BREAST FEEDING AND THE INTESTINAL MICROFLORA OF THE INFANT—IMPLICATIONS FOR PROTECTION AGAINST INFECTIOUS DISEASES

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Abstract: Human breast milk contains an array of factors with anti-infectious potential, such as immunoglobulins (especially secretory IgA), oligosaccharides and glycoproteins with anti-adhesive capacity, and cytokines. Breast-feeding is associated with protection from the following infections or infection-related conditions: gastroenteritis, upper and lower respiratory tract infection, acute otitis media, urinary tract infection, neonatal septicaemia and necrotizing enterocolitis. Some of the protective effects may derive from an altered mucosal colonization pattern in the breast-fed infant. In other instances breast-fed infants develop less symptoms to the same microbe which causes disease in the bottle-fed infant. An example of an altered colonization pattern is that breast-fed infants have less P-fimbriated, but more type 1-fimbriated E. coli. This may protect against urinary tract infection in the breast-fed infant since P fimbriae are the major virulence factor for urinary tract infection. An example of changed consequences of the same microbial colonization is that secretory IgA in the breast-milk protects very efficiently from translocation of intestinal bacteria across the gut mucosa by coating intestinal bacteria and blocking their interaction with the epithelium. This mechanism may protect the infant from septicaemia of gut origin and, possibly, necrotizing enterocolitis. Breast-milk is also highly anti-inflammatory and contains hormone like factors which counteract diarrhea. Thus, breast-fed infants may be colonized by recognized diarrheal pathogens and still remain healthy. Due to a less virulent intestinal microflora and decreased translocation breast-fed infants will obtain less stimuli for the gut immune system, resulting, in e.g., lower salivary IgA antibody titres.
1. INTRODUCTION

Breast-feeding is associated with protection from a range of infections or infection-related conditions (Table 1). For infants in developing countries, breast-feeding is in many cases life saving, but also in developed countries excess morbidity due to lack of breast-feeding may be substantial. Some of the protective effects may derive from an altered mucosal colonization pattern in the breast-fed infant. In other instances breast-fed infants develop less symptoms to the same microbe which causes disease in the bottle-fed infant. This might relate either to a changed behaviour of the colonizing microbe, e.g. alteration of toxin or adhesin production, or to altered host responsiveness. For example, anti-diarrheal hormones or anti-inflammato-genic compounds in the milk might render the infant less sensitive to microbes and their toxins. Some mechanisms of importance for the protection of the breast-fed infants against infection will be reviewed here.

2. COMPONENTS OF HUMAN MILK WITH POTENTIAL TO AFFECT MICROBES OR HOST RESPONSES TO THEM

An adult human being produces approximately 2-3 g of secretory IgA per day. The fully breast-fed infant is supplemented with 0.5-1 g per day. Thus, the breast-fed infant's mucosal membranes are equally effectively covered by secretory IgA as are those of an adult, despite a very low production of secretory IgA by the newborn infant. Secretory IgA in the milk derives from dimeric IgA produced by plasma cells in the mammary gland which acquires secretory component during passage through the mammary gland duct epithelial cells. Secretory IgA is highly resistant to proteolytic degradation in the gastrointestinal tract. IgA antibodies do not activate complement or other inflammatogenic effector functions, but are thought to exert their action by agglutinating bacteria and blocking their too close interaction with mucosal epithelial cells. IgM and IgG antibodies together make up only a few per cent of milk immunoglobulin. Breast milk antibodies are directed against a multitude of antigens: microbial surface structures, toxins and food proteins.

A component of human milk with potential capacity to influence microbial colonization and pathogenicity is the large amounts of receptor-active structures both in the form of soluble oligosaccharides and as protein- or lipid-bound glycosyl chains. Human breast milk contains 4-6 g/l of complex oligosaccharides, which are virtually absent from cow's milk. The free oligosaccharides consist of a variety of linear and branched structures based on