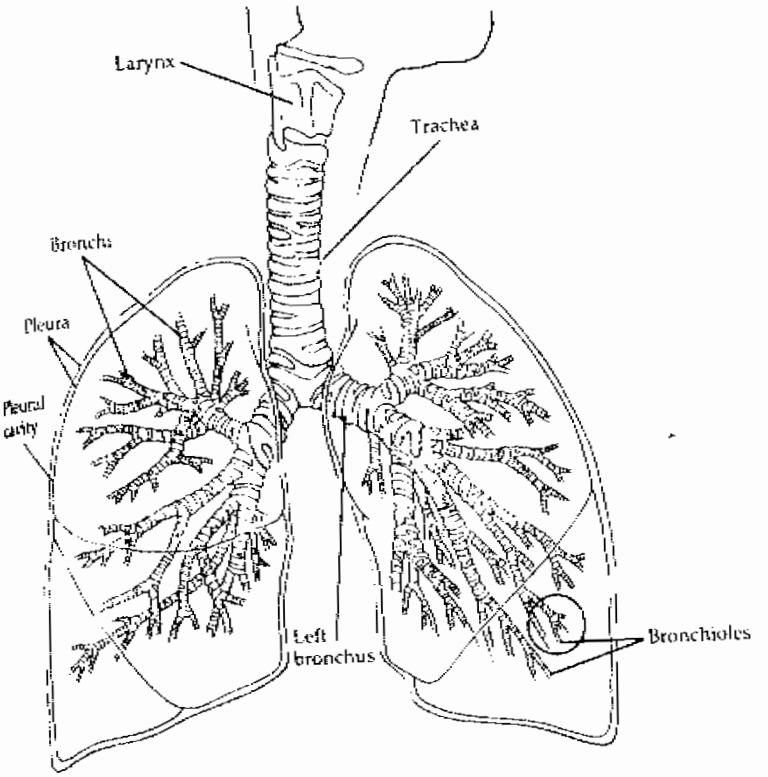
The embryonic lung bud arises from the primitive endodermal tube in the 4th. week of gestation and progress by asynchronous branching to form all conducting airways (terminal brochioles and all larger airways) by the end of the fourth month of gestation.

The airways are fully mature in their structure and branching pattern at birth *(Phelan et al., 1982)*. Postnatal lung growth is characterized by formation of alveoli, maturation of the structures in the lung and production and secretion of a variety of substances within the lung.

Design and structure of the human lung:

The lower respiratory tract begins at the junction of the larynx with the trachea and includes the trachea, bronchi, bronchiales, and alveoli *(Murray, 1976)*.

Particles deposited in conducting airways are cleared within hours by the mucociliary mechanisms, while clearance of these reaching the alveoli may take several days to months, the later may be phagocytosed by alveolar machrophages *(Phelan et al., 1982)*.



Phagocytosis and mucociliary clearance may not be a sufficient protection from living agents, such as bacteria and viruses. The principal antibody in respiratory secretions is secretory IgA, which is produced by plasma cells in the submucosa of the airways *(Murray, 1976)*.

IgA can neutralize certain viruses and toxins and help in the lysis of bacteria. A small fraction of the antibodies of the respiratory surface is made up of immunoglobulin E (IgE), which is attached to mast cells and relatively concentrated in respiratory mucosa, it plays an important role in allergic reactions *(Green, 1970)*.

AETIOLOGY OF LOWER RESPIRATORY TRACT INFECTIONS

In 1930s investigators in North America and U.K. assumed that pediatric pneumonias were bacterial in origin *(Luria et al., 1967)*.

In 1950s, with the discovery of new infective agents and because of the general effectiveness of the antibacterial chemotherapy, research naturally focused upon the respiratory viruses and mycoplasma *(Foy, 1973)*. However, recent reports have disregarded bacterial pneumonia and have concentrated on the role of respiratory viruses and mycoplasma in pediatric acute lower respiratory tract infections (ALRTI) *(Murphy et al., 1981)*.

In the early 1960s, it was realized that the respiratory syncytial virus (RSV) was responsible for considerable respiratory illness in young children *(Lauria et al., 1967)*.

RSV is the leading cause of lower respiratory tract illness in infants and young children *(Foy et al., 1973)* and it is responsible for repeated attacks of acute respiratory illness throughout life.

Its presence may be witnessed in most countries by the yearly up occurrence of bronchiolitis, pneumonia, tracheobronchitis in the very young *(Foy et al., 1973)*.

Studies on viral aetiology of lower respiratory infections (LRI) in children were carried out in Beijing from winter, 1967 to spring 1981, and 596 children under five years old with lower respiratory infections were observed. This study showed that respiratory syncytial virus (RSV) was the most common agent causing lower respiratory infection in children *(Chretien et al., 1984)*.

The high incidence of pneumonia and other respiratory illness caused by these organisms posses a major public health problem *(Mufson et al., 1983)*. The mechanism by which viruses spread from upper to lower respiratory tract is not clear, but it is assumed that the route of spread is via the respiratory epithelium or through aspirated secretions *(Hall et al., 1984)*.

DISEASES OF THE LOWER RESPIRATORY TRACT INFECTIONS

The air we breath contains microorganisms, so the upper respiratory system is the major portal entery for pathogens. In fact, respiratory system infections are the most common type of infection *(Glezen et al., 1973)*. Some pathogens that enter the body via the respiratory system can infect other parts of the body for example viruses causing measles, mumps, and chicken pox *(Glezen, 1973)*.

Another very serious aspect of respiratory infection is the ease with which they are spreads, both by direct contact with droplet emitted during sneezing, coughing, talking, kissing and by fomites (contaminated objects) *(Tortora et al., 1988)*.

As the bronchi become involved, bronchitis or bronchiolitis develops. Mycoplasma pneumoniae and a number of common respiratory viruses are suspected cause. In infants, the most common agent is probably the respiratory syncytial virus (RSV) *(Foy, 1973)*.

Diseases such as whooping cough are also forms of bronchitis. A severe complication of bronchitis is pneumonia, in which the pulmonary alveoli become involved. These often inter-related diseases are sometimes are called "croup" *(Tartora et al., 1988)*.

I. Pneumonia:

Pneumonia is one of the commonest disease in infancy and childhood. It is defined as an acute or chronic inflammation of the lung. About 80% of all childhood deaths from pneumonia occur during the first year of life *(Forfar and Arneil, 1984)*.

Classification of pneumonia:

Pneumonia is usually derived into categories based on aetiological, anatomical and historical classification *(Costals, 1992)*.

A. Historical classification:

In 1920s, all primary pneumonias were classified as either lobar or atypical (not lobar) although children often had pneumococcal pneumonia that was atypical by this classification. Bronchopneumonia is a term that also been used to apply to any pneumonia that was not lobar.

In 1930s, increased use of roentography led to the detection of clinically unsuspected pneumonia and the term viral pneumonia was used to describe this part of the clinical spectrum of minor respiratory tract infections *(Lewis, 1944)*.