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MATHEMATICAL MODELLING OF MUCUS TRANSPORT IN THE LUNG DUE TO PROLONGED COUGH: EFFECT OF RESISTANCE TO FLOW BY SEROUS FLUID IN THE CILIA BED

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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 cough is modelled and analysed to study mucus transport in an airway due to prolonged cough. In the central core air is assumed to flow under quasisteady state turbulent condition and the mucus layer surrounding this central core is also assumed to flow under quasisteady state turbulent condition while the serous fluid surrounding this mucus layer is assumed to flow under unsteady laminar condition. It is found that for fixed thickness of air and mucus, the mucus transport increases as its total thickness increases and serous fluid flow rate decreases. It is depicted that mucus transport increases as the porosity of cilia bed saturated with serous fluid increases. It is also observed that mucus transport increases as the viscosity of serous fluid decreases. Keeping in view that the time dependent pressure gradient function representing prolonged cough, increases, takes a maximum value during cough and then decreases to almost zero, It has been found that the flow rates also follow the same pattern.

1. INTRODUCTION

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[1,2,3,4]. 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[5,6,7,8,9]. In particular, Clarke *et al.*,[5] 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[7], Scherer[8] 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 $\rho_a UT/\mu$ (where ρ_a is the density of air, μ 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 ρ_a, U, T, transport efficiency decreases as viscosity μ increases. Kim *et al.*,[9] 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.

Several other experimental investigations in a cough machine (a parallel plate channel) under turbulent flow condition have also been conducted by simulating mucus transport in the trachea due to cough [13,1,2,3,11,12]. In particular, King *et al.*,[10] in their experiments found no apparent relationship between elasticity of mucus and its transport. Zahm et al.[11] in their experimental studies in a cough machine pointed out that mucus transport increases due to the presence of a sol phase at bottom plate. Agarwal *et al.*,[13] have studied the mucus gel transport in a constricted simulated cough machine and found that mucus transport increases in presence of serous fluid. Agarwal *et al.*,[14] have also studied, experimentally, the transport of mucus gel in a simulated cough machine where the bottom plate was grooved and, flooded with serous fluid. They found that mucus transport increases as the cross-sectional area formed by grooves saturated with serous fluid increases, suggesting the importance of topography and slipperiness of the bottom surface.

Though in the past few decays 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[15]:

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 assuned to behave as an incompressible Newtonian fluid due to high shear rate during cough[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[7,8].

6. The coaxial mucus layer surrounding the central core region where air is flowing under turbulent condition during cough and in contact with air, flows under turbulent conditions as the Reynold number corresponding to this region is very large due to high mucus velocity here.
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.

2. MODEL

In view of the above considerations and using Prandtl mixing length theory, the means of quasisteady state equations in the turbulent layers can be written in cylindrical coordinates as follows[16]. Further the unsteady state equation of serous fluid in the laminar layer is governed by the generalised Darcy's law.

Governing Equations With Boundary And Matching Conditions

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

$$-\frac{\partial p}{\partial z}+\frac{1}{r}\frac{\partial}{\partial r}(r\tau_a)=0 \tag{2.1}$$

$$\tau_a=\rho_a l_a^2\left|\frac{\partial u_a}{\partial r}\right|\frac{\partial u_a}{\partial r}=-\rho_a l_a^2\left(-\frac{\partial u_a}{\partial r}\right)^2 \tag{2.2}$$

Region II: Quasi steady turbulent flow of mucus ($R_a \le r \le R_m$):

$$-\frac{\partial p}{\partial z}+\frac{1}{r}\frac{\partial}{\partial r}(r\tau_m)=0 \tag{2.3}$$

$$\tau_m=\rho_m l_m^2\left|\frac{\partial u_m}{\partial r}\right|\frac{\partial u_m}{\partial r}=-\rho_m l_m^2\left(-\frac{\partial u_m}{\partial r}\right)^2 \tag{2.4}$$

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

$$-\frac{\partial p}{\partial z}-\frac{\mu_s}{\phi_s}u_s=\rho_s\frac{\partial u_s}{\partial t} \tag{2.5}$$

In system (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 and 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, mucus and serous fluid in the z direction respectively, τ_a is the mean shear stress in the air, τ_m is the mean shear stress in mucus layer and ρ_a, ρ_m and ρ_s are the densities of air, mucus and serous fluid respectively, μ is serous fluid viscosity, ϕ_s is the coefficient of porosity of cilia bed.

The mixing lengths l_a and l_m are assumed as follows: [Schlichting (1960)]

$$l_a = l_0 (R - r) \tag{2.6}$$

$$l_m = l_1 (R - r) \tag{2.7}$$

where l_0 and l_1 are constants and are determined experimentally.

Initial Condition

$$u_s = 0 \quad \text{at} \quad t = 0 \tag{2.8}$$

Boundary Condition

$$\frac{\partial u_a}{\partial r} = 0 \quad \text{at} \quad r = 0 \tag{2.9}$$

Matching Conditions

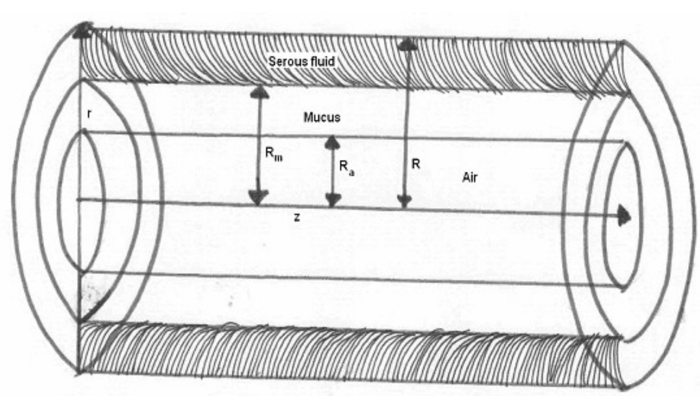
$$u_a = u_m;\ \tau_a = \tau_m \quad \text{at} \quad r = R_a \tag{2.10}$$

$$u_m = u_s \quad \text{at} \quad r = R_m \tag{2.11}$$

Equations (2.10) and (2.11) represents the continuity of the velocity and stress components at the two interfaces.

$$-\frac{\partial p}{\partial z} = P = P_0 f(t) \tag{2.12}$$

where t is time, P_0 is a constant, the magnitude of which depends upon the intensity of prolonged cough.

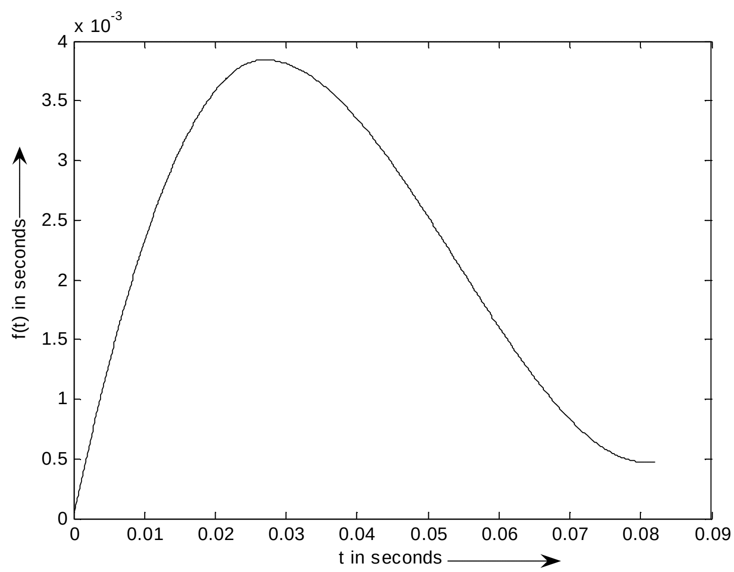


2.13: Mucus Transport in a Circular Tube

The function $f(t)$ in (2.12) is assumed to be given by,

$$f(t)=\begin{cases}\dfrac{41}{144}t\left(1-\dfrac{t}{2T_m}\right) & 0\le t\le T_m\\[2ex] \dfrac{9}{32}t\left(1-\dfrac{10t}{27T}\right)^2+\dfrac{T}{64} & T_m\le t\le \dfrac{T}{\alpha}\\[2ex] \dfrac{T}{64} & t\ge\dfrac{T}{\alpha}\end{cases} \tag{2.14}$$

where $\alpha = 0.37$ and Tm = .027 and T is the duration of cough. This function represents the prolonged cough as discussed by Leith[17].



2.15: Graphical Representation of *f*(t) for Various Values of *t*

3. ANALYSIS OF MODEL

3.1 Method of Solution

Now on solving the model (2.1)-(2.5) using the initial conditions (2.8), boundary condition (2.9), and matching conditions (2.10), (2.11), the stress and velocity components in each layer are given as follows:

$$\tau_a = -\frac{\Pr}{2} \tag{3.1.1}$$

$$\tau_m = -\frac{\Pr}{2} \tag{3.1.2}$$

$$u_a = \frac{\phi_s P}{\mu_s}\left[1 - e^{-\frac{\mu_s}{\rho_s\phi_s}t}\right]$$
$$+\frac{1}{l_0}\left(\frac{2PR}{\rho_a}\right)^{\frac{1}{2}}\left[\ln\frac{R^{\frac{1}{2}}+R_a^{\frac{1}{2}}}{R^{\frac{1}{2}}+r^{\frac{1}{2}}} - \frac{1}{2}\ln\frac{R-R_a}{R-r} - \frac{R_a^{\frac{1}{2}}-r^{\frac{1}{2}}}{R^{\frac{1}{2}}}\right]$$
$$+\frac{1}{l_1}\left(\frac{2PR}{\rho_m}\right)^{\frac{1}{2}}\left[\ln\frac{R^{\frac{1}{2}}+R_m^{\frac{1}{2}}}{R^{\frac{1}{2}}+R_a^{\frac{1}{2}}} - \frac{1}{2}\ln\frac{R-R_m}{R-R_a} - \frac{R_m^{\frac{1}{2}}-R_a^{\frac{1}{2}}}{R^{\frac{1}{2}}}\right] \tag{3.1.3}$$

$$u_m = \frac{\phi_s P}{\mu_s}\left[1 - e^{-\frac{\mu_s}{\rho_s\phi_s}t}\right]$$
$$+\frac{1}{l_0}\left(\frac{2PR}{\rho_a}\right)^{\frac{1}{2}}\left[\ln\frac{R^{\frac{1}{2}}+R_a^{\frac{1}{2}}}{R^{\frac{1}{2}}+r^{\frac{1}{2}}} - \frac{1}{2}\ln\frac{R-R_a}{R-r} - \frac{R_a^{\frac{1}{2}}-r^{\frac{1}{2}}}{R^{\frac{1}{2}}}\right] \tag{3.1.4}$$

From equation (2.5), using the initial condition $u_s = 0$ at $t = 0$, we get that

$$u_s = \frac{\phi_s P}{\mu_s}\left[1 - e^{-\frac{\mu_s}{\rho_s\phi_s}t}\right] \tag{3.1.5}$$

The volumetric flow rates in each layer can be defined as

$$Q_a = \int_0^{R_a} 2\pi r u_a dr, \quad Q_m = \int_{R_a}^{R_m} 2\pi r u_m dr, \quad Q_s = \int_{R_m}^{R} 2\pi r u_s dr \tag{3.1.6}$$

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

$$\frac{Q_a}{2\pi} = \frac{\phi_s R_a^2 P}{2\mu_s}\left[1 - e^{-\frac{\mu_s}{\rho_s\phi_s}t}\right]$$
$$+\frac{R^2}{2l_0}\left(\frac{PR}{2\rho_a}\right)^{\frac{1}{2}}\left[\ln\frac{R^{\frac{1}{2}}+R_a^{\frac{1}{2}}}{R^{\frac{1}{2}}-R_a^{\frac{1}{2}}} - 2\left(\frac{R_a}{R}\right)^{\frac{1}{2}}\left\{1+\frac{R_a}{3R}+\frac{R_a^2}{5R^2}\right\}\right]$$
$$+\frac{R_a^2}{2l_1}\left(\frac{PR}{2\rho_m}\right)^{\frac{1}{2}}\left[\ln\frac{R^{\frac{1}{2}}+R_m^{\frac{1}{2}}}{R^{\frac{1}{2}}-R_m^{\frac{1}{2}}} - \ln\frac{R^{\frac{1}{2}}+R_a^{\frac{1}{2}}}{R^{\frac{1}{2}}-R_a^{\frac{1}{2}}} - 2\frac{R_m^{\frac{1}{2}}-R_a^{\frac{1}{2}}}{R^{\frac{1}{2}}}\right] \tag{3.1.7}$$

$$\frac{Q_m}{2\pi} = \frac{Q_m}{2\pi} = \frac{\phi_s P}{2\mu_s}\left[1 - e^{-\frac{\mu_s}{\rho_s\phi_s}t}\right][R_m^2 - R_a^2]$$

$$+\frac{1}{l_1}\left(\frac{PR}{2\rho_m}\right)^{\frac{1}{2}}\left[\begin{array}{l}\frac{R^2 - R_a^2}{2}\left\{\ln\frac{R^{\frac{1}{2}} + R_m^{\frac{1}{2}}}{R^{\frac{1}{2}} - R_m^{\frac{1}{2}}} - \ln\frac{R^{\frac{1}{2}} + R_a^{\frac{1}{2}}}{R^{\frac{1}{2}} - R_a^{\frac{1}{2}}}\right\} \\ +\left(\frac{R_a}{R}\right)^{\frac{1}{2}}\left(\frac{15R^2 + 5R_aR - 12R_a^2}{15}\right) \\ -\left(\frac{R_m}{R}\right)^{\frac{1}{2}}\left(\frac{15R^2 + 5R_mR + 3R_m^2 - 15R_a^2}{15}\right)\end{array}\right] \quad (3.1.8)$$

$$\frac{Q_s}{2\pi} = \frac{\phi_s P}{2\mu_s}[R^2 - R_m^2]\left[1 - e^{-\frac{\mu_s}{\rho_s\phi_s}t}\right]. \quad (3.1.9)$$

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 varied the parameter $(R_m - R_a)$ in such a way that the radial thickness of the turbulent mucus zone increases and the corresponding laminar layer thickness decreases. To study this aspect we have drawn the graph of Q_a, Q_m and Q_s with respect to $(R_m - R_a)$ for fixed values of viscosity and porosity coefficient.

We have applied the model analysis to the larger airways (second generation) and considered the case where $R = 46.45 \times 10^{-2}$ cm. To study the effect of various parameters on air flow rate and mucus transport quantitatively the expressions for Q_a, Q_m and Q_s have been calculated and plotted by using the following set of parameters.

$T = .03$sec,	$t = 0 - 0.08$ sec,
$l_0 = l_1 = 0.40$	$R_a = 31.45 \times 10^{-2}$ cm,
$R_m = 38.45 \times 10^{-2}$ cm,	$\mu_m = 1.00 - 10.00$ poise
$\rho_a = 1.00 \times 10^{-3}$ gm cm^{-3}	$\mu_s = 1.00 - 10.00 \times 10^{-2}$ poise
$\rho_m = 1.00$ gm cm^{-3}	$\phi_s = 0.01 - 0.10$ gm^{-1} cm^2 sec
$\rho_s = 0.9$ gm cm^{-3}	$P_0 = 1.00 \times 10^5$ gm cm^{-2} sec^{-2}

Figure 3.2.1 illustrates the effect of time on air, mucus and serous fluid flow rates for $\mu_s = 0.05$ poise, $\phi_s = 0.05$ gm^{-1} cm^2 sec and various values of R_m and so from these figures it is observed that for fixed radial thickness of mucus $(R_m - R_a)$ and air core radius R_a, the

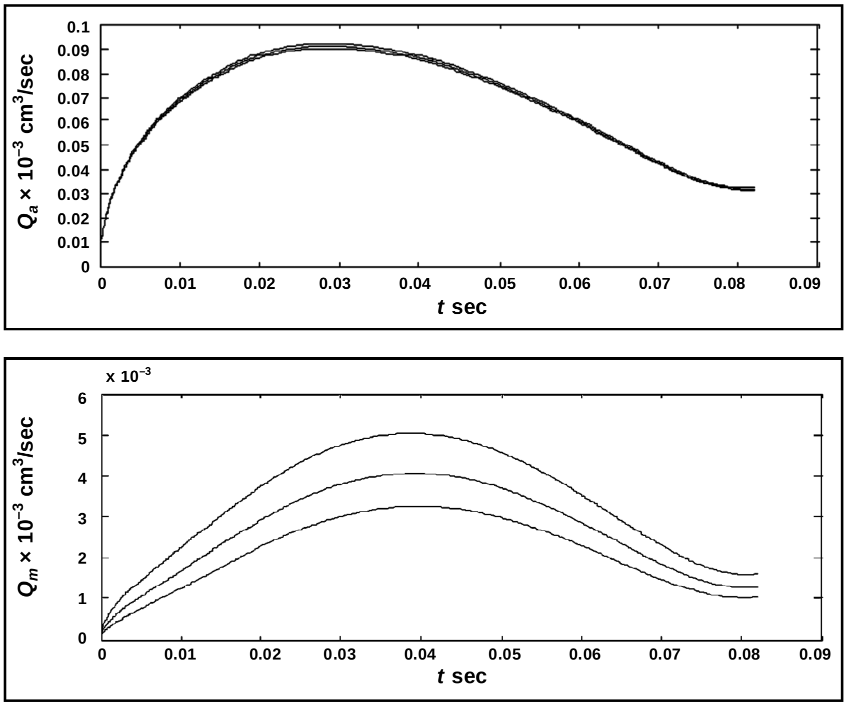


Figure 3.2.1(a): Variation of Q_a, Q_m with t for Different $(R_m - R_a)$
($\mu_s = 0.05$ Poise, $\phi_s = 0.05$ gm^{-1} cm^2 sec)
Upper denotes $(R_m - R_a) = 0.09$ cm
Middle denotes $(R_m - R_a) = 0.08$ cm
Lower denotes $(R_m - R_a) = 0.07$ cm

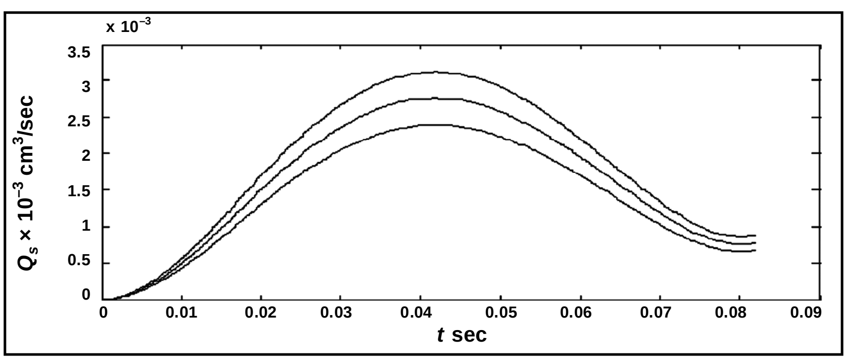
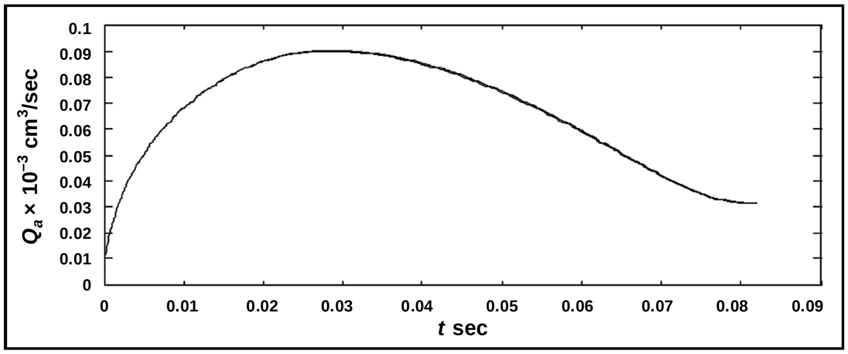
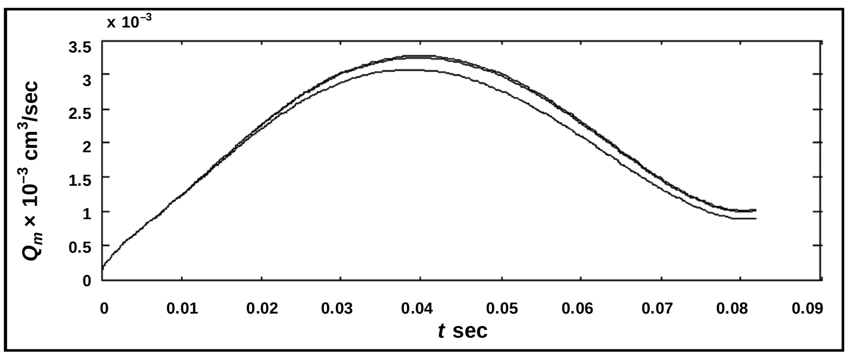


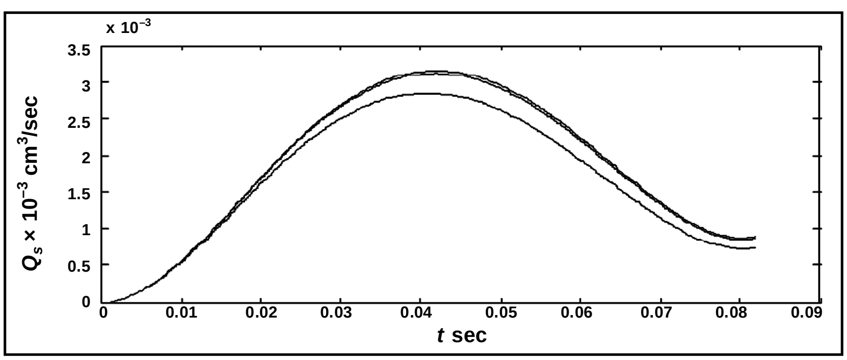
Figure 3.2.1(b): Variation of **Q_s with t for Different $(R_m - R_a)$**
($\mu_s = 0.05$ Poise, $\phi_s = 0.05$ gm^{-1} cm^2 sec)
Upper denotes $(R_m - R_a) = 0.07$ cm
Middle denotes $(R_m - R_a) = 0.08$ cm
Lower denotes $(R_m - R_a) = 0.09$ cm



(a)

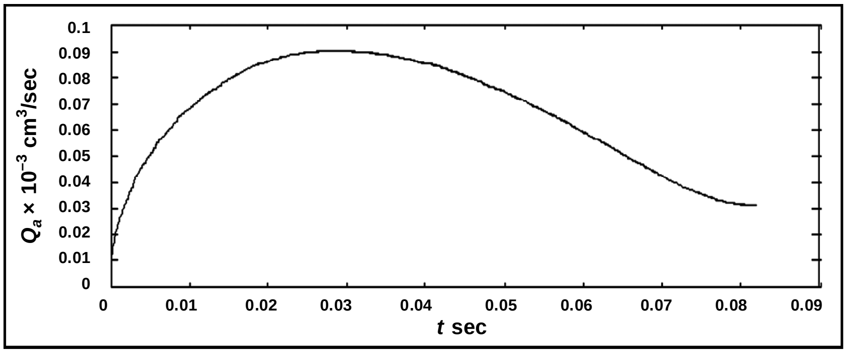


(b)

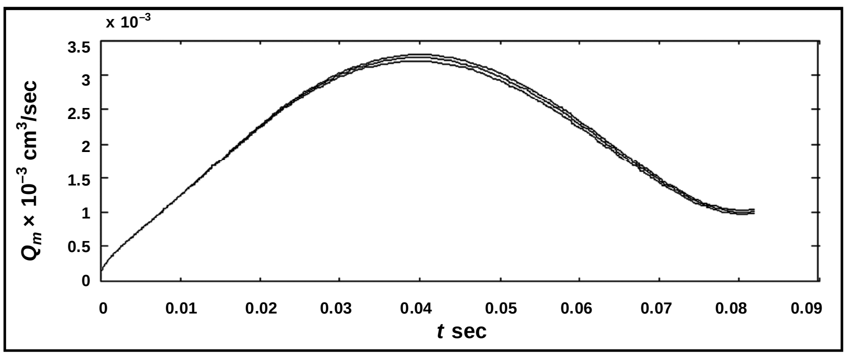


(c)

Figure 3.2.2: Variation of Q_a, Q_m, Q_s with t for different ($\mu_s = 0.05$ Poise, $\phi_s = 0.07$ cm)
Upper denotes $\phi_s = 0.1$ gm^{-1} cm^2 sec
Middle denotes $\phi_s = 0.05$ gm^{-1} cm^2 sec
Lower denotes $\phi_s = 0.01$ gm^{-1} cm^2 sec



(a)



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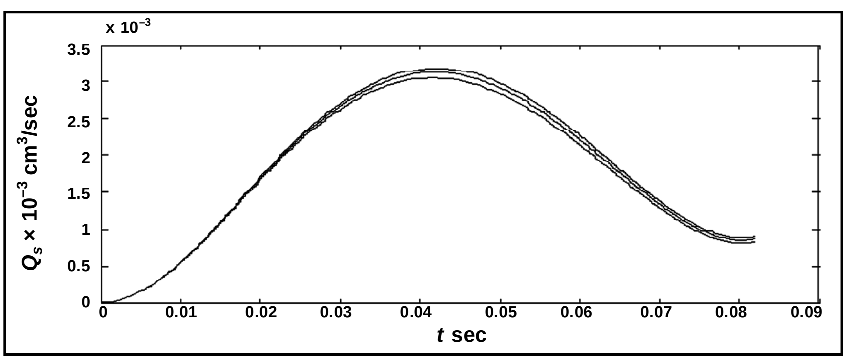

(c)

Figure 3.2.3: Variation of Q_a, Q_m, Q_s with t for Different μ_s (ϕ_s = 0.05 gm^{-1} cm^2 sec, ($R_m - R_a$) = 0.07 cm)
Upper Denotes μ_s = 0.01 Poise
Middle Denotes μ_s = 0.05 Poise
Lower Denotes μ_s = 0.1 Poise

flow of mucus increases as its thickness increases [Figure 3.2.1(a)]. While the serous fluid flow rate decreases as the radial thickness of mucus increases [Figure 3.2.1(b)]. Figure 3.2.2 illustrates the effect of time on air, mucus and serous flow rates for fixed $\mu_s = 0.05$ poise, and varying ϕ_s and it is clear that as ϕ_s increases these flow rates also increase but there is a negligible change in air flow rate as compare to the mucus and serous fluid flow rates. It is observed from Figure 3.2.3 that for fixed coefficient of porosity, mucus and serous fluid flow decrease with increasing serous viscosity and again there is a very negligible change in air flow rate.

4. CONCLUSIONS

In this paper, we have studied mucus transport in an airway due to prolonged cough by representing it as a circular tube. The prolonged cough has been represented by a time dependent pressure gradient. The simultaneous and coaxial flow of air and mucus in a tube are considered to flow under quasisteady turbulent conditions while serous fluid surrounding mucus layer coaxially is assumed to flow under unsteady laminar condition.

From the analysis of the model the following results have been obtained.

1. It is found that for fixed thickness of air and mucus, the mucus transport increases as its total thickness increases and serous fluid flow rate decreases.
2. It is depicted that mucus transport increases as the porosity of cilia bed saturated with serous fluid increases.
3. It is also observed that mucus transport increases as the viscosity of serous fluid decreases.
4. It has been found that the flow rates also follow the same pattern as the time dependent pressure gradient function representing prolonged cough.

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