Keloid is a tumorlike mass with an excessive formation of a fibrous scar with frequent recurrence after surgical extirpation. Granulomatous lesion marked by capillary proliferation is one of hallmarks in early phases of keloid formation. The present study was conducted in anticipation of a possible involvement of vascular endothelial cell growth factor (VEGF) in the pathogenesis of keloid.

Materials and Methods: Fibroblasts were cultured by an explant method from surgically resected keloid and hypertrophic scar tissues. Control fibroblasts were cultivated from normal dermal tissue pieces attached to resected pigmented nevus and lipoma. Full informed consent to the present experiment was obtained from all the patients. Fibroblasts were grown and propagated in Dulbecco's modified Eagle medium (DMEM) containing 5% fetal calf serum. Subconfluent cells with 4 to 9 passages made quiescent in serum-free DMEM for 24 h were used throughout the present experiment. Concentration of VEGF and transforming growth factor (TGF)-β1 in the conditioned medium from fibroblast culture for 24 h was measured by enzyme-linked immunosorbent assay (ELISA). Biological activity of VEGF in the conditioned medium was assayed by chemotaxis as measured by the number of dermal microvessel endothelial cells migrating through pore membrane in a modified Boyden chamber. Expression of VEGF mRNA in fibroblasts was determined by Northern blot.

Results with Discussion: Concentration of VEGF was elevated 5 to 8-fold in the conditioned medium from keloid fibroblast culture as compared to controls. Upregulation of VEGF mRNA expression was evident in keloid fibroblasts. A significant increase in total TGF-β1 concentration was further noted in keloid fibroblasts. The conditioned medium from keloid fibroblasts elicited a greater chemotactic activity of endothelial cells than that from normal counterparts. Anti-VEGF antibody completely abolished the chemotaxis. Fibroblasts derived from hypertrophic scar remained at values within a range of controls. TGF-β1 stimulated VEGF production in keloid, hypertrophic scar and control fibroblast cultures. A neutralizing antibody to TGF-β1 inhibited VEGF secretion, indicating a possible involvement of TGF-β1-mediated VEGF expression. A higher production and an enhanced expression of VEGF by keloid fibroblasts are at least in part attributable to their upregulation of TGF-β1. VEGF-induced angiogenesis may play a role in facilitating growth of keloid fibroblasts and their resultant overproduction of collagenous fibers.