MARGINATION OF A LARGE STIFF CELL IN A MODEL MICROVESSEL

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In the inflammation response, leukocytes (white blood cells) are recruited to the walls of vessels in the microcirculation, typically the post-capillary venules. There, they chemically attach, eventually binding firmly and emigrating out of the vessel through its walls. The basic chemical mechanisms of this have been well studied,[1] but the chemical interactions are short range, too short to bring the leukocyte to the wall in the first place. Thus inflammation also appears to depend upon a mechanical process call leukocyte margination, in which the interactions of the leukocyte with the red cells flowing in the blood bring the leukocyte to the wall. At low flow rates, this processes can be remarkably robust with a large fraction of the leukocytes reaching and binding to the wall.[2] However, attachment rates are observed to decrease rapidly with increasing flow rate at otherwise fixed conditions.[2,3] The well known clumping of red cells into aggregates at low strain rates has been pointed to as a driving mechanism for this margination (*e.g.* Pearson & Lipowsky[4]), but this hypothesis is difficult to assess directly because the aggregation promoting or inhibiting agents used also alter the blood's rheology. Direct observations of aggregation simultaneously with counts of leukocytes on the wall suggest that increasing aggregation indeed promotes leukocyte margination,[4] but they have not demonstrated that it is necessary.

We investigate this using numerical simulation of a two-dimensional model microvessel. The red cells are modeled as fluid filled capsules whose membranes resist bending and stretching according to linear constitutive models; the leukocytes are stiffer and larger than the red cells. The flow both inside the cells and in the surrounding plasma is assumed to be Stokians with the same Newtonian viscosity inside and out. The flow is solved using an efficient boundary integral method that allows us to simulate ~ 1000 of leukocyte flow-throughs of our vessel which is $27r_o$ long and $8r_o$ wide, where r_o is the radius of hypothetically circular red cell. The red cell volume fraction (hematocrit) is 0.45. These long simulations permit statistical analysis of the margination process under various flow conditions and red cell material properties.

Despite the approximations this model, it reproduces key experimental observations: the leukocytes marginate readily at low flow rates but their on-wall probability decreases rapidly with increasing flow rate. They do this despite the fact that the model lacks aggregation. We also find that the margination process is insensitive to the material properties of the red cells, behaving in a similar fashion for nearly rigid or highly flexible cells.

References

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