Role of bovine IgG in human immunity

A review by Ulfman et al 2018 (1) shows that studies involving infants and adults have found that bovine immunoglobulin G (IgG) and colostrum that is very rich in bovine IgG may have a role in the prevention of gastrointestinal tract (GIT) infections (2-7) and upper respiratory tract (URT) infections (8-17). However, these studies vary with regard to target group, design, source of bovine IgG, dosage, and endpoints measured; making it difficult to draw firm conclusions. With that in mind, the review focuses on the effects of orally ingested bovine IgG and their potential mechanisms of action on the immune system of children and adults.

Researchers have discovered that orally ingested bovine immunoglobulin G (IgG) can be recovered in faeces, indicating that it can be functionally active throughout the gastrointestinal tract. The levels recovered are higher in infants than in adults and this is most likely due to differences in gastrointestinal conditions such as pH. Studies involving both infants and adults have shown that bovine IgG can prevent gastrointestinal (GIT) infections (2-7) and upper respiratory tract (URT) infections (8-17).

The review by Ulfman et al 2018 is a state-of-the-art review on mechanisms and nutritional studies performed with products containing bovine IgG. The review explains that most human studies used colostrum, colostrum- and milk-derived IgG, and serum-derived immunoglobulins as the source of bovine IgG. IgG from both vaccinated cows and nonimmunized animals were used, depending on the study aim and setup.
Effects of bovine IgG on the immune system

Gastrointestinal tract (GIT) infections
Four studies on on-going GIT infections in infants and children suggest bovine IgG—which is isolated from cows that were vaccinated with the specific organism—plays a role in reducing the duration of GIT infections (18,20). Besides its therapeutic effect (18-24), the prophylactic effect (2-7) of bovine IgG has also been examined. The concept of preventing GIT infections in infants using pathogen-specific bovine immunoglobulins has been tested for several enteropathogens such as Escherichia coli and Helicobacter pylori (44-47). The most extensively researched enteropathogen in this area is rotavirus, and there are both animal and human studies that support the ingestion of rotavirus-specific bovine immunoglobulins for the prevention of rotavirus diarrhea (7, 18-21, 42, 43). Bovine IgG has also been shown to confer a prophylactic effect against GIT infections in immune compromised individuals (48-54). Studies involving HIV-infected individuals with recurrent diarrhea found that ingestion of bovine IgG led to reduction in stool frequency, lower fatigue scores and increased body weight and CD4+ T-cell counts.

Respiratory tract infections
Breastfed infants are less likely to develop respiratory tract infections and otitis media compared to formula fed infants. However, more research is needed to determine the optimal duration and amount of breastfeeding to confer protection against respiratory tract infections and otitis media.

There are 11 studies that showed bovine IgG and colostrum can prevent URT infections in children, adults, elderly people and athletes (8-17,55, 56). These studies mostly used normal IgG from non-vaccinated cows as vaccination was only done for gastrointestinal pathogens. Interestingly, an epidemiological study on the consumption of unprocessed cow milk as weaning food in the first year of life found a reduced risk for respiratory infections and otitis media, compared to ultra heat-treated (UHT) milk. A possible explanation is that intact milk protein, which is present in unprocessed cow milk, is responsible for the protective effect (57-59).

Allergy
There is a complex link between early respiratory tract infection and the development of allergy. The hygiene hypothesis states that early infection is linked to reduced allergy and allergy disease (60). The proposed immunological mechanism is interferon gamma (IFN-g) generated during infection down-regulates T-helper 2 (Th2) activity associated with the production of interleukin-4 (IL-4) which promotes IgE production. In addition, infection also upregulates T-regulatory cell (T-reg) activity, which has additional controlling effects on Th2 and Th1 responses. The latter may explain why allergy, which correlates with Th2 response, and autoimmune diseases, which are associated with Th1 cells, are increasingly more common and co-exist in relatively affluent communities. In some communities where active infection such as measles has been linked to less allergy, it is possible that the commensal human microbiome plays a major role in promoting normal immune regulation. As such, a more accurate term has been coined: “the microbial exposure hypothesis.”

In line with the microbial exposure hypothesis, the findings of epidemiological cohort studies showing an increased frequency of respiratory infections in children who subsequently develop allergic sensitization and disease need to be interpreted with care. The underlying defects in immune response that increases the risk of infection may be responsible for allergy as well; this suggests that the relationship between infection and allergy may not be cause and effect.

Nevertheless, some viral infections in infants have been specifically linked to the later development of asthma. For instance, rhinovirus induced wheezing in infancy predicts a high probability of later asthma. To a lesser extent, asthma has also been linked to infant bronchiolitis caused by respiratory syncitial virus (RSV) infections. Of special interest is the fact that bovine IgG binds strongly to human RSV and can in in vitro assays prevent the infection of human cells with human RSV, thus speculatively linking bovine IgG to reducing RSV infections and subsequently asthma (61).

Generally, acute gastroenteritis in infancy increases the risk of allergic sensitization to food proteins, especially if the exposure to allergenic proteins occurs while there is intense gut inflammation.
The latter provides co-stimulatory signals to trigger a sensitizing response. Thus, breastfeeding with its protective effects against gastrointestinal and RSV infections will reduce such events.

**Mechanism of action**

Bovine IgG binds to many human pathogens and prevent their adhesion to the intestinal epithelium. Moreover, bovine IgG can neutralize experimental infection of human cells and limits gastrointestinal inflammation. It exerts anti-inflammatory effects directly on the intestinal epithelium and blocks the translocation of bacterial components across the epithelial layer. Bovine IgG also binds to human Fc receptors, which leads to enhanced phagocytosis, killing of bacteria and antigen presentation. In vitro models, bovine IgG was shown to support gastrointestinal barrier function. (33-41)

**The authors conclusion**

The review suggests that bovine IgG, when taken orally, may play a role in supporting the immune function in vulnerable groups such as infants, children, the elderly and immunocompromised persons (1).

- The review analysed studies on bovine IgG and colostrum, and showed that they have a prophylactic and therapeutic effect on GIT and URT infections (2-28).
- Bovine IgG may also reduce the risk of otitis media (29,30) and allergy (31,32).
- Bovine IgG confer their effect on the immune system by binding to pathogens and allergens, enhancing their clearance, limiting gastrointestinal inflammation, and in some cases even neutralizing infections.
- In in vitro models, bovine IgG also enhances phagocytosis by targeting the pathogens to phagocytes that express receptors for IgG; killing of bacteria; and antigen presentation (33, 34), and supports gastrointestinal barrier function (35-41).

**References:**

The FrieslandCampina Institute provides nutrition and health professionals with extensive information about dairy, nutrition and health following the most recent scientific developments. This information is solely meant for professionals and not for consumers, clients or patients.

Are you a nutrition or health professional who wants to know all about dairy, nutrition and health? Contact the FrieslandCampina Institute to find out more. www.frieslandcampina.institute

Follow us on social media

@FCInstitute_int
@FrieslandCampinaInt

Disclaimer
© FrieslandCampina 2019
Although the FrieslandCampina Institute has taken the greatest possible care in preparing this document, the information provided and/or displayed in this document may be incomplete or incorrect.

The FrieslandCampina Institute assumes no responsibility or obligation whatsoever with respect to any printing, spelling, typographical or other similar errors of any kind in materials published by it.

Version February 2019