Chapter 1

Introduction

Nature has provided highly complex system in the human body and the human lung is no exception [1]. The lung, the lower part of the respiratory tract known as bronchial tree, a complex system of branching of tubes, starting from trachea dividing into two bronchi and continuing up to the alveoli (23rd generation) where the gas exchange process occurs with cardiovascular system (Figure 1). The walls of the trachea and bronchi consist of epithelium, cartilage, gland, mucosa, sub-mucosa and adventitia. From the trachea to the beginning of the respiratory bronchioles (17-20th generation), the respiratory tract is lined by the ciliated columnar epithelium. During normal breathing, large quantities of air are transported into the lungs by the airways. This air is contaminated with a variety of pollutants, bacteria and particles that deposited in the airways. Clearance mechanisms in the lungs work to fight this constant accumulation of material by removing these particles from the body. These particles may be toxic and harmful to health or harmless and beneficial.

Figure 1. Anatomy of lung[20]
1.1 Mucus

Mucus is treated as a protective blanket over the lungs, mouth, throat, nose and gastrointestinal tract surfaces. It also prevents the tissue underneath from drying out. Fluid of mucus is typically produced from the cells found in mucus glands. Cells of mucus secrete products which are rich in glycoprotein and water. Fluid of mucus may be originated from mixed glands containing both serous and mucus cells. Viscosity of mucus may range from 10 poise to $10^3$ poise at low shear rate ($1 \text{ sec}^{-1}$) and magnitude of mucus is about 0.01 poise at high shear rate ($100 \text{ sec}^{-1}$), [2,3,4,5]. Mucus is treated as Newtonian fluid by Yates et al. [6] and it is considered as a Maxwell fluid by Ross et al. [7].

1.2 Cilia and Cilia Beating

The cilia are microscopic, contractile filaments which act as sensory organs and perform many mechanical functions of the cell (Figure 2). Cilia protect a person from germs, which are present in the lung. Cilia are classified into two types - Motile cilia and Non-Motile cilia. We can found motile cilia in the respiratory tract, lungs and middle ear. As cilia can perform rhythmic beating or waving motion, therefore its function is to keep the airways clear by removing dirt along with mucus to make ease in breathing without irritation. The size, the structure and the pattern of motion of cilium [8]. They are grown on ciliated cells of the epithelium at the rate of 200 cilia/cell i.e. 1500-2000 million cilia/cm$^2$. The length of cilia is 6-7 µm in man. The diameter of cilium is about 0.16 - 0.20 µm.

![Figure 2. Effective stroke (a) and Recovery stroke (b) of a cilium][21]
In the respiratory tract, cilia beat in a continuous coordinated manner; generate a metachronal wave [9], moving the overlying mucus towards the Pharynx. The rate of ciliary beat varies and it is approximately 20 beats/second. In the terms of pattern, ciliary beat consists of two parts, the effective stroke and the recovery stroke. During an effective stroke, the cilium remains fully extended and moves through an arc in a plane approximately perpendicular to the cell surface while in the recovery stroke, a bend is propagated through the length of the cilium from base to tip and the cilium swings around near the cell surface to reach the starting position for the next effective stroke. The cilia tip velocity is 0.03 cm/sec and the force exerted by single cilium is 4x10^{-7} dyne [10]. By combining many cilia together, the stiffness of the organelles can be increased and have much higher tip speeds than a single cilium. The rates of beating as well as cilia tip velocity are strongly influenced by the viscosity of serous fluid in which they beat.

1.3 The Forced Expiration

Coughing is the body's best way of removing mucus from the lungs or foreign material or reacting to an irritated airway. Traits of cough are common to recognize. A cough is not a disease, it is a symptom. The human lung under pathological conditions is affected by various diseases such as, Chronic bronchitis, Bronchial asthma, Lung cancer, etc. Loss of cilia mass may occur in the case of cancer. Diseases in lungs are caused by either removal of serous fluid or cilia. The cough reflex is associated with Asthma, Chronic bronchitis, [11] etc.

The human cough has mainly two functions:

1. It helps to protect the lungs against expiration, and
2. It helps to propel secretions and other materials upward through the airways.

1.4 Mechanism of Mucus Transport in a Normal Lung

Cilia and mucus form the primary defence system of the lung for cleaning the inspired air contaminants and entrapped particles in normal condition of lung. During a forced expiration, high expiratory flow is developed, which creates a high shear rate. Variation of mucus transport is inversely with shear rate. This phenomenon is called pseudo-plastic flow or shear thinning. A temporary realignment of macromolecular glycoprotein by the applied force results in decrease of viscosity. Therefore repeated coughing with short intervals between the expirations may result in reduction of viscosity and improvement of mucus transport more than coughs with long intervals. Repetitive forced expirations with shorter interval are more efficient [12].

King et al. [5] have proposed a planar non-symmetrical two layer fluid laminar flow model to study mucus transport in the respiratory tract due to cilia beating and air
motion by considering mucus as a visco-elastic, its thickness, pressure drop, air stress and serous layer viscosity, etc. on mucus transport have been studied. It may be noted here that the thickness of the serous layer has been assumed to be constant during beating.

1.5 Mechanism of Mucus Transport in Diseased Lung

It is known that under pathological conditions of the lung, caused by diseases such as Chronic bronchitis, Cystic fibrosis, etc. excessive mucus is formed and it is transported by forced expiration or cough [13,14,15]. Also when airways are affected by immotile cilia syndrome (dyskinesia), cough is the main mechanism by which mucus is transported. Mucus transport is decreased in patients with pulmonary diseases such as chronic obstructive pulmonary disease, asthma and in patients with dysfunctional cough control.

1.5.1 Asthma

Asthma is a long term disease due to which air passage becomes narrow and inflamed. During asthma, muscles of the bronchial tube thicken and tighten. Air passage become inflamed and filled with mucus which make it difficult to move air. In a non-asthmatic person, muscles around the bronchial tube are become less stiff and tissues are thinner for allowing air to move easily (Figure 3).

![Normal and Asthmatic Bronchiole](image-url)

Figure 3. Normal and Asthmatic Bronchiole[22]
1.5.2 Chronic Obstructive Pulmonary Disease

COPD is also known as Chronic Obstructive Lung Disease. It is a long term lung disease, blocks airway and makes us hard to breathe. It damages the breathing tubes which carry air in and out of the lungs. Shortness of breath, sputum and cough production is its symptoms. It is mainly caused by cigarette and tobacco smoke. Air pollution, Chemical fumes and dust also contribute to COPD. It is treated by quitting smoking and keeps away from air pollution and dust. In an asthmatic patient, mucociliary transport does not fully recover and it may progressively decrease due to a loss of ciliated epithelium. It is due to recurrent infections and progressive severe airway instability [12].

1.5.3 Chronic Bronchitis

Chronic bronchitis is a long-term inflammation of the bronchi in the lungs. Due to this, mucus production increases and respiratory passage gets swollen and become irritated. Chronic bronchitis is caused by smoking cigarette, inhaling irritants and underlying disease processes such as asthma or congestive heart failure. Cough shortness of breath and wheezing are its symptoms. It is treated by bronchodilators and steroids.