# PROTECTIVE ELEMENTS OF BREAST MILK IN THE PREVENTION OF GASTROINTESTINAL AND RESPIRATORY DISEASES

### ELEMENTOS PROTETORES DO LEITE MATERNO NA PREVENÇÃO DE DOENÇAS GASTRINTESTINAIS E RESPIRATÓRIAS

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### **ABSRACT**

**Objective**: to identify the protective elements of breast milk that work in the prevention of gastrointestinal and respiratory diseases. **Sources**: the search was performed on Bireme, Lilacs, Medline and Scielo databases, using keywords breast milk, gastrointestinal disease and respiratory disease, with limits of languages (English, Portuguese and Spanish) and period (1996 to 2009). 46 papers were selected for achieving the objectives of this work. **Summary of the findings**: the IgA is the immunoglobulin with more protective capability against both types of disease, to survive the intestinal and respiratory mucosa. Breast milk also contains other immunoglobulins, antibodies, oligosaccharides, lipids, bioactive peptides, among other components with unique mechanisms that besides the protection against these diseases, stimulate the development of infants' immune systems. No other milk has these properties, and may even be the cause of these diseases. Campaigns and actions in Public Health to encourage breastfeeding should be continuously developed and encouraged considering all the benefits it provides.

Key words: milk, human; gastrointestinal diseases; respiratory tract diseases; breast feeding.

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### **RESUMO**

Objetivos: identificar os elementos protetores do leite materno que atuam na prevenção de doenças gastrintestinais e respiratórias. Fonte dos dados: a busca foi realizada nas bases de dados Bireme, Lilacs, Medline e Scielo, utilizando os descritores *leite materno*, *doenças gastrintestinais* e *doenças respiratórias*, com limites de idiomas (português, inglês e espanhol) e de período (1996 a 2009). Foram selecionados 46 materiais por atenderem aos objetivos deste trabalho. Síntese dos dados: A IgA é imunoglobulina com maior capacidade protetora contra ambos os tipos de doenças, por sobreviver às mucosas intestinal e respiratória. O leite materno também possui outras imunoglobulinas, anticorpos, oligossacarídeos, lipídeos, peptídeos bioativos, entre outros constituintes exclusivos com mecanismos específicos que, além da proteção contra essas doenças, estimulam o desenvolvimento do sistema imune do lactente. Conclusões: Nenhum outro leite possui essas propriedades, e podem até ser a causa destas doenças. Campanhas e ações em Saúde Pública que incentivam o aleitamento materno devem ser continuamente desenvolvidas e estimuladas, considerando todos os beneficios que o mesmo proporciona.

**Palavras-chave**: Leite Humano. Gastroenteropatias. Doenças Respiratórias. Aleitamento Materno.

### INTRODUCTION

Breastfeeding is one of the earliest nutritional experiences of the newborn child<sup>1</sup>. No other food or modified formula is able to provide the infant with all the ingredients of breast milk. Breast milk has a specific composition that meets the nutritional needs of infants and is compatible with their metabolic and physiological limitations<sup>2,3</sup>. Furthermore, breast milk represents no additional cost to the family budget<sup>4,5</sup>.

The frequency and duration of breastfeeding have risen favorably over the past 30 years<sup>6</sup>. Despite this positive trend, consensus on the numerous advantages of breastfeeding, and the global movement to recover the culture of breastfeeding in recent decades, early weaning remains a common practice worldwide<sup>7,8</sup>.

The indices of the frequency and duration of breastfeeding do not reflect the efforts of numerous governmental and non-governmental programs to foster breastfeeding throughout Brazil<sup>9</sup>. Only 35% of infants under four months old are exclusively breastfed and early we-

aning continues to be still associated with high rates of infant mortality due to malnutrition and diarrhea<sup>8</sup>.

Recent estimates regarding the various forms of action and their repercussions on child health have shown that the promotion of exclusive breastfeeding is potentially the single most effective public health intervention for reducing child mortality 10 since exclusive breastfeeding contributes toward lowering both child morbidity and mortality 11. According to Betrán et al. 12, 13.9% of all causes of infant mortality in Latin America are preventable by exclusive breastfeeding in infants aged 0-3 months, and by partial breastfeeding during the first year of life.

In Brazil, most mothers start out breastfeeding but by the first month of life more than half of the infants are no longer being exclusively breastfed. This early weaning goes against WHO<sup>13</sup> guidelines recommending exclusive breastfeeding for at least the first six months of life<sup>5</sup>.

The first two years of life is a critical period for promoting optimal growth, he-

alth and development of the infant. Breastfeeding is an excellent means of ensuring that children go through this vulnerable period of life, allowing normal future development<sup>14</sup> and preventing against disease during childhood and into adult life<sup>15</sup>.

Breastfeeding confers numerous health benefits for the child, representing the best way of promoting full development since breast milk supplies all the nutrients a child needs to make the healthiest start in life<sup>16</sup>. Human milk fully meets the needs of the infant up to the sixth month of life<sup>17,18</sup>, and is one of the most efficient means of meeting their nutritional and immunological requirements during the first year<sup>19</sup>.

Besides having the ideal composition of nutrients, breast milk contains other components that strengthen organism defenses such as immunoglobulins, anti-inflammatory factors and immunostimulators. Their mechanisms include specific activity against infectious agents and cell growth of intestinal mucosa which increases resistance to infections<sup>2,3</sup>. Reports describe approximately 250 protective components in human milk, besides growth factors of the gastrointestinal tract<sup>18</sup>.

Breastfeeding decreases the incidence and/or severity of diarrhea, botulism, necrotizing enterocolitis, allergies, infectious and respiratory diseases, and of other types of diseases<sup>3,5,11,12,20,21</sup> such as autoimmune diseases<sup>20</sup>, while also encourages development of the baby's immune system<sup>18</sup>.

Other types of milk increase the risk of developing diseases and allergies<sup>17</sup> and can cause damage to the immature infant gut<sup>22</sup>. The entry point of most infections in humans is mucosal surfaces, especially gastrointestinal and respiratory tracts. Through feeding and breathing, the organism comes into contact with pathogenic microorganisms as well as potentially allergenic or harmful substances<sup>23</sup>. Exclusive breastfeeding saves millions of children every year by preventing acute and chronic

infectious diseases, especially respiratory and intestinal diseases<sup>7</sup>.

In view of the numerous beneficial effects of exclusive breastfeeding and the protection it confers against various diseases, the aim of this study was to identify the protective elements of breast milk that help prevent against gastrointestinal and respiratory diseases.

### **METHOD**

The present study consisted of a literature review of the subject based on information obtained through systematic screening of the literature by the Boolean technique using the *and* operator together with the following key words: *leite materno* and *doenças gastrintestinais*, as well as *leite materno* and *doenças respiratórias*. The search was based on research sources including publications and the specific search databases Bireme, Lilacs, Medline and Scielo. The scope of the search was limited in terms of language of publication (Portuguese, Spanish and English) and publication date (1996-2009).

Using these screening criteria, the search yielded 302 articles. Of these articles, 46 met the study inclusion criteria and were therefore selected.

## PROTECTIVE ELEMENTS OF BREAST MILK

Newborns and infants are more vulnerable to infections, especially during the first six months of life, due to immaturity of the immune system and greater intestinal permeability. Thus, during this critical period of relative immunologic incompetence, human milk has valuable attributes to help meet infants' immunobiological needs and protect them from a range of diseases<sup>2,23,24</sup>.

Neither chronological age nor nutritional status of mothers has a significant influen-

ce on the concentrations of total proteins, albumins, IgG and IgA present in their colostrum<sup>25</sup>. The mammary gland appears to have specific mechanisms to regulate the concentration of trace elements in the milk, even under specific conditions of a variable maternal diet<sup>26</sup>.

However, the composition of the milk from mothers of premature newborns differs in that it promotes greater anti-inflammatory effects than milk from mothers with term newborns<sup>27</sup>. This different composition can provide immunoprotection by inducing maturation of the gut in premature infants<sup>27</sup> given that preterm infants have a higher risk of developing complications in the gastrointestinal and respiratory tracts<sup>28</sup>. The nutritional and anti-infectious properties of milk from mothers of preterm infants cater to the physiological and immunological needs of the immature gut of the newborn, containing greater amounts of IgA, lysozyme and lactoferrin<sup>2</sup>.

The anti-infective properties of human milk comprise soluble and cell components. The soluble components include immunoglobulins IgA, IgM, IgD, IgE, IgG, predominantly IgA, lysozyme, lactoferrin, components of the complement system (C'3, C'4), bioactive peptides, oligosaccharides, and lipids (antistaphylococcal factor and inactivation virus). The immunologically active cell components consist of polymorphonuclear phagocytes, lymphocytes, macrophages, nucleotides, plasma cells, and epithelial cells<sup>2,18,27,29,30,31,32</sup>.

Human milk also contains lactoperoxidase which oxidizes bacteria with antimicrobial action<sup>18,29</sup>. Macrophages and lymphocytes are responsible for phagocytosis and the production of complement factors<sup>27</sup>.

The antibodies present in breast milk target numerous microorganisms which the mother was exposed to throughout her life, representing a kind of immunological "repertoire". Most of these microorganisms had previously come into contact with the mucosal surfaces

of the mother's gastrointestinal or respiratory tracts<sup>20</sup>.

Besides antibodies, human colostrum contains many immunocompetent cells and biochemical factors. These interact with each other and with the mucosa of the digestive and respiratory tracts of infants, providing not only passive immunity, but also stimulating the development and maturation of the neonate's mucosal immune system<sup>11</sup>.

Glycoconjugates and oligosaccharides display anti-adherent activity for many microorganisms that cause gastrointestinal and respiratory diseases<sup>23</sup>. Cow's milk has no immune component beneficial to infants<sup>27</sup> and the introduction of food or pre-milk supplements increases the risk of infections in infants<sup>4</sup>.

### **GASTROINTESTINAL DISEASES**

In 1989, the year of publication of the study by Brown et al.<sup>3</sup>, it was known that pacifier use and the administration of teas and other non-nutritious fluids to infants, besides provoking early weaning, predisposed infants to the onset of diarrhea due to exposure to risk of contamination.

The prolongation of breastfeeding is especially beneficial at the end of the first and second years of life when the incidence of diarrhea reaches its highest<sup>17</sup>. The presence of milk in the intestinal lumen stimulates the development of its mucosa<sup>17,28</sup> and the activity of the enzyme lactase<sup>34</sup>. According to the review by Toma & Rea<sup>10</sup>, exclusively breastfed infants had lower morbidity from diarrhea compared with those who were fed on breast milk in combination with complementary foods at 3-4 months.

From the first hours of life, different strains of *Escherichia coli* colonize the human gut, becoming part of its normal flora. However, some of these strains can cause severe intestinal disease<sup>23</sup>. In neonates, the immaturity

of the intestinal epithelium, low gastric acidity and lower activity of digestive enzymes limit the effectiveness of the barrier against the entry of microorganisms<sup>35</sup>.

Since the 1970s, following the discovery of the *bifidus* factor, the mechanism by which the intestinal mucosa is protected against pathogenic agents has become elucidated. Several types of oligosaccharides and glycoconjugates in breast milk (known as prebiotic agents) stimulate the colonization of the gut by beneficial microorganisms. These agents act in the first essential step of pathogenesis by preventing microorganisms from attaching to cell walls<sup>36</sup>.

Exclusively breastfed infants have beneficial intestinal flora with higher bifidobacteria and lower *Clostridium dificile* and *Escherichia* coli, according to Penders et al.<sup>37</sup>. In their study, which examined the feces of 1032 Dutch infants up to one month old, infant feeding was found to be a major determinant of intestinal microflora in early life. Records from as early as 1905 describe differences in the composition of intestinal microflora in breastfed children compared to weaned children.

Carbohydrates present in human milk include oligosaccharides and lactose. The oligosaccharides, in the presence of peptides, form a *bifidus* factor (carbohydrate with dialysable nitrogen). In the lactose-rich environment, this produces lactic acid and succinic acid, lowering intestinal pH and creating conditions inconducive for the growth of pathogenic bacteria, fungi and parasites. Thus, lactose also exerts a protective effect against the development of gastrointestinal disorders by promoting this beneficial colonization<sup>2,38</sup>.

These nitrogen oligosaccharides allow population by the bifid flora which prevents, through selective action, new recent bacteria to the intestinal lumen and potential pathogens of diarrhea such as *E. coli*, among other enterobacteria, from colonizing the intestinal tract<sup>18,29,31</sup>.

Mucin is a protein found in colostrum which binds to fat globules and whose main function is to inhibit bacterial adhesion to the intestinal epithelium<sup>39</sup>.

Some polyunsaturated fats such as linoleic and arachidonic acids are important for the syntheses of the prostaglandins involved in biological functions active in digestion and intestinal cell maturation, decreasing the prevalence of intestinal allergy and boosting infant defenses<sup>2,40</sup>. The lipids present in human milk are hydrolyzed into fatty acids and monoglycerides that act against some types of viruses, bacteria and protozoa<sup>39</sup>.

Nucleotides, glutamine and lactoferrin present in breast milk influence gastrointestinal development and the body's defenses<sup>3,21,35,41</sup>. Glutamine acts as the principal fuel for the growth of intestinal epithelium during periods of stress<sup>28</sup>.

One of the functions of lactoferrin is to chelate iron ions, which are essential for the multiplication of pathogenic microorganism, thereby decreasing their bioavailability in the intestinal microenvironment, a process favored by the presence of bicarbonate in human milk<sup>39,42</sup>. Lactoferrin is found intact in both feces and urine of breastfed infants, and may thus exert a systemic protective role<sup>23</sup>.

Lysozyme is an enzyme with bactericidal action, interacting synergistically with lactoferrin and IgA<sup>39,42</sup>. Protection against gastroenteritis results in a lower incidence of diarrhea due to the presence of IgA antibodies in breast milk which are reactive against pathogens and toxins<sup>20</sup>.

IgA is the main immunoglobulin in colostrum<sup>23,28,43</sup>. It is present in the intestines of infants fed human milk, and prevents the invasion and adhesion of viruses and bacteria in the intestinal mucosa, and also neutralizes toxins and virulence factors<sup>28</sup>.

The main action of IgA is to bind to macromolecules and microorganisms, inhibiting the interaction between bacteria and epithelial cells and impeding their adherence to mucosal surfaces thereby preventing contact of pathogens with the epithelium<sup>44</sup>. Thus, IgA protects the mucosa against diarrhea by forming a protective coating on mucosal surfaces in infants<sup>23</sup>.

IgA antibodies in colostrum survive the gastrointestinal tract of the newborn and can be found intact in feces, retaining the same reactivity against antigens they displayed in the mother's colostrum, and preserving their anti-infective activity throughout the gastrointestinal tract of the newborn<sup>23,39,42,45</sup>. The peculiar structure of IgA confers this class of antibodies with greater resistance to the action of proteolytic enzymes which are abundant in mucous secretions<sup>44</sup>.

The other immunoglobulins are found in colostrum and human milk, albeit at much lower concentrations than IgA. IgM is the second most abundant of these immunoglobulins. In the event of insufficient IgA in breast milk, IgM acts as a compensatory mechanism. Consequently, IgM antibodies may play an important role in defending the mucosal surfaces in infants<sup>23</sup>.

In the course of lactation, even with the decline in secretion of IgA in breast milk, the biological activity of inhibition of bacterial adhesion remains unchanged. This finding is consistent with the fact that children remain protected from gastroenteritis throughout the entire period of breastfeeding. Diarrhea is more prevalent after weaning, regardless of age of onset. Therefore, these data serve to highlight the importance of breast milk in premature and small for gestational age infants<sup>23</sup>.

The casein in human milk is also one of several constituents that helps protect the child from gastrointestinal infections by preventing bacteria adherence to cells of the intestinal mucosa<sup>2</sup>.

Secretory antibodies reactive against the virulence factors of some bacteria are able to inhibit bacterial adhesion to the intestinal mu-

cosa and thus prevent the colonization of the host and impede the chain of events that would ultimately culminate in infection and diarrhea. This is an important protection mechanism conferred by breast milk that prevents various infections initiated by the adherence of microorganisms to mucosal surfaces<sup>45</sup>.

### RESPIRATORY DISEASES

Exclusive breastfeeding protects infants against progression to severe respiratory infection<sup>10,46</sup>. The practice of breastfeeding for between six months and one year of age may also reduce the prevalence of respiratory infections in childhood<sup>47,48</sup>. Breast milk is able to reduce both intestinal exposure and absorption of allergens responsible for respiratory diseases<sup>49,50</sup>.

The protective effects of breastfeeding against both ear and lung infections have become more evident in recent years. Secretary IgA, an antibody resulting from the mother's response to prior exposure to infectious agents, plays a particularly important role. It is characterized by being able to survive in the membranes of the respiratory mucosa and by its resistance to proteolytic digestion. Besides preventing pathogens from establishing in the cells of the breastfed infant, IgA attenuates the damaging effects of the inflammatory process<sup>32,49,51</sup>.

Cytokine concentrations have a key role in the immunogenicity of milk. The IL-4, IL-5 and IL-3 cytokines, principally involved in the production of IgE and induction of eosinophil response, may protect infants against respiratory diseases<sup>52</sup>. The transforming growth factor beta, a cytokine predominant in human milk, enhances the infant's ability to produce IgA<sup>53</sup>.

The oligosaccharides block pneumococci through receptor cells of the pharynx<sup>28</sup>. Several types of antibodies protect against the viruses that cause bronchitis. Lipids and some macroglobulins possess antiviral action, pro-

tecting the infant against the *influenza* virus. These macroglobulins also protect the newborn from causative agents of acute respiratory infection<sup>54</sup>.

Soluble CD14 is present in high concentrations in breast milk and has an important role in the induction of helper T lymphocyte response to bacteria, and may also protect against the development of allergies<sup>55</sup>. The high level of cationic eosinophil protein also confers this protection<sup>56</sup>. Lymphocytes protect infants against respiratory diseases, especially asthma<sup>57,58,59</sup>.

Breastfeeding also decreases the involution of the thymus gland during childhood<sup>60</sup>, which in turn stimulates the effects

### REFERENCES

- 01. Simon VGN, Souza JMP, Souza SB. Aleitamento materno, alimentação complementar, sobrepeso e obesidade em pré-escolares. Rev Saúde Pública. 2009; 43: 60-9.
- Lamounier JA, Vieira GO, Gouvêa LC. Composição do Leite Humano - Fatores Nutricionais. In: Rego JD. Aleitamento Materno. Rio de Janeiro: Atheneu; 2001. p. 47-58.
- 3. Ribeiro LC, Kuzuhara JSW. Lactação. In: Silva SMCS, Mura JD'AP. Tratado de alimentação, nutrição e dietoterapia. São Paulo: Roca, 2007. p. 293-318.
- OMS Organização Mundial da Saúde. Organização Pan-Americana da Saúde. Evidências científicas dos dez passos para o sucesso no aleitamento materno. Brasília; 2001.
- 5. WHO World Health Organization. The optimal duration of exclusive breastfeeding: a systematic review. Geneva; 2001.
- Abrão ACFV. Amamentação: uma prática que precisa ser aprendida. Pediatria (São Paulo). 2006; 28: 79-80.

of T cells, protecting the infant from respiratory diseases<sup>48</sup>.

### **CONCLUDING REMARKS**

Breast milk is the only food that can protect infants from various diseases in the first months of life because it is rich in nutritional and immunological compounds that confer this protection. Other types of milk, formula or food are not only devoid of these protective compounds but can also cause diseases in the newborn.

Campaigns and actions in Public Health that foster breastfeeding should be continuously developed and encouraged in light of the numerous benefits of this practice.

- 7. Venâncio SI, Escuder MML, Kitiko P, Rea MF, Monteiro CA. Frequência e determinantes do aleitamento materno em municípios do Estado de São Paulo. Rev Saúde Pública. 2002; 36: 313-8.
- 8. WHO World Health Organization. Global strategy for infant nf young child feeding. Geneva; 2003.
- 9. Silva IA. Enfermagem e aleitamento materno: combinando práticas seculares. Rev Esc Enf USP. 2000; 34: 362-9.
- 10. Toma TS, Rea, MF. Benefícios da amamentação para a saúde da mulher e da criança: um ensaio sobre as evidências. Cad Saúde Pública. 2008; 24(Supl 2): 235-46.
- 11. Hanson LA, Telemo E. Immunobiology and epidemiology of breastfeeding in relation to prevention of infections from a global perspective. In: Ogra PL, Mestecky J, Lamm ME, Strober W, Bienenstock J, McGhee J. Mucosal Immunology. San Diego: Academic Press, 1999. p. 1501-10.
- 12. Betrán AP, Onís M, Lauer JA, Villar J. Ecological study of effect of breast feeding on infant mortality in Latin America. BMJ. 2001; 323: 1-5.

- 13. Venâncio SI. Dificuldades para o estabelecimento da amamentação: o papel das práticas assistenciais das maternidades. J Pediatr (Rio J). 2003; 79: 1-2.
- 14. UNICEF. Oficina de Uruguay, RUANDI, Ministerio de Salud Pública. Programa Nacional de Salud de la Niñez. Encuesta de lactancia, estado nutricional y alimentación complementaria en niños menores de 24 meses atentidos por servicios público y mutuales de Montevideo e interior del país / María Isabel Bove, Florencia Cerutti. – Montevideo; 2007.
- 15. Brasil. Ministério da Saúde. Município que promove a amamentação promove a saúde. Prêmio Bibi Vogel. Pacto nacional pela redução da mortalidade materna e neonatal. Brasília; 2005.
- Vieira GO, Silva LR, Vieira TO, Almeida JAG, Cabral VA. Hábitos alimentares de crianças menores de um ano amamentadas e não amamentadas. J Pediatr (Rio J). 2004; 80: 411-6.
- 17. Brasil. Ministério da Saúde, Organização Pan-Americana de Saúde. Dez passos para uma alimentação saudável. Guia alimentar para crianças menores de dois anos. Brasília; 2002a.
- 18. Devincenzi UM, Mattar MJG, Cintra EM. Nutrição no primeiro ano de vida. In: Silva SMCS, Mura JD'AP. Tratado de alimentação, nutrição e dietoterapia. São Paulo: Roca, 2007. p. 319-45.
- 19. Saliba NA, Zina LG, Moimaz SAS, Saliba O. Frequência e variáveis associadas ao aleitamento materno em crianças com até 12 meses de idade no município de Araçatuba, São Paulo, Brazil. Rev Bras Saúde Matern Infant. 2008; 8: 481-90.
- 20. Hanson LA. Breastfeeding provides passive and likely long-lasting active immunity. Ann Allergy Asthma Immunol. 1998; 81: 523-37.

- Teruya K, Coutinho SB. Sobrevivência infantil e aleitamento materno. In: Rego JD. Aleitamento materno. São Paulo: Atheneu, 2001. p. 5-20.
- 22. Edmond KM, Zandoh C, Quigley MA, Amenga-Etego S, Owusu-Agyei S, Kirkwood BR. Delayed breastfeeding initiation increases risk of neonatal mortality. Pediatrics. 2006; 117: 380-6.
- Carbonare SB, Carneiro-Sampaio MMS.
  Composição do Leite Humano Aspectos Imunológicos. In: Rego, JD. Aleitamento Materno. São Paulo: Atheneu, 2001. p. 83-97.
- Carneiro-Sampaio MMS, Silva MLM, Carbonare SB, Palmeira P, Delneri MT, Honório AC, Trabulsi LR. Breast-feeding protection against enteropathogenic Escherichia coli. Rev Microbiol. 1996; 27: 120-5.
- 25. Costa COM, Queiroz SS, Nóbrega FJ, Vitolo MR, Sole D. Total proteins, albumin, globulin, immunoglobulins (A, M, G) and C3 complement fraction in the colostrum of adolescent nursing mothers of preterm infants. In: Nóbrega FJ. Human milk composition. São Paulo: Revinter, 1996. p. 83-98.
- Lönnerdal B. Regulation of mineral and trace elements in human milk: exogenous and endogenous factors. Nutr Rev. 2000; 58: 223-9.
- 27. Brasil. Ministério da Saúde. Secretaria de Políticas de Saúde. Área de Saúde da Criança. Atenção humanizada ao recémnascido de baixo-peso: método mãecanguru: manual do curso. Brasília; 2002b.
- 28. Vinagre RD, Diniz EMA. O leite humano e sua importância na nutrição do recémnascido prematuro. São Paulo: Atheneu, 2001. p. 142.
- 29. Feferbaum R, Quintal VS. Nutrição enteral do recém-nascido pré-termo. Pediatr Modern. 2000; 36: 133-40.

- 30. Fernandes RM, Carbonare SB, Carneiro-Sampaio MM, Trabulsi LR. Inhibition of enteroaggregative Escherichia coli adhesion to Hep-2 cells by secretory immunoglobulin A from human colostrum. Pediatr Infect Dis J. 2001; 20: 672-8.
- 31. Novak FR, Almeida JAG, Vieira GO, Borba LM. Colostro humano: fontes naturais de probióticos? J Pediatr (Rio J). 2001; 77: 265-71.
- 32. Jackson KM, Nazar AM. Breastfeeding, the immune response, and long-term health. J Am Osteopath Assoc. 2006; 106: 203-7.
- 33. Brown KH, Black RE, Romaña GL, Kanashiro HC. Infant-feeding practices and their relationship with diarrheal and other diseases in Huascar (Lima), Peru. Pediatrics. 1989; 83: 31-40.
- 34. Rego JD. Amamentando um prematuro. In: Rego JD. Aleitamento materno: um guia para pais e familiares. São Paulo: Atheneu, 2002. p. 179-86.
- 35. Bernt KM, Walker WA. Human milk as a carrier of biochemical messages. Acta Paediatr. 1999; 88 (suppl 430): 27-41.
- 36. Newburg DS, Ruiz-Palacios GM, Morrow AL. Human milk glycans protect infants against enteric pathogens. Annu Rev Nutr. 2005; 25: 37-58.
- 37. Penders J, Thijs C, Vink C, Stelma FF, Snijders B, Kummeling I, et al. Factors influencing the composition of the intestinal microbiota in early infancy. Pediatrics. 2006; 118: 511-21.
- 38. Vitolo MR. Aspecto nutricional do leite humano. In: Anais do VII Encontro Paulista de Aleitamento Materno. São Paulo; 1997. p. 33.
- 39. Goldman AS, Ogra PL. Anti-infectious and infectious agents in human milk. In: Ogra PL, Mestecky J, Lamm ME, Strober W, Bienenstock J, McGhee J. Mucosal Immunology. San Diego: Academic Press, 1999. p. 1511-21.

- 40. Nóbrega, FJ. A importância nutricional do leite materno. In: Rego JD. Aleitamento Materno. Rio de Janeiro: Atheneu, 2001. p. 59-82.
- 41. Gouvêa LC. Aleitamento materno. In: Lopez FA, Brasil ALD. Nutrição e Dietética em Clínica Pediátrica. São Paulo: Atheneu, 2003. p.17-36.
- 42. Xanthou M. Immune protection of human milk. Biol Neonate. 1998; 74: 121-33.
- 43. Honório-França AC, Carvalho MPSM, Isaac L, Trabulsi LR, Carneiro-Sampaio MMS. Colostral mononuclear phagocytes are able to kill enteropathogenic Escherichia coli opsonized with colostral IgA. Scand J Immunol. 1997; 46: 59-66.
- 44. Russel MW, Kilian M, Lamm ME. Biological actives of IgA. In: Ogra PL, Mestecky J, Lamm ME, Strober W, Bienenstock J, McGhee J. Mucosal Immunology. San Diego: Academic Press, 1999. p.225-40.
- 45. Carbonare SB, Silva MLM, Palmeira P, Carneiro-Sampaio MMS. Human colostrum IgA antibodies reacting to Enteropathogenic Escherichia Coli (EPEC) antigens and their persistence in the faeces of a breast-fed infant. J Diarrhoeal Dis Res. 1997; 15: 53-8.
- 46. Carvalho CF, Silva MGF. Avaliação do desmame precoce e suas implicações infecciosas nas crianças atendidas no ambulatório de um hospital terciário. Arq Ciênc Saúde. 2005; 12: 129-32.
- 47. Broor S, Pandey RM, Ghosh M, Maitreyi RS, Lodha R, Singhal T, Kabra KS. Risk factors for severe acute lower respiratory tract infection in under-five children. Indian Pediatr. 2001; 38: 1361-9.
- 48. Oddy WH, Sly PD, Klerk NH, Landau LI, Kendall GE, Holt PG, Stanley FJ. Breast feeding and respiratory morbidity in infancy: a birth cohort study. Arch Dis Child. 2003; 88: 224-8.

- 49. Kerner JA Jr. Use of infant formulas in preventing or postponing atopic manifestations. J Pediatr Gastroenterol Nutr. 1997; 24: 442-6.
- 50. Wold AE, Adlerberth I. Does breastfeeding affect the infant's immune responsiveness? Acta Paediatr. 1998; 87: 19-22.
- 51. Carvalho Júnior, FF. Apresentação clínica da alergia ao leite de vaca com sintomatologia respiratória. J Pneumol. 2000; 27: 17-24.
- 52. August A, Mueller C, Weaver V, Polanco TA, Walsh ER, Cantorna MT. Nutrients, nuclear receptors, inflammation, immunity lipids, PPAR, and allergic asthma. J Nutr. 2006; 136: 695-9.
- 53. Kalliomäki M, Ouwehand A, Arvilommi H, Kero P, Isolauri E. Transforming growth factor-beta in breast milk: a potential regulator of atopic disease at an early age. J Allergy Clin Immunol. 1999; 104: 1251-7.
- 54. Carbajal CC. Estado de salud en los niños lactados por más de 4 meses. Rev Cubana Pedriatr. 2000; 72: 275-80.
- 55. Savilahti E, Siltanen M, Kajosaari M, Vaarala O, Saarinen KM. IgA antibodies, TGF-beta1 and -beta2, and soluble CD14 in the colostrum and development of atopy by age 4. Pediatr Res. 2005; 58: 1300-5.

- 56. Osterlund P, Smedberg T, Hakulinen A, Heikkilä H, Järvinen KM. Eosinophil cationic protein in human milk is associated with development of cow's milk allergy and atopic eczema in breast-fed infants. Pediatr Res. 2004; 55: 296-301.
- 57. Pabst HF, Spady DW, Pilarski LM, Carson MM, Beeler JA, Krezolek MP. Differential modulation of the immune response by breast- or formula-feeding of infants. Acta Paediatr. 1997; 86: 1291-7.
- 58. Hawkes JS, Neumann MA, Gibson RA. The effect of breast feeding on lymphocyte subpopulations in healthy term infants at 6 months of age. Pediatr Res. 1999; 45: 648-51.
- 59. Busse WW, Lemanske RF Jr. Asthma. N Engl J Med. 2001; 344: 350-62.
- 60. Hasselbalch H, Engelmann MD, Ersboll AK, Jeppesen DL, Fleischer-Michaelsen K. Breast-feeding influences thymic size in late infancy. Eur J Pediatr. 1999; 158: 964–7.

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