DIABETES

Modified LDLs linked to progression of retinopathy in T1DM

High circulating levels of immunocomplexes containing oxidized LDLs or advanced glycation end product (AGE)-LDLs are associated with an increased risk of progression of retinopathy in patients with type 1 diabetes mellitus (T1DM).

Oxidized LDLs and AGE-LDLs are found in the retina of patients with T1DM owing to damage of retinal barriers and extravasation of these modified lipoproteins from the plasma. The presence of oxidized LDLs and AGE-LDLs elicits the production of autoantibodies and the formation of immunocomplexes containing these molecules. The results of this study indicate that immunocomplexes containing oxidized LDLs and AGE-LDLs have a role in the pathogenesis of retinopathy in people with T1DM.

These findings are the result of a 16-year follow-up of a subgroup of 517 patients enrolled in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) cohort. At study entry, these patients had their serum tested for

levels of oxidized LDLs and AGE-LDLs in their immunocomplexes. Severity of retinopathy was graded according to the Early Treatment Diabetic Retinopathy Study (ETDRS) scores. Over the course of the study, 121 patients progressed to proliferative diabetic retinopathy and 137 to severe nonproliferative diabetic retinopathy, 113 patients developed clinically significant macular oedema and 323 experienced a three-step progression in their ETDRS score.

Individuals who had retinopathy at baseline were more likely to experience progression than those individuals who did not. However, high baseline levels of immunocomplexes containing oxidized and AGE-LDLs were significantly associated with increased risk of disease progression in both groups.

Further studies are required to fully elucidate the mechanisms by which immunocomplexes containing oxidized LDLs and AGE-LDLs contribute to the pathogenesis of retinopathy in patients with T1DM. The investigators suggest that these immunocomplexes enhance the build up of white blood cells that could

lead to the endothelial cell damage, retina vascular leakage and lack of perfusion that characterize retinopathy in T1DM.

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Original article Lopes-Virella, M. F. *et al.* High concentrations of AGE-LDL and oxidized LDL in circulating immune complexes are associated with progression of retinopathy in type 1 diabetes. *Diabetes Care* doi:10.2337/dc11-2040