



## Role of leukocytes in the pathogenesis of diabetic retinopathy

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Increasing interests have been recently directed toward the role of leukocytes in microvascular disorders including diabetic retinopathy because their large cell volume, high cytoplasmic rigidity, natural tendency to stick to the vascular endothelium, and capacity to generate toxic superoxide radicals and proteolytic enzymes. Leukocytes from diabetic patients are reported to be less deformable and more activated, and may be involved in capillary non-perfusion, endothelial cell damage, and vascular leakage. Histological studies showed the evidences of capillary occlusion by leukocytes and capillary dropout or degeneration associated with leukocytes in diabetic retina.

We have developed acridine orange fluorography to visualize leukocytes in the retinal microcirculation in the living eyes. We have shown the increased leukocyte entrapment (leukostasis) in the retinal capillaries of early diabetic rats using this technique. It was confirmed that the leukocyte entrapment preceded the vascular leakage and damage of the retinal vascular endothelial cells. Trapped leukocytes caused non-perfusion of downstream capillaries which was reversible in the early stages. The studies demonstrated that adhesion molecules of the retinal vascular endothelium and leukocytes were both upregulated in the diabetes. Increased expression of the adhesion molecules was considered as one of the mechanisms of retinal leukostasis in the diabetic rats. Recent studies suggested that the VEGF-induced vascular leakage is mediated through the increased expression of adhesion molecules of retinal vascular endothelium and the interaction with leukocytes. Leukocyte-endothelial interaction in the diabetic retina was inhibited with antibodies to the adhesion molecules and other agents. Anti-adhesion therapy to inhibit the retinal leukostasis may be a promising approach for the prevention and treatment of diabetic retinopathy.