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A MODEL FOR THE INTERACTION BETWEEN INTIMAL HYPERPLASIA AND BLOOD FLOW

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INTRODUCTION

The interaction between blood flow and the transport of cholesterol through the arterial wall is critical in the formation of atherosclerosis. We have developed a mathematical model of a large artery which describes the early stages of the disease, i.e. intimal hyperplasia and the evolution of fatty streaks which are the precursors to the formation of atherosclerotic plaques.

THE MODEL

The arterial wall is modelled by two layers, the innermost layer (the intima) and the media, through which cholesterol both diffuses and is advected with the slow flow of water through the wall. Within the intima, cholesterol is converted to oxidised cholesterol and is then consumed in situ by macrophages which bind to the substrate and turn into fatty foam cells. These processes are described by

$$\frac{\partial c_L}{\partial t} = -\nabla . j_I - kc_L \quad \text{and} \quad \frac{\partial c_{LO}}{\partial t} = kc_L - \gamma c_{LO}$$

where c_L and c_{LO} are the concentrations in the intima of native cholesterol (L) and oxidised cholesterol (LO) respectively. k is the rate of conversion to LO and γ is the constant background decay rate for LO. j_I is the flux of L in the intima and is given by

$$j_I = -D_I . \nabla c_L - c_L U \chi_I \hat{z},$$

where D_I is a diffusion tensor, χ_I is the slip coefficient (the mean velocity of the molecule relative to that of the fluid), $-U\hat{z}$ is the mean fluid velocity through the vessel wall, which is taken to be constant. No conversion takes place in the media which has relatively low diffusion and advection coefficients and thus acts a barrier to the transport of cholesterol so that the governing equation is

$$\frac{\partial c_M}{\partial t} = -\nabla . j_M,$$

where

$$j_M = -D_M . \nabla c_M - U \chi_M \hat{z},$$

c_M is the concentration of L in the media, D_M a diffusion tensor and χ_M is the slip coefficient.

The key concepts are that the permeability, κ, of the endothelial layer (which lines the inside of the artery) to cholesterol in the blood depends on the local wall shear stress due to the flow of blood, and that the presence of LO in foam cells leads to swelling of the arterial wall and changes the flow producing a feedback mechanism. Specific functional forms need to be specified for these two processes.

As a first step, the permeability of the endothelial cells is given by the quadratic formula

$$\kappa = \kappa_0 (\tau - \tau_0)^2 + \kappa_{\min},$$

where τ_0 is the value of the wall shear stress giving the minimum enodothelial permeability, $\kappa_{\min}$, and τ is the wall shear stress. This functional form gives high permeability at both low and very high wall shear stresses but in our simulations $\tau < \tau_0$ always.

The swelling of the arterial wall is described by a simple first order process in which the increase in the height of the endothelium is made proportional to the excess of LO in the intima below it i.e.

$$h(x,t) = \eta \int_{-H_I}^{h} \left[c_{LO}(x,z,t) - c_0(x,z,t) \right] dz$$

where the integral is positive and 0 otherwise. Here η is the constant of proportionality, h is the height of the endothelial layer above the mean height $z = 0$, H_I is the depth of the intima, and c_0 is the background concentration of LO within the intima.

RESULTS

For simplicity a two-dimensional channel geometry has been used. Both steady and pulsatile flows are simulated using standard asymptotic results for high Reynolds number flows [1,2]. The results confirm that changes in the structure of the wall with age increase the likelihood of incidence of atherosclerosis, and show a good correlation between the likelihood of atherosclerosis occurring at the most common sites in man and the persistence of fatty streaks when we use the physiological parameter values for those sites in our model. We also find an unexpected connection with the early stages of the formation of another important arterial disease — abdominal aortic aneurysms.

REFERENCES

1. Smith, F.T., 1976, "Flow through constricted or dilated pipes and channels: part 2", Quarterly Journal of Mechanics and Applied Mathematics, Vol. 29, pp. 365-376.
2. Duck, P.W., 1978, "Oscillatory flow through constricted channels and axisymmetric pipes", Proceedings of the Royal Society of London, Vol. A363, pp. 335-355.