



Circular Model for Mucus Transport in the Airways due to Air Motion

Dipak Kumar Satpathi, A Ramu

Department of Mathematics

Birla Institute of Technology and Science, Pilani Hyderabad Campus

Jawahar Nagar, Shameerpet, RR Dist., AP-500078

INDIA

Abstract: In this paper, a three layer flow model is proposed to study the mucus transport in the airways due to air motion caused by forced expiration or mild coughing (by considering the circular geometry of the airways). The flow is governed by the instantaneous pressure gradient generated during air motion. Mucus is represented by viscoelastic Maxwell fluid, whereas serous fluid and air are considered as Newtonian fluids. For fixed air flow rate, it is shown that mucus transport is more in the viscoelastic case. It is also shown that for fixed air flow rate and fixed airway dimensions; mucus transport is more in the presence of serous fluid. This increase is further enhanced in the presence of surfactant.

Keywords: Mucus, viscoelastic, serous, surfactant, airways

I. Introduction

The mucocilliary system consists of a mucus layer, a serous layer and cilia embedded in the epithelium. The first line of defense of human lungs against inhaled debris is mucus. Inhaled viruses, bacteria and particulates land on mucus layer and diffuse within. These foreign particles are cleared if flow of the mucus layer toward the larynx dominates particle diffusion through the layer. The system consists of two layers-the lower layer, a non-viscid serous fluid that lines the airway epithelium and in which the cilia beat and the upper layer, the mucus, which lies on the top. Under normal conditions of the lung, contaminants of the inspired air, occluded particles and cellular debris are removed by cilia beating. However, during various diseases such as chronic bronchitis, cystic fibrosis and bronchial asthma, the number of mucus secreting cell increases. This results in excessive mucus formation due to which lung mucocilliary clearance is either impaired or absent. Mucus in that case is transported mainly by air motion caused by forced expiration or cough.

To understand the mechanism of mucus transport in the lung due to coughing, there have been many simulated experimental studies [1-6]. These investigators have brought several points in focus regarding the role played by rheological properties of mucus which is rheologically characterized by viscoelastic material [7-9]. The role of serous fluid and air flow rate has been also studied ([1], [4], [10]). Reference [5] studied the clearance of fluid by simulated cough using a section of clear, non-collapsible tubing and Newtonian liquids of various viscosities to represent the airway and the mucus. They found that the fraction of liquid slug blown out of the tube, increased as the liquid viscosity decreased [6]. They assumed that the flow is quasi-steady by taking the flow of air as turbulent. References [2]-[4] studied the clearance of mucus by simulated cough with emphasis on mucus/airflow interaction during coughing pointed out that cough clearance increases with the decrease of viscosity or elastic modulus of mucus gel. Reference [1] in their experiment regarding mucus transport observed that mucus gel transport is more in the presence of serous layer simulant [10].

It is noted that bronchial surfactant is essential for bronchoalveolar transport mechanisms including ciliary and non-ciliary mucus transport and surfactant therapy appears to improve mucus clearability ([11]-[14]).

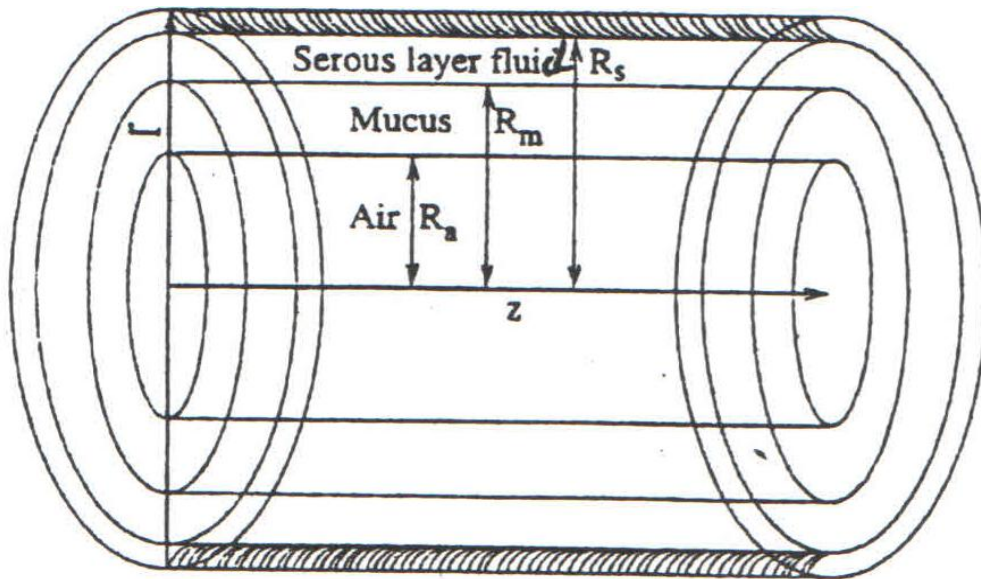
It may be pointed out here that little effort has been made to study the mucus transport in the airways using mathematical model. Therefore, in this paper, a three layer laminar flow model is proposed to study mucus transport in the circular airways by considering the following aspects into account.

1. Cilia are immotile during coughing and they float in the serous fluid close to the epithelium. No flow is assumed in this region.
2. For simplicity mucus is represented by viscoelastic Maxwell fluid, whereas air and serous fluid are considered as Newtonian fluids
3. The presence of surfactant in the mucus and serous layer interface causes slipperiness.

II. Mathematical Formulation

Consider the flow of air, mucus and serous fluid in a circular tube simulating the flow in the airways. The flow is caused due to air motion during coughing. Air and serous fluids are considered as Newtonian fluids whereas

mucus is viscoelastic Maxwell fluid. The flow geometry is shown in the following figure [16], where, air flows in the region $0 \leq r \leq R_a$, and serous fluid flows in the region $R_m \leq r \leq R_s$ and mucus flows in the region $R_a \leq r \leq R_m$.



The equation governing the quasi-steady flow of air, mucus and serous layers in a circular tube can be written as follows:

Region I ($R_m \leq r \leq R_s$) Serous fluid:

$$\phi_p + \frac{1}{r} \frac{\partial}{\partial r} (r \tau_s) = 0, \tau_s = \mu_s \frac{\partial u_s}{\partial r} \quad (1)$$

Region II ($R_a \leq r \leq R_m$), Mucus:

$$\phi_p + \frac{1}{r} \frac{\partial}{\partial r} (r \tau_m) = 0 \quad (2)$$

$$\tau_m + \frac{\mu_m}{G} \frac{\partial \tau_m}{\partial t} = \mu_m \frac{\partial u_m}{\partial r} \quad (3)$$

Region III ($0 \leq r \leq R_a$), Air:

$$\phi_p + \frac{1}{r} \frac{\partial}{\partial r} (r \tau_a) = 0, \tau_a = \mu_a \frac{\partial u_a}{\partial r} \quad (4)$$

Where τ_a, τ_m, τ_s are the stresses in the air, mucus and serous layer, respectively; u_a, u_m and u_s are the respective velocity of air, mucus and serous fluid in the z direction; ρ_a and μ_a are the respective density and viscosity of air; μ_m is the viscosity of mucus, G is the elastic modulus of mucus and μ_s is the viscosity of serous fluid. Equation (3) written by assuming that mucus behaves as a viscoelastic Maxwell fluid [15]. From Equation (4) we may note that when $G \rightarrow \infty$ mucus behaves as a Newton fluid.

Since during mild coughing or forced expiration the pressure gradient in the lung is time dependent, therefore we assume that $-\frac{\partial p}{\partial z} = \phi_p = \phi_0 f(t)$ (where t is the time, p is the pressure which is constant across the layers, z is axial coordinate, and ϕ_0 is constant).

Since initially there is no pressure gradient, one can assume that the velocities and stresses are zero, therefore, the initial conditions are

$$u_a = u_m = u_s = 0, \tau_a = \tau_m = \tau_s = 0, \frac{\partial u_m}{\partial r} = 0 \quad (5)$$

Again the velocities and stresses are continuous at the interfaces $r = R_a$ and $r = R_m$. Therefore, the matching conditions are

$$u_a = u_m, \tau_a = \tau_m \text{ at } r = R_a \quad (6)$$

$$u_m = u_s - \beta \tau_s, \tau_m = \tau_s \text{ at } r = R_m \quad (7)$$

To take in to account the effect of slipperiness caused by the presence of surfactant in the mucus and serous fluid interface we have considered slip velocity in equation (7), where β is the slip coefficient [16].

Due to symmetry at $r = 0$ and no-slip at $r = R_s$ we have the boundary conditions as

$$\frac{\partial u_a}{\partial r} = 0 \text{ at } r = 0 \quad (8)$$

$$u_s = 0 \text{ at } r = R_s \quad (9)$$

III. Results and Discussion

Now solving Equations (1) – (4) along with the conditions (5) – (9) the velocity components are obtained as follows:

$$u_a = \frac{\varphi_p}{4\mu_a}(R_a^2 - r^2) + \frac{\varphi_p}{4\mu_s}(R_s^2 - R_m^2) + \left(\frac{\varphi_p}{\mu_m} + \frac{\varphi_p'}{G}\right)\frac{R_m^2 - R_a^2}{4} + \frac{\varphi_p}{2}\beta R_m \quad (10)$$

$$u_m = \frac{\varphi_p}{4\mu_s}(R_s^2 - R_m^2) + \left(\frac{\varphi_p}{\mu_m} + \frac{\varphi_p'}{G}\right)\frac{R_m^2 - r^2}{4} + \frac{\varphi_p}{2}\beta R_m \quad (11)$$

$$u_s = \frac{\varphi_p}{4\mu_s}(R_s^2 - r^2) \quad (12)$$

where φ_p' denotes the derivative of φ_p with respect to t .

The volumetric flow rates in each layer can be defined as

$$Q_s = \int_{R_m}^{R_s} 2\pi r u_s dr, Q_m = \int_{R_a}^{R_m} 2\pi r u_m dr, Q_a = \int_0^{R_a} 2\pi r u_a dr$$

Which after using Equations (10) – (12) can be found as

$$Q_a = \frac{\pi\varphi_p}{2}R_a^2 \left[\frac{R_a^2}{4\mu_a} + \frac{R_m^2 - R_a^2}{2\mu_m} + \frac{R_s^2 - R_m^2}{2\mu_s} + \beta R_m \right] + \frac{\pi\varphi_p'}{4G}R_a^2(R_m^2 - R_a^2) \quad (13)$$

$$Q_m = \frac{\pi\varphi_p}{2}(R_m^2 - R_a^2) \left[\frac{R_m^2 - R_a^2}{4\mu_m} + \frac{R_s^2 - R_m^2}{2\mu_s} + \beta R_m \right] + \frac{\pi\varphi_p'}{8G}(R_m^2 - R_a^2)^2 \quad (14)$$

$$Q_s = \frac{\pi\varphi_p}{8\mu_s}(R_s^2 - R_m^2)^2 \quad (15)$$

In a particular case, when mucus behaves as a Newtonian fluid (*i.e.* $G \rightarrow \infty$), the expressions for Q_a , Q_m and Q_s reduce to

$$Q_a = \frac{\pi\varphi_p}{2}R_a^2 \left[\frac{R_a^2}{4\mu_a} + \frac{R_m^2 - R_a^2}{2\mu_m} + \frac{R_s^2 - R_m^2}{2\mu_s} + \beta R_m \right]$$

$$Q_m = \frac{\pi\varphi_p}{2}(R_m^2 - R_a^2) \left[\frac{R_m^2 - R_a^2}{4\mu_m} + \frac{R_s^2 - R_m^2}{2\mu_s} + \beta R_m \right]$$

$$Q_s = \frac{\pi\varphi_p}{8\mu_s}(R_s^2 - R_m^2)^2$$

From equation (14), we may note that Q_m increases as β increases. This shows that mucus transport is more in the presence of surfactant mucus. Thus, the role of surfactant is to spread and cover the entire surface of the relevant airway and thereby serve as an adhesive forming an interface or interlayer between mucus and the airway wall [18, 19]. Therefore the role of surfactant in the mucus transport can be speculated as a lubricating agent acting as a serous layer and reducing the friction between the mucus layer and the surfaces of the epithelium embedded with cilia.

It is also observed (from equation (14)) that Q_m increases as the viscosity of mucus and serous fluid decrease. Therefore, mucus flow rate is enhanced as the viscosity of serous fluid decreases. This is in agreement of analytical and experimental observation of [1, 2, 10, 16]. The flow rate also increases as the viscosity of mucus decreases [15-18]. It can be further noted that the flow rate increases as the elastic modulus (G) decreases [3]. This suggests that mucus transport will be more in the case mucus behaves as viscoelastic fluid. Rheological properties of mucus are important to cough clearance; elasticity impedes forward motion and results in recoil after the cough event.

For fixed airway dimension (R_s) and serous layer ($R_s - R_m$) we have (from equation (14))

$$\frac{\partial Q_m}{\partial R_a} = \frac{\pi \phi_p}{2} \left[-\frac{R_a(R_m^2 - R_a^2)^2}{\mu_m} - \frac{R_a(R_s^2 - R_m^2)^2}{\mu_s} - 2\beta R_a R_m \right] - \frac{\pi R_a}{2G} \phi_p' (R_m^2 - R_a^2) < 0$$

This shows that Q_m decreases as R_a increases (for fixed airway dimension and serous layer thickness. Therefore mucus transport increases with its thickness [1,3,15-18].

Forced expiration or coughing is a short time phenomenon. During this time, instantaneous pressure gradient (ϕ_p) is generated. From equation (14) it is observed that mucus flow rate increases as the magnitude of pressure gradient increases.

From equation (14) it can be further noted that for fixed airway dimension, mucus transport is more in the presence of serous fluid. It has been reported by [20] that bacterial infection increases the secretion of tracheal mucus macromolecules and reduce the transport of ions and water into the tracheobronchial lumen. Reduced water movement across the airway will likely alter the hydration of mucus and serous fluid. This shows that in absence of serous fluid mucus transport is reduced (see equation (14)).

IV. Conclusion

In this paper, a quasi steady state three layer laminar flow model to study mucus transport in the smaller airways is presented. Serous fluid and air are considered as Newtonian fluids while mucus is treated as Maxwell fluid. It is assumed that surfactant is present in the mucus and serous layer interfaces. The results of the study can be summarized as follows:

- Mucus transport increases as the magnitude of pressure gradient increases.
- For airway dimension and serous layer thickness, mucus transport increases with its thickness. This increase is further enhanced as the viscosity of mucus decreases.
- Mucus transport increases as the viscosity of serous fluid decreases. This transport also increases as the elastic modulus decreases. This shows that mucus transport is more in the viscoelastic case as compared to Newtonian case.

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