BIOCHEMISTRY OF SPUTUM : IRON IN SPUTUM IN PATIENTS WITH BRONCHIAL ASTHMA

Thesis

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BY
Ola Ahmed Hassan
M.B.,B.Ch.

Supervised by

Prof. Dr. Foze Abas El-Shayeb
Prof. of Medicine and Allergy
Ain-Shams University

Prof. Dr. Hassan El-Sayed Soliman
Prof. of Medicine and Allergy
Ain - Shams University

Prof. Dr. El-Said Mostafa Abou Gamrrah
Prof. of Medicine and Allergy
Ain - Shams University

Faculty of Medicine
AIN SHAMS UNIVERSITY
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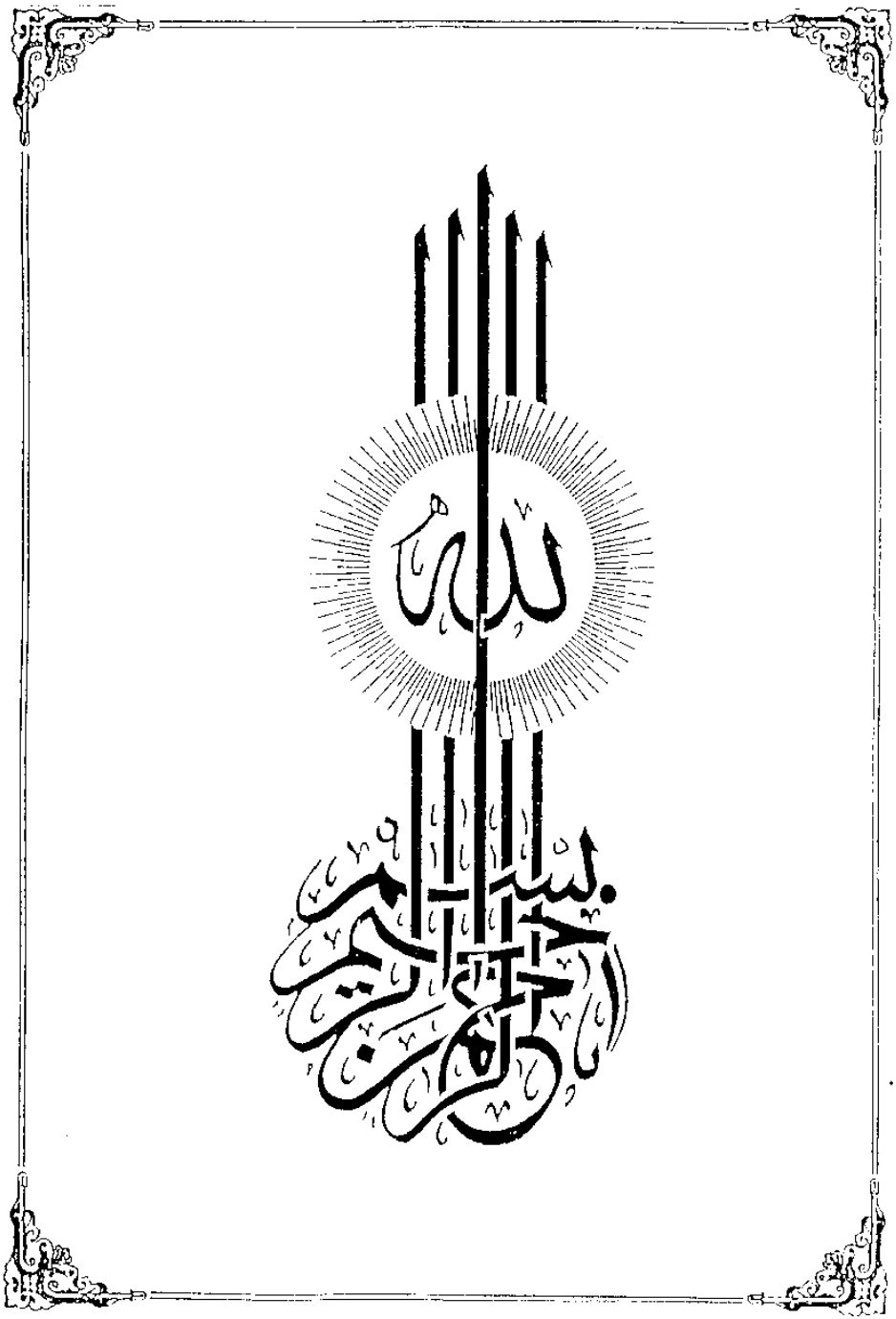

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INTRODUCTION AND AIM OF THE WORK

INTRODUCTION

* Biochemistry of sputum in bronchial asthma is not well established. There are many studies about the lipid. protein, carbohydrates and trace elements contents of sputum in bronchial asthma.

Some sporadic studies were done e.g. Shimura et al.,1988 who studied the pH, NaCl and potassium in the sputum and saliva in 8 normal cases and 17 asthmatic persons. The result was not confirmed and not satisfactory.

In 1980 Volkov, studied the contents of sputum for trace elements in 12 patients, he found the abscence of Zinc and disturbance in the results of Calcium.

There are other sporadic works about the lipid and protein structure.

THE AIM OF THE WORK:

Iron is an important element in human metabolism. It has a control role in erythropoiesis and is also involved in other intracellular processes. A number of additional functions of the immune system have been proposed which involve iron and iron binding proteins. Iron deficiency induced by chronic inflammation has been associated with impaired immuno-competence in many infectious, inflammatory and neoplastic states (***Weinberg, 1981***).

The aim of this work is to study Iron content in sputum in patients with bronchial asthma whether intrinsic or extrinsic.

REVIEW OF LITERATURE

Biochemistry of Sputum

Sputum may be defined as any abnormal secretion produced in or expectorated from, the bronchopulmonary system. It is not saliva, and it is not nasopharyngeal in origin. It is a variable mixture of cellular, non cellular pulmonary material dependent on the underlying pathologic process. The cellular elements may be inflammatory or red blood cells from the airways, exfoliated bronchial and alveolar cells, or malignant cells shed from tumors. Non pulmonary cells may be:

A. Oropharyngeal squamous cells.

B. Vegetative cells.

C. Animal cells may become part of the sputum if they have been aspiratd into the lungs and subsequently coughed up.

Acellular bodies in the sputum:

Various acellular bodies are present in the sputum. They are round to oval bodies and they are mostly concentrically structured, partly amorphous,and partly crystalline. They are usually positive for periodic acid-Schiff stain (***Ackerman et al., 1980***).

Most of them showed a concentric lamination of layers that vary greatly in size and number, and lamination was not observed in some cases (***Badge et al., 1955***).

Occasional bodies displayed central cores, they are also ring shaped forms, sometimes filled with crystalline material, these bodies corresponded to mucus condensations. Occasional groups of sputum bodies are seen closely attached to or included in curshman's spirals ***(Coffery and Altman, 1965)***.

The acellular bodies in the sputum are:

1- Microliths.

2- Psammoma Bodies.

3- Corpora amylacea.

4- Calcium oxalate crystals.

5- Charcot - Leyden crystal protein (*CLC*)

6- Eosinophil granule major basic protein ***(MBP)***.

Bronchial mucus is produced by goblet cells and by submucosal glands consisting of mucous and serous cells ***(Roussell et al., 1978)***. These different cell types are not equally distributed along the respiratory tract ***(Reid, 1965)***.

The number of goblet cells is also greater proximally than distally. The volume of glands exceed that of goblet cells about forty folds *(Reid, 1960)*.

Volume of Sputum:

The volume of sputum expectorated usually reflects the severity of the disease process. Poorly understood but complex interaction among the various constituents determine the physical properties of the material which relate to the patients ability to clear the secretions.

The thickness and stickness of the sputum are partly related to the amounts of extracellular mucopolysaccharide and deoxyribonucleic acid molecules present. The colour of sputum is due to green perioxidases released from degenerated neutrophils or eosinophils. Rather than providing a reliable index for infection, it is an excellent indicator of the speed of clearing secretions. Mucoid sputum indicates prompt clearance.

In health, the volume of tracheobronchial secretion has been variously estimated to be 0.1 - 0.75 ml/kgm body weight in 24 hrs *(Boyd, 1973)*, suggesting that in 70 kgm

individual the daily volume varies between 8 ml to 50 ml, and the sputum volume correlated with the degree of gland hypertrophy even in subjects who produce only traces of sputum in the morning.

In spite the discrepancies in the former figures one thing is certain, a normal individual does not cough up or expectorates any bronchial secretion, this secretion is normally swallowed.

Constituents of Sputum

Water is the major constituent of sputum usually accounting for over 95% of its weight. The remaining 5% which is the macromolecular material is distributed as follows: Glycoprotein 2-3%, protein 0.1-0.5% and fats 0.3-0.5% (***Creeth, 1978***), enzymes, carbohydrates making up the balance.

A. glycoproteins

The normal airway is capable of producing glycoproteins on cholinergic stimulation (***Reid and Bhaskar, 1989***).

The major glycoprotein present in tracheobronchial secretion is large carbohydrate rich glycoprotein whose macromolecular structure regulates the viscoelastic properties of mucus ***(Woodward et al., 1982)***. Carbohydrates are present in varying amounts attached in short or long (up to 15 units) branched or unbranched chains.

The Carbohydrates Include The Following Types:

a) Hexoses : e.g. mannose, galactose.

b) Acetyl hexosamines as acetyl glucosamine, acetyl galactosamine.

c) Methyl pentose as fructose

d) Sialic acid which is a derivative of neuraminic acid (a 9 Carbon Sugar).

Hexosamines are sugars containing - NH_3 group (amine group) ***(Murray, 1988)***.

Glucosamine and galactosamine form complexes with proteins called glycosaminoglycans ***(Frisell, 1982)***.

Fructose and sulfate are present in purified bronchial mucous glycoprotein and are virtualy absent from serum glycoproteins. Whereas mannose is present in considerable amount in serum glycoproteins.

N-acetyl neuraminic acid is present in similar amounts in both mucous and serum glycoproteins. So fructose and sulfate are markers of mucous glycoproteins *(Creeth et al., 1977)*.

N-acetylneuraminic acid and fructose are important terminal units of carbohydrates prosthetic groups of glycoprotein molecule. The concentration of markers of mucous and serum glycoproteins in sputum sample are correlated with the viscosity of sputum, in infected sputum both mucous and serum components contribute to its viscosity *(Lopez and Reid, 1978)*.

B. *Proteins*

Ryley and Brogan (1973), studied by immunoelectrophoretic methods the free protein component of sputum. Their studies showed the presence of secretory IgA, albumin, IgG, they were most significant together with lysozymes and amylase.

Querinjean et al. (1971), showed also the presence of lactoferrin which was also called lactotransferrin.

However, with two exceptions, the ratios of the concentration in the plasma to the concentration in the sputum were remarkably constant. The exception were IgA and α_1 antichymotrypsin. It was concluded that plasma proteins were generaly present through transudation, whereas IgA and α_1 antichymotrypsin must be secreted. A positive protective role seems likely for these proteins in addition to IgA. ***(Creeth, 1978).***

C. Lipids

Lipids form a significant portion of airway mucus, yet they have not received the same attention that epithelial glycoproteins have ***(Montreuil and Spik, 1975).***

Analysis by thin layer chromatography from healthy volunteers by broncho-alveolar lavage showed that cholesterol was found to be the predominant lipid ***(Bhaskar et al., 1987).***

Reid and Bhaskar (1989), again showed that lesser amounts of phospholipids were detected. Its role mainly as surfactant is to reduce surface tension of mucus films, so alveoli remain open, and the special mix of macromolecules (glycoproteins) and lipids gives the bronchial epithelial mucus its physical and chemical properties.