MATHEMATICAL MODELLING OF MUCUS TRANSPORT IN THE LUNG DUE TO PROLONGED MILD COUGH: EFFECTS OF MUCUS AND SEROUS FLUID VISCOSITY

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ABSTRACT: In this paper, the simultaneous and coaxial flow of moist air, mucus and serous fluid in a circular tube under time dependent pressure gradient representing prolonged mild cough is modelled and analysed to study mucus transport in an smaller airway due to prolonged mild cough. In the central core air is assumed to flow under quasisteady state turbulent condition and the mucus layer surrounding this central core is assumed to flow under unsteady laminar condition and the serous fluid surrounding this mucus layer is also assumed to flow under unsteady laminar condition through cilia bed by considering the resistance term and ignoring viscous term. It is shown that flow rates of mucus in two layers increase as the magnitude of the pressure gradient increases. It has been found that the mucus flow rate decreases as the mucus and serous fluid viscosities increase but mucus flow increases as its thickness increases. It is observed that mucus and serous fluid flow rates increase as the coefficient of porosity increases.

1. INTRODUCTION

Nature has provided highly complex system in human body and the human lung is no exception\textsuperscript{1}. The lung, the lower part of 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, where the gas exchange occurs in cardiovascular system. The walls of trachea and bronchi consist of epithelium, gland, cartilage, mucosa, submucosa and adventitia. From the trachea to the beginning of the respiratory bronchioles, the respiratory tract is lined by ciliated columnar epithelium. The epithelium of the airways consists of ciliated cells, serous cells, goblet cells, clara cells, brush cells etc. Each ciliated cell contains at least 200 cilia. The goblet cells produce mucus while serous cells produce serous fluid, a water like substance. The serous fluid behaves like a Newtonian fluid. Its viscosity varies from 0.01-0.1 Poise. A mixture of lipoproteins called surfactant is secreted by special surfactant cells that are part of the alveolar epithelium and bronchioles, useful in mucus transport by causing slip at the inner wall of each 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\textsuperscript{2,3,4,5}. Also when airways are affected by immotile cilia syndrome (dyskinesia), cough is the main mechanism by which mucus is transported.
In recent decades, several experiments related to two phase flow in tubes under externally applied pressure have been studied to simulate mucus transport in airways due to cough\textsuperscript{6,7,8,9,10}. In particular, Clarke \textit{et al.},\textsuperscript{6} have shown that the resistance to air flow through a liquid lined tube is markedly increased at all flow rates in comparison to the case of a dry tube. They have noted that at all flow rates compatible with laminar flow conditions the pressure flow relationship in liquid lined tube is nonlinear and the resistance to flow being greater than that expected from narrowing alone. This result is expected as the high viscous fluid occupies the corresponding air-space in the tube under dry condition. They have pointed out further that after the onset of turbulence there is a considerable increase in flow resistance which occurs simultaneously with wave formation on the surface of liquid film. These effects are more marked in case of thicker liquid layer and with lower viscosity. They have also found that the effect of gravity is negligible on mucus transport. Scherer and Burtz\textsuperscript{8}, Scherer\textsuperscript{9} have conducted fluid mechanical experiments relevant to cough, using air and liquid blown out of a straight tube by turbulent air jet. By assuming that the turbulent flow is quasi steady and the turbulent stress in the air is equal to viscous stress in the liquid flowing under laminar condition, they have shown that the liquid transport efficiency has positive correlation with the parameter $\rho_a U T/\mu$ (where $\rho_a$ is the density of air, $\mu$ is the viscosity of liquid, $U$ is the air velocity, $T$ is the cough duration) and the liquid transport decreases as this parameter decreases. They have further pointed out that for fixed values of $\rho_a$, $U$, $T$, transport efficiency decreases as viscosity $\mu$ increases. Kim \textit{et al.},\textsuperscript{10} have studied mucus transport in vertical tubes by two phase (gas, liquid) flow mechanism and noted that the elasticity of mucus does not affect its transport.

Though in the past few decades some review articles and research papers have been written relevant to the problem under consideration, it may be noted here that hardly any attempt has been made to study mucus transport in lung due to cough by using mathematical models. Therefore, in this paper, we study the simultaneous flow of air and mucus in a pipe simulating mucus transport in airways due to cough under the following assumptions\textsuperscript{11}:

1. The fluid flow is symmetrical about the central axis.
2. The applied pressure gradient is assumed to be a time dependent function representing cough.
3. Mucus is assumed to behave as an incompressible Newtonian fluid due to high shear rate during cough.\textsuperscript{12}
4. Since air is saturated with watery liquid during cough, it is also assumed to behave as an incompressible Newtonian fluid in the lung during cough.
5. Air flow is turbulent and is quasi steady during cough.$^{8,9}$
6. The coaxial mucus layer surrounding the central core region where air is flowing under turbulent condition during cough and in contact with air, assumed to flow under unsteady laminar conditions.

7. In large airways, during cough immotile cilia form an oriented porous matrix saturated with serous fluid, through which this fluid flows due to pressure gradient generated by cough under unsteady laminar conditions through cilia bed.

2. Model

In view of the above considerations and using Prandtl mixing length theory, the means of quasisteady state equations in the turbulent layer and the unsteady state equations of mucus and serous fluid in the laminar layer can be written in cylindrical coordinates as follows\textsuperscript{13}. Further the equation of serous fluid is governed by the generalised unsteady Darcy’s law.

**Region I:** Quasi steady turbulent flow of air ($0 \leq r \leq R_a$):

$$-rac{\partial p}{\partial z} + \frac{1}{r} \frac{\partial}{\partial r} (r \tau_a) = 0$$

(2.1)

$$\tau_a = \rho_a l_a^2 \left| \frac{\partial u_a}{\partial r} \right| \frac{\partial u_a}{\partial r} = -\rho_a l_a^2 \left( -\frac{\partial u_a}{\partial r} \right)^2.$$  

(2.2)

**Region II:** Unsteady laminar flow of mucus ($R_a \leq r \leq R_m$):

$$-\frac{\partial p}{\partial z} + \frac{1}{r} \frac{\partial}{\partial r} (r \tau_m) = \rho_m \frac{\partial u_m}{\partial t}$$

(2.3)

$$\tau_m = \mu_m \frac{\partial u_m}{\partial r}.$$  

(2.4)

**Region III:** Unsteady laminar flow of serous fluid ($R_m \leq r \leq R$):

$$-\frac{\partial p}{\partial z} - \frac{\mu_s}{\phi_s} u_s = \rho_s \frac{\partial u_s}{\partial t}.$$  

(2.5)

In equation (2.1)-(2.5), $t$ is the time, $z$ is the coordinate along the axis of the tube in the flow direction, $r$ is the coordinate in the radial direction and perpendicular to fluid flow, $R_a$ is the thickness up to air-mucus interface, $R$ is the radius of the tube, $p$ is the mean pressure which is constant across three layers, $u_a$, $u_m$, $u_s$ are the mean velocity components of air (under turbulent flow), mucus (under laminar flow) and serous fluid (under laminar flow) in the $z$ direction respectively, $\tau_a$ is the mean shear stress in the air
and $\tau_m$ is the mean shear stress in the laminar mucus layer, $\rho_a$, $\rho_m$ and $\rho_s$ are the densities of air, mucus and serous fluid respectively, $\mu_s$ and $\mu_m$ are viscosities of serous fluid and mucus respectively. Here $\phi_s$ is the coefficient of porosity of cilia bed.

The mixing length $l_a$ is assumed as follows:

$$l_a = l_0 (R - r),$$

where $l_0$ is a constant and determined experimentally.

Initial Condition:

$$u_s = 0 \quad \text{at} \quad t = 0. \quad (2.6)$$

Boundary Condition:

To simplify the model, since the viscosity of serous fluid is very small, in (2.5), the viscous term has been assumed to be negligible in comparison to the resistance term caused by cilia bed. So the boundary condition is:

$$\frac{\partial u_s}{\partial r} = 0 \quad \text{at} \quad r = 0. \quad (2.7)$$

Matching Conditions:

$$u_a = u_m; \quad \tau_a = \tau_m \quad \text{at} \quad r = R_a$$

$$u_m = u_s; \quad \text{at} \quad r = R_m \quad (2.8)$$

Equations (2.8) and (2.9) represent the continuity of the velocity and stress components at the two interfaces.

$$-\frac{\partial p}{\partial z} = P = P_0 f(t). \quad (2.10)$$

Here $P_0$ is the strength of prolonged mild cough and as this increases the flow rates increases proportionally.

2.11: Mucus Transport in a Circular Tube
The function in (2.10) is given by,

$$f(t) = \begin{cases} \frac{321t^2}{640T_m^2} \left( 1 - \frac{2t}{3T_m} \right) & 0 \leq t \leq T_m \\ \frac{9}{32} t \left( 1 - \frac{9t}{10T} \right)^2 + \frac{T}{64} & T_m \leq t \leq \frac{T}{\alpha} \\ \frac{T}{64} & t \geq \frac{T}{\alpha} \end{cases}$$  \hspace{1cm} (2.12)$$

Where $T$ is the duration of cough and $\alpha$ is the constant which is 0.9 and $T_m = 0.011$ sec. This function represents the prolonged mild cough as discussed by Leith\textsuperscript{14}.

![Graphical Representation of the Function]

2.13: Graphical Representation of the Function

3. **Analysis of Model**

3.1 **Method of Solution**

We solve the model (2.1)-(2.5) using the boundary conditions (2.7) and the matching conditions are given by (2.8), (2.9). Thus the stress and velocity components in each layer are given by the following set of equations:

$$\tau_u = -\frac{\text{Pr}}{2}$$  \hspace{1cm} (3.1.1)
\[ \tau_m = -\frac{Pr}{2} + \frac{\rho_m \Psi_m}{2} \left[ r - \frac{R_a^2}{r} \right] \]  

\[ u_a = \frac{P \phi_s}{\mu_s} \left( 1 - e^{-\frac{\mu_s}{\rho_s \phi_s} t} \right) + \left( \frac{R_m^2 - R_a^2}{4 \mu_m} \right) P - \frac{\rho_m \Psi_m}{2 \mu_m} \left[ R_m^2 - R_a^2 + R_a^2 \ln \frac{R_a}{R_m} \right] + \frac{1}{l_0} \left( \frac{2PR}{\rho_a} \right)^{\frac{1}{3}} \left[ \ln \frac{R_m^2 + R_a^2}{R_m^2 + r^2} - \frac{1}{2} \ln \frac{R - R_a}{R - r} - \frac{R_a^2 - r^2}{R^2} \right] \]  

\[ u_m = \frac{P \phi_s}{\mu_s} \left( 1 - e^{-\frac{\mu_s}{\rho_s \phi_s} t} \right) + \left( \frac{R_m^2 - r^2}{4 \mu_m} \right) P - \frac{\rho_m \Psi_m}{2 \mu_m} \left[ R_m^2 - r^2 + R_a^2 \ln \frac{r}{R_m} \right]. \] 

The equation (2.5) is solved by using the initial condition (2.6) as follows:

\[ u_s = \frac{P \phi_s}{\mu_s} \left( 1 - e^{-\frac{\mu_s}{\rho_s \phi_s} t} \right). \] 

The volumetric flow rates in each layer can be defined as

\[ Q_a = \int_0^{R_a} 2\pi r u_adr, \quad Q_m = \int_{R_a}^{R_m} 2\pi r u_madr, \quad Q_s = \int_{R_m}^R 2\pi r u_sadr. \] 

Which after using equations (3.1.3)-(3.1.5) can be written as

\[ \frac{Q_a}{2\pi} = \frac{PR_m^2}{2\mu_s} \left( 1 - e^{-\frac{\mu_s}{\rho_s \phi_s} t} \right) + \left( \frac{R_m^2 - R_a^2}{8 \mu_m} \right) P R_m^2 - \frac{\rho_m \Psi_m}{2 \mu_m} \left[ R_m^2 - R_a^2 + R_a^2 \ln \frac{R_a}{R_m} \right] + \frac{R^2}{2l_0} \left( \frac{2PR}{\rho_a} \right)^{\frac{1}{3}} \left[ \ln \frac{R_m^2 + R_a^2}{R_m^2 + r^2} - \frac{1}{2} \ln \frac{R - R_a}{R - r} - \frac{R_a^2 - r^2}{R^2} \right] \] 

\[ \frac{Q_m}{2\pi} = \frac{P}{2} \left( R_m^2 - R_a^2 \right) \left[ \frac{\phi_s}{\mu_s} \left( 1 - e^{-\frac{\mu_s}{\rho_s \phi_s} t} \right) + \frac{R_m^2 - R_a^2}{8 \mu_m} \right] - \frac{\rho_m \Psi_m}{2 \mu_m} \left[ \frac{R_m^2 - R_a^2}{8} \right] + \frac{R_a^4}{2} \ln \frac{R_m}{R_a} \] 

\[ \frac{Q_s}{2\pi} = \frac{P \phi_s}{2\mu_s} \left( 1 - e^{-\frac{\mu_s}{\rho_s \phi_s} t} \right). \] 

To solve the unsteady equations in laminar layer we use the method of averaging as done by Sestak and Charles. Thus, by substituting the acceleration term on the right hand side of equations (2.3) by its mean value across the thickness i.e.
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\[
\frac{\partial u_m}{\partial t} \approx \Psi_m = \frac{1}{R_m - R_a} \int_{R_a}^{R_m} \frac{\partial u_m}{\partial t} \, dr \quad (3.1.10)
\]

then equation (2.3) reduces to

\[
\frac{\partial}{\partial r} (r \tau_m) = -(P - \rho_m \Psi_m) r . \quad (3.1.11)
\]

Where \( \Psi_m \) is a function of time only, and \( P \) as given in equation (2.10).

To determine \( \Psi_m \) we differentiate Equation (3.1.4) with respect to \( t \) to get

\[
\frac{\partial u_m}{\partial t} = \frac{P' \phi_s}{\mu_s} \left( 1 - e^{-\frac{\mu_s}{\rho_s} t} \right) + \frac{P}{\rho_s} e^{-\frac{\mu_s}{\rho_s} t} + \left( \frac{R_m^2 - r^2}{4 \mu_m} \right) P' \\
- \frac{\rho_m \Psi_m'}{2 \mu_m} \left[ \frac{R_m^2 - r^2}{2} + R_a^2 \ln \frac{r}{R_m} \right] \quad (3.1.12)
\]

where (') denotes the derivative with respect to \( t \).

Now on solving (3.1.10) using (3.1.12) we get,

\[
\psi_m' + \frac{\psi_m}{a_2} = \frac{P' a_1}{a_2} + \frac{1}{a_2} e^{-\frac{\mu_s}{\rho_s} t} \left( \frac{P}{\rho_s} - \frac{P' \phi_s}{\mu_s} \right) \quad (3.1.13)
\]

where,

\[
a_1 = \left[ \frac{(2R_m + R_a)(R_m - R_a)}{12 \mu_m} - \frac{\phi_s}{\mu_s} \right] \\
a_2 = \frac{\rho_m}{2} \left[ \frac{(2R_m + R_a)(R_m - R_a)}{6 \mu_m} - \frac{R_a^2}{\mu_m} \left( 1 + \frac{R_a}{R_m - R_a} \ln \frac{R_a}{R_m} \right) \right] .
\]

On solving (3.1.13) using (2.10) and (2.12) we get the value of \( \psi_m \).

3.2 Discussion and Results

We now study the flow rates \( Q_a \), \( Q_m \) and \( Q_s \) with respect to various parameters. We have drawn the graph of \( Q_a \), \( Q_m \) and \( Q_s \) with respect to \( t \) for various values of viscosities of mucus and serous fluid by using the following set of parameters\(^6\).

\[
T = 0.03 \text{ sec} \quad t = 0 - 0.035 \text{ sec}, \\
l_0 = l_1 = 0.40 \quad \mu_s = (1.00 - 10.00) \times 10^{-2} \text{ poise}. \\
R_a = 31.45 \times 10^{-2} \text{ cm}, \quad R_m = 38.45 \times 10^{-2} \text{ cm}
\]
\[ \mu_m = 1.00 - 10.00 \text{ poise} \quad \rho_m = 1.00 \text{ gm cm}^{-3} \]
\[ \rho_a = 1.00 \times 10^{-3} \text{ gm cm}^{-3} \quad \rho_s = 0.9 \text{ gm cm}^{-3} \]
\[ P_0 = 1 \times 10 \text{ gm cm}^{-2} \text{ sec}^{-2} \quad \phi_f = 0.01 - 0.1 \text{ gm}^{-1} \text{ cm}^{2} \text{ sec}. \]

Figure 3.2.1 illustrates the effect of time on air, mucus and serous fluid flow rates for \( \phi_f = .05 \text{ gm}^{-1} \text{ cm}^{2} \text{ sec} \) and for various values of \( \mu_s \). So from these figures it is observed

Figure 3.2.1: Variation of \( Q_a, Q_m \) and \( Q_s \) with \( t \) for Different \( \mu_s: \mu_m = 5 \text{ poise}, \phi_f = .05 \text{ gm}^{-1} \text{ cm}^{2} \text{ sec} \)

Upper Denotes \( \mu_s = 0.01 \text{ poise} \)
Middle Denotes \( \mu_s = 0.05 \text{ poise} \)
Lower Denotes \( \mu_s = 0.1 \text{ poise} \)
that for fixed air core radius $R_a$, the flow of mucus and serous fluid decreases as $\mu_m$ increases. It can be seen from Fig. 3.2.2 that as mucus viscosity increases mucus, air and serous flow rates decrease. Also from these figures it can be seen easily that mucus and serous fluid flow rates increase as the porosity increase for fixed values of mucus

Figure 3.2.2: Variation of $Q_a$, $Q_m$ and $Q_s$ with $t$ for Different $\mu_m$ ($\mu_s = 0.05$ poise, $\phi_s = 0.05$ gm$^{-1}$ cm$^2$ sec)

Upper Denotes $\mu_m = 1$ poise
Middle Denotes $\mu_m = 5$ poise
Lower Denotes $\mu_m = 10$ poise
and serous fluid viscosities [Fig. 3.2.3 (b), (c)]. Figure 3.2.4 illustrates the effect of mucus layer thickness and it is clear from Fig. 3.2.4(a), (b) that as the thickness of mucus layer increases its flow rate also increases for fixed $R$ and $R_a$ whereas the serous fluid flow rate decreases [Fig. 3.2.4(b,c)].
In this paper, we have studied mucus transport in an airway due to prolonged mild cough by representing it as a circular tube. The prolonged mild cough has been represented by a time dependent pressure gradient. The simultaneous and coaxial flow of air in a tube is considered to be quasisteady turbulent while serous fluid and mucus surrounding air coaxially are assumed to flow under unsteady laminar conditions.

4. CONCLUSIONS

In this paper, we have studied mucus transport in an airway due to prolonged mild cough by representing it as a circular tube. The prolonged mild cough has been represented by a time dependent pressure gradient. The simultaneous and coaxial flow of air in a tube is considered to be quasisteady turbulent while serous fluid and mucus surrounding air coaxially are assumed to flow under unsteady laminar conditions.
The following results about flow rates have been concluded from the analytical and computational study:

1. Air, mucus and serous fluid flow rates decrease with increase in serous fluid viscosity.
2. Mucus and serous fluid flow rates increase as mucus viscosity decreases and there is a very negligible effect on air flow rate.
3. It is observed that mucus and serous fluid flow rates increase as the coefficient of porosity increases.
4. As the thickness of mucus increases its flow rate increases on the other hand the serous fluid flow rate decreases.

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