

Mother-Child Breastfeeding

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Abstract

Pro- and anti-inflammatory defence of the neonate

The sterile newborn starts to get colonized with microbes from delivery on. Preferably much of the early microbial exposure will be with bacteria from the mother's stool in connection with the delivery next to the mother's anus. Much of those bacteria are of no or low virulence, but potentially virulent microbes are also present .

The neonate has a good level of trans-placentally obtained maternal IgG antibodies in its circulation and tissues. To function efficiently in the defence these IgG antibodies need to activate the complement system and bring in stimulated neutrophils. But complement levels remain low for about the first 3 months of life and neutrophils are present in lower numbers, respond less well to activation signals than later and there is a reduced production of neutrophils in early life. Furthermore, activation of complement and neutrophils result in an inflammatory response with tissue damage and clinical symptoms like fever, pain, tiredness and loss of appetite, as well as increased energy consumption.

The defence provided via breastfeeding is, in contrast, efficiently protective without inflammation; partly it is even anti-inflammatory. In addition, some of the host defence factor of the human milk has long lasting stimulatory effects on the infants.

Breastfeeding and protection against infections

One of the major milk proteins is secretory IgA (SIgA). Such antibodies, which make up about 80% of antibodies in man are present to defend mucosal membranes. They do so by being relatively resistant to proteolysis compared to serum antibodies and by binding microbes preventing their attachment to and passage through mucosal membranes into the circulation and tissues. This form of defence does not cause inflammation. The SIgA antibodies in milk are produced in the mammary glands by lymphocytes, which at least partly originate from the lymphoid tissues of the mother's gut, especially from the Peyer's patches. As a consequence a mother's milk SIgA antibodies are primarily directed against her microbial gut flora. Thus the breastfed infant is well protected against the potential pathogens from the mother's gut flora, which may colonize the infant after delivery.

Human milk also contains numerous oligosaccharides, which prevent infections by blocking the adherence of microbes to mucosal membranes in the upper respiratory tract and the gastrointestinal tracts of the breastfed infant, as well as the urinary tracts, since some of the milk oligosaccharides come out that way. Several glycoconjugates in the milk also block mucosal attachment of toxins and microbes in the gut, like *Escherichia coli*, *Vibrio cholerae*, *Shigella dysenteriae* and *Campylobacter jejuni*.

Another major milk protein, lactoferrin, can kill bacteria, viruses and fungi. Bactericidal peptides can be obtained from an exposed α -helix loop in the molecule. At the same time lactoferrin has the remarkable capacity of blocking the transcription factor NF κ B in leucocytes. Thus the production of pro-inflammatory cytokines like IL-1 β , TNF- α , IL-6 is blocked and inflammation prevented or down-regulated. In experimental models in mice we have shown that lactoferrin and certain fragments thereof given perorally can prevent urinary tract infections since they are excreted also in the urine, not only in the stool. The same components prevented inflammation in an experimental model of colitis as well.

Human milk contains numerous cytokines, chemokines, hormones and growth factors. The possible effects of all these components on the breastfed offspring is largely unknown today, although it is suggested for instance that the IL-7 in milk may be involved in the fact that the thymus is twice as large in fully breastfed compared to non-breastfed infants. The consequence of this is presently unknown, but the thymus is the central organ in the immune system and is important for the appearance of peripheral T lymphocytes.

Lately we have been interested in the anti-secretory factor (AF), which can be found, or be induced in human milk. This 41 kD protein prevents secretion induced for instance by enterotoxins from *V. cholerae* or *E. coli*. Its production can be induced by these enterotoxins and by specially treated cereals (SPC). We investigated whether induction of AF in the milk of breastfeeding mothers could decrease the presently very high prevalence of mastitis in Western countries. In a small study in Sweden we found that the SPC induced AF in the milk and that it gave significant protection against acute mastitis. A similar study of larger size is presently running in Lahore, Pakistan. It might be that the AF in the milk can add to the many protective factors in the milk, which help to prevent acute diarrhoea in breastfed infants. As a first experiment to study this we have in a double blind randomized study in Lahore given children with acute diarrhoea during the first three days after admittance to hospital either egg yolk from hens fed or not fed with SPC. Those fed with SPC have AF in the egg yolk, the others not. We found significantly protective effects measured as improvement in the

consistency of stools, frequency of stools/day and mean number of days requiring hospitalizations. All parameters showed significant improvement by giving AF.

It is obvious even from this short review that human milk contains numerous factors which support the protection of the infant against infections. Some of the many components of the milk seem to have long term effects, so that certain vaccine responses are enhanced up through school age and the enhanced protection against certain infections during breastfeeding seems to last for some years after the termination of feeding with mother's milk.

To illustrate some of the many various capacities of human milk I end by discussing the fact that breastfeeding provides significant protection against necrotizing enterocolitis (NEC). This condition appears in prematures where intestinal colonization results in microbes reaching an intestinal mucosa with an immature immune defence and an unbalanced capacity to respond with inflammation. The result can be a violent inflammatory reaction which may end with necrosis of the intestinal mucosa and often the death of the infant. Human milk may provide defence in many ways, first by SIgA antibodies against the colonizing microbes decreasing their capacity to reach the mucosal membranes. The many receptor analogues in the milk, like oligosaccharides and glycoconjugates may help preventing the bacteria from attaching to the gut mucosa. Lactoferrin may block production of pro-inflammatory cytokines as discussed above and the platelet-activating factor (PAF)-acetylhydrolase of the milk may degrade the PAF produced which otherwise would cause tissue damage. The anti-inflammatory IL-10 from mother's milk might help protecting the gut mucosa of the premature.

It is obvious that at this time we still do not have a very complete picture of the effects in the breastfed infant of the numerous potentially protective factors present in human milk