OBJECTIVE: To determine the effects of pretreatment with alpha-linolenic acid, an omega-3 polyunsaturated fatty acid, on equine synovial explants challenged with lipopolysaccharide (LPS). ANIMALS: 8 mature mixed-breed horses (4 mares and 4 geldings). PROCEDURE: Synovial explants were assigned to receive 1 of 7 concentrations of alpha-linolenic acid, ranging from 0 to 300 microg/mL. At each concentration, half of the explants were controls and half were challenged with 0.003 microg of LPS as a model of synovial inflammation. Cell inflammatory response was evaluated by measurement of prostaglandin E2 production via an ELISA. Synovial cell viability, function, histomorphologic characteristics, and cell membrane composition were evaluated by use of trypan blue dye exclusion, hexuronic acid assay for hyaluronic acid, objective microscopic scoring, and high-performance liquid chromatography, respectively. RESULTS: Challenge with LPS significantly increased production of prostaglandin E2 and decreased production of hyaluronic acid. Treatment with alpha-linolenic acid at the highest dose inhibited prostaglandin E2 production. Cell viability and histomorphologic characteristics were not altered by treatment with alpha-linolenic acid or LPS challenge. Treatment with alpha-linolenic acid increased the percentage of this fatty acid in the explant cell membranes. CONCLUSIONS AND CLINICAL RELEVANCE: Results suggest that investigation of alpha-linolenic acid as an anti-inflammatory medication for equine synovitis is warranted.