IL-12 and IFN-γ Deficiencies in Human Neonates

A review of: Joyner JL, Augustine NH, Taylor KA, et al. 2000 Effects of group B streptococci on cord and adult mononuclear cell interleukin-12 and interferon-γ mRNA accumulation and protein secretion. J Infect Dis 182:974-977

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An effective form of innate immunity involves naive T-cells initiating a specific response to a pathogen (1). Mononuclear phagocytes producing IL-12 upon stimulation by microbial products or direct infection are central to this response. IL-12 induces the production of IFN-γ by T-cells and NK-cells, and naive T-cells develop preferentially into T-helper-1 (Th1) lymphocytes (1).

Neonates are deficient in the production of IFN-γ, a potent macrophage-activating agent in vivo (2). Memory T cell deficiency in neonatal blood compared to adult blood (12.3 % *versus* 55.2 % memory cells and 87.6% vs 44.8% naive cells in cord and adult blood, respectively) has been suggested to be responsible for the neonatal deficiency of IFN-γ production (3). In a recent study, Joyner *et al.* proposed that decreased production of IL-12 may also be linked to IFN-γ deficiency in newborns (4). They studied group B streptococcus (GBS)-stimulated mRNA accumulation and protein secretion of both IFN-γ and IL-12 in mononuclear cells from cord and adult blood. By using reverse transcriptase polymerase chain reaction and quantitative densitometry assays, the authors compared kinetics of GBS-stimulated accumulation of IFN-γ mRNA and IL-12 mRNA (both p40 and p35 subunits) in cord and adult cells. After 12-18 h of incubation, they detected significantly decreased mRNA accumulation for both IFN- and IL-12 in cord cells compared to adults. The concentration of IFN-γ and IL-12 in suspensions of GBS-induced cord mononuclear cells was also significantly lower than in adults at 12 and 18 h. The data presented in this paper suggest that IFN-γ deficiency in neonates may be attributed, in addition to lymphocyte immaturity, to decreased production of IL-12 by cord mononuclear phagocytes.

IL-2, another potent IFN-γ-inducing cytokine, is produced in nearly equal amounts by both memory and naive T cells from neonatal and adult blood (2). Therefore, the striking discrepancy between neonatal and adult IFN-γ production does not seem to be related to deficient IL-2 induction of IFN-γ. However, IL-2 receptor-mediated signaling and IFN-γ release by IL-2-induced neonatal T cells have not been studied.

The main conclusion that can be drawn from the work by Joyner *et al.* is that strategies to enhance neonatal host defense against intracellular pathogens may include administration of IL-12. Much remains to be answered, however, about cellular responsiveness of neonatal T-cells and monocytes/macrophages to cytokines critical to Th1 differentiation. For example, neonatal macrophages cannot be fully activated by IFN-γ, which may represent developmental immaturity (5).

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3. D'Arena G, Musto P, Cascavilla N, Di Giorgio G, Fusilli S, Zendoli F, Carotenuto M 1998 Flow cytometric characterization of human umbilical cord blood lymphocytes: immunophenotypic features. Haematologica 83:197-203
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