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**Beneficial effects of post-transfusional hepatitis in acute myelogenous leukemia may be mediated by lipopolysaccharides, tumor necrosis factor alpha and interferon gamma.**

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Post-transfusional hepatitis is often a complication in patients with acute myelogenous leukemia (AML) in whom survival is paradoxically prolonged. The etiology is unknown. In previous studies, we showed that impaired hepatic endotoxin (lipopolysaccharide, LPS) clearance in patients with acute viral hepatitis A, B, or C versus controls results in endotoxemia and tumor necrosis factor alpha (TNF-alpha) release. TNF-alpha mediates anti-proliferative and differentiating effects in AML cell lines. Interferon-gamma (IFN-gamma) released in acute viral hepatitis, acts in synergy with TNF-alpha. HL60, KG1, and U937 AML cells treated 3, 6, and 9 days with physiologically attainable TNF-alpha (10 U/ml), IFN-gamma (100 U/ml) and LPS (10 ng/ml) levels, have significantly diminished viability and cell growth versus controls. Treatment of HL60 AML cells with LPS/TNF-alpha/IFN-gamma also resulted in significantly increased monocytic pathway differentiation not seen with KG1 or U937 AML cells. HL60 AML cells treated with TNF-alpha/IFN-gamma for 6 days released endogenous TNF-alpha (1.57 U/10(6) cells) upon LPS stimulation compared to less than 0.01 U/10(6) cells in non-LPS-stimulated TNF-alpha/IFN-gamma-treated cells or untreated cells (p less than 0.0001). Untreated HL60 AML cells co-cultured with HL60 cells pretreated for 6 days with TNF-alpha/IFN-gamma and then subjected to LPS stimulation had significantly diminished cell growth compared to controls (p less than 0.0001). This effect could be reversed with anti-TNF-alpha antibody, supporting the concept that endogenous TNF-alpha release by LPS/TNF-alpha/IFN-gamma treated HL60 AML cells may act by paracrine means to suppress growth of other AML cells. The beneficial effects of post-transfusional hepatitis in AML patients may be mediated via LPS/TNF-alpha/IFN-gamma-induced AML cell growth suppression and/or terminal differentiation in which AML cells participate by releasing TNF-alpha after being acted upon by LPS/TNF-alpha/IFN-gamma. Endogenously released TNF-alpha might then act by autocrine/paracrine means to mediate further suppression and terminal differentiation.