Evidence-Based Adjunctive Strategies for Diagnosis and Treatment of Neonatal Sepsis

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The first step in the innate immune response is the processing of foreign antigens by dendritic cells, or monocyte derived macrophage.

TH1, TH2 & TH17 (CD4) Immune Responses

- TH1:
  - Activates NK cells
  - Activates macrophages
  - IL-12, IFN-γ, TNF-β
  - Immunity to extracellular bacteria, allergens, toxins and parasites

- TH2:
  - Activates T & B cells
  - IL-4, IL-5, IL-6, IL-9, IL-10
  - Immunity to extracellular bacteria, allergens, toxins and parasites

- TH17:
  - Activates T & B cells
  - IL-17, IL-21 & IL-22
  - Immunity at epithelial & mucosal surfaces

- TH0:
  - Resting T cell (naive)
  - IL-12

- APC:
  - Antigen
  - IL-1 (+ IL-2)

- IL-17, IL-23

- IL-21

- IL-22

- IL-4

- IL-6

- IFN-γ

- TNF-β

- IL-2
null
IFN-γ: A Cautionary Tale

- Improves neutrophil phagocytosis and killing by inducing Fc receptors
- Primary macrophage activator
  - Improves intracellular killing
  - Improves antigen processing
  -Induces macrophage gene expression
  -Induces production of TNF-α and NO
  -Stimulates TH₂ and suppresses TH₁ cells
IFN-$\gamma$: A Cautionary Tale

- Phase I safety clinical trials started in neonates in the 80’s
- IFN-$\gamma$ cytotoxic to oligodendroglial cells in culture (Volpe and others)
- Increased circulating IFN-$\gamma$ is associated with periventricular leukomalacia in preterm infants (Hansen-Pupp, Pediatr Res, 2005)

**Cautionary Note:** Treatment with cytokines may be fraught with peril, both for upsetting the pro-anti-inflammatory balance, and for unpredictable effects on multiple organ systems
Diagnostic Biomarkers for Infection in Premature Neonates: 8 of 142 markers Significantly Elevated in Neonatal Sepsis

Kingsmore SF. Molecular & Cellular Proteomics, 2008