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**Low density lipoprotein uptake by macrophages in multiple sclerosis plaques: implications for pathogenesis.**

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**Source**

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**Abstract**

Low density lipoprotein (LDL), the major carrier of plasma cholesterol, may enter the parenchyma of early multiple sclerosis (MS) lesions as a result of blood-brain barrier damage. We have used antibodies against LDL and epitopes found in LDL oxidized by two peroxidative end-products, malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE), to immunocytochemically stain MS plaques at different stages of pathology. Native LDL, epitopes of MDA-LDL, peptides of myelin basic protein and neutral lipid oil red O (ORO) staining were found to be co-localized within foamy macrophages in early and actively demyelinating MS plaques. Thus cholesterol esters, which are seen as Maltese crosses under polarized light in a proportion of foamy macrophages, appear to be derived from both LDL and myelin. ORO-negative astrocytes were strongly stained with the antibodies against 4-HNE-LDL and MDA-LDL, suggesting uptake of oxidatively modified protein products alone. Our findings suggest that a large proportion of the plasma LDL which enters the parenchyma of MS plaques is oxidatively modified in the lesion. Lipid peroxidation and oxidized LDL uptake by activated microglia and infiltrating macrophages in the early stages of MS plaque development may play important roles in demyelination.