Host Defense against Infection in the Newborn

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It has long been recognized that newborn infants exhibit a predisposition to infection by a variety of microorganisms. Infection remains one of the major threats to the neonate even today. In some cases, infection might be explained by massive exposure to the infecting organism in utero or during the birth process, e.g., syphilis, group B streptococcus, and herpes simplex virus. In general, however, it appears likely that newborn infants carry an undue susceptibility to infection because they cannot mount normal host defense. A large number of studies have been conducted in an attempt to discover specific abnormalities. Many of these have detected subnormal function of various aspects of the newborn's inflammatory response, yet no single defect can explain why newborns sustain serious infection so commonly.

The barrier function of skin and mucous membranes is clearly important in the neonatal period, but the function of antimicrobial peptides such as magainins and defensins has not been described in the human newborn.

The maternal dowry of antibodies in the IgG class reflects the mother's experience with infection except in preterm babies, especially those born at less than about 32-34 weeks of gestation, who start at antibody deficit. The active antibody response by the baby to new polysaccharide antigens is blunted, and the baby lacks memory lymphocytes that expedite a rapid response to familiar microbial products. This problem undoubtedly plays a role in the predisposition of the newborn to bacterial infections, but to date prophylactic infusion of immunoglobulin had not been shown conclusively to reduce the threat of infection.

Complement, to other key system involved in opsonization, is clearly deficient in newborns, and the deficiency is more pronounced in pre-term babies. The alternative pathway, which allows complement activation in the absence of specific antibody, is relatively more defective than the classical pathway. Thus, the effect of antibody deficiency is compounded by defective function of the complement system.

Newborns generally begin life with normal or increased numbers of circulating phagocytes (neutrophils and monocytes), as well as lymphocytes. However, the reserve supply of

killing can be depressed. Certain components of signal transduction are deficient in newborn neutrophils, including IP3 and Ca²⁺ release, and deficient signalling undoubtedly underlies at least some of the functional abnormalities.

Cell-mediated immunity, effected by T lymphocytes, natural killer cells, and macro-phages, is also blunted in newborn infants. Essential to this process is release of the major macrophage-activating factor interferon- γ by T cells and upregulation of macrophage microbicidal activity in response to this lympho-kine. Both the release and response phases of this process are profoundly deficient in the newborn; the macrophage abnormality is not due to deficient receptors for interferon- γ . Release and response to many other cytokines are currently under study in newborn cells.

All of the abnormalities in host defense described to date in the neonate are partial, even in pre-term babies. None of these abnormalities, if present as an isolated defect in an older child or adult, would be likely to predispose that individual to infection. These abnormalities act in combination, however, and reduce the substantial immunologic reserve that develops in infancy and that has allowed humans to evolve in a world of microbes. More understanding of the basic mechanisms that underlie host defense may eventually permit us to accelerate development of the immune system and prevent infections in this special host.

Extended Abstracts

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