Bovine Colostrum: HEALTH BENEFITS

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General Benefits of Bovine Colostrum

Intestinal Permeability/Leaky Gut Syndrome

Immune Health

Bacterial Infections

Viral Infections
  Rotavirus
  Influenza
  Poliovirus
  Hepatitis
  Herpes
  HIV/AIDS

Autoimmune Disorders
  Arthritis
  Asthma
  Inflammatory Bowel Disease
  Type 1 Diabetes
  Type 2 Diabetes
  Multiple Sclerosis
  Sjogren’s Syndrome

Anti-Aging Benefits

Alzheimer’s Disease

Bone Health/Osteoporosis

Cardiovascular Disease

Brain Injury/Stroke
Cancer

Athletic Performance

Mental Health / Psychiatric Disorders

Autism

Wound Healing & Tissue Repair

Pain Management

Sexual Health

Colostrum Supplementation in Infants & Children

Colostrum Supplementation in Dogs & Cats

General Benefits of Bovine Colostrum

Bagwe S, et al. Bovine colostrum: an emerging nutraceutical. Journal of Complementary & Integrative Medicine. 2015 Mar 12. pii: /j/jcim.ahead-of-print/jcim-2014-0039/jcim-2014-0039.xml. There is emerging evidence that bovine colostrum (BC) may be one of the promising nutraceuticals which can prevent or mitigate various diseases in newborns and adults. Immunity-related disorders are one of the leading causes of mortality in the world. BC is rich in immunity, growth and antimicrobial factors, which promote tissue growth and the maturation of digestive tract and immune function in neonatal animals and humans. The immunoglobulins and lactoferrin present in colostrum are known to build natural immunity in newborns which helps to reduce the mortality rate in this population. Also, the side-effect profile of colostrum proteins and possible lactose intolerance is relatively less in comparison with milk. In general, BC is considered safe and well tolerated.

Rathe M, et al. Clinical applications of bovine colostrum therapy: a systematic review. Nutrition Reviews. 2014 Apr;72(4):237-54. Bovine colostrum may provide gastrointestinal and immunological benefits, but further studies are required before recommendations can be made for clinical application. Animal models may help researchers to better understand the mechanisms of bovine colostrum supplementation, the dosage regimens required to obtain clinical benefits, and the optimal methods for testing these effects in humans.

Struff WG, Sprotte G. Bovine colostrum as a biologic in clinical medicine: a review. Part I: biotechnological standards, pharmacodynamic and pharmacokinetic characteristics and principles of treatment. Int J Clin Pharmacol Ther. 2007 Apr;45(4):193-202. It has long been known that the consumption of bovine colostrum by humans has therapeutic effects e.g. in gastrointestinal infections, but only since the second half of the last century has it been possible to prepare stable, standardized preparations of colostrum. These biologics are administered to patients in combination with standard therapies as so-called balanced supportive diets. Investigations with standardized colostrum
preparations in animal models of human disease and estimates of bovine IgG activity in the human GI-tract, described in this review, have provided preclinical data supporting the use of bovine colostrum in human diseases.

Struff WG, Sprotte G. Bovine colostrum as a biologic in clinical medicine: a review—Part II: clinical studies. Int J Clin Pharmacol Ther. 2008 May;46(5):211-25. The value of bovine colostrum as a biologic in medicine is documented in clinical trials and supported by relatively large databases containing case reports and anecdotal findings. The main actions include an antibacterial effect and modulation of the immune response. The ability of bovine colostrum concentrates (BCC are polyvalent bovine colostrum concentrates produced from the colostrums of several 100 cows) to neutralize lipopolysaccharides, i.e. endotoxins arising from Gram-negative bacterial pathogens and to inhibit enterogenic endotoxemia in animal models as shown in the last review to have its counterpart in patient therapy. Clinical trials with BCC provide evidence that oral application reduces the influx of LPS from the gut and this appears to be a major mechanism underlying its therapeutic effect in patients at risk for Gram-negative septic shock.

Artym J, Zimecki M. Milk-derived proteins and peptides in clinical trials. Postepy Hig Med Dosw (Online). 2013 Aug 6;67:800-16 Clinical trials are reviewed, involving proteins and peptides derived from milk (predominantly bovine), with the exception of lactoferrin, which will be the subject of another article. The most explored milk fraction is α-lactalbumin (LA), which is often applied with glycomacropeptide (GMP) - a casein degradation product. These milk constituents are used in health-promoting infant and adult formulae as well as in a modified form (HAMLET) to treat cancer. Lactoperoxidase (LCP) is used as an additive to mouth hygiene products and as a salivary substitute. Casein derivatives are applied, in addition, in the dry mouth syndrome. On the other hand, casein hydrolysates, containing active tripeptides, found application in hypertension and in type 2 diabetes. Lysozyme is routinely used for food conservation and in pharmaceutical products. It was successfully used in premature infants with concomitant diseases to improve health parameters. When used as prophylaxis in patients with scheduled surgery, it significantly reduced the incidence of hepatitis resulting from blood transfusion. Lysozyme was also used in infected children as an antimicrobial agent showing synergistic effects in combination with different antibiotics. Proline-rich polypeptide (PRP) was introduced to therapy of Alzheimer's disease patients. The therapeutic value of PRP was proved in several clinical trials and supported by studies on its mechanism of action. Concentrated immunoglobulin preparations from colostrum and milk of hyperimmunized cows showed efficacy in prevention of infections by bacteria, viruses and protozoa. A nutrition formula with milk-derived TGF-β2 (Modulen IBD®) found application in treatment of pediatric Crohn's disease. In conclusion, the preparations containing milk-derived products are safe and effective measures in prevention and treatment of infections as well as autoimmune and neoplastic diseases.

Kelly GS. Bovine colostrums: a review of clinical uses. Alternative Medicine Review. 2003 Nov;8(4):378-94. Bovine colostrums (“early" milk”) has a nutrient profile and immunological composition that differs substantially from "mature" milk. Included in the nutrient profile are higher amounts of immunoglobulins, growth factors, cytokines, and nucleosides than are found in milk. Bovine colostrums are also rich in oligosaccharides, antimicrobials, and immune-regulating factors. Available evidence suggests a beneficial effect of supplementation of bovine colostrums in improving body composition, aspects of athletic performance, diarrhea in persons with immune-deficiency syndromes, NSAID-induced gastrointestinal disturbances, and aspects of the acute phase response that occurs secondary to surgery. Specific hyperimmune bovine colostrums, produced to have high neutralizing titer
activity against Cryptosporidia, H. pylori, measles, rotavirus, and Shigella sp., appear to have clinical utility in conditions associated with these infectious organisms. **FULL TEXT.**

**Intestinal Permeability/Leaky Gut Syndrome**

Bodammer P, et al. **Bovine colostrum increases pore-forming claudin-2 protein expression but paradoxically not ion permeability possibly by a change of the intestinal cytokine milieu.** *Public Library of Science One* 2013;8(5):e64210. Bovine colostrum was shown to be a prophylactic agent with properties that strengthen barrier function and favor epithelial restitution in IBD. Modulation of the intestinal transforming growth factor-β expression might have compensated the claudin-2 increase and contributed to the observed barrier strengthening effects of colostrum in vivo and in vitro. **FULL TEXT.**

Leclercq S, et al. **Role of intestinal permeability and inflammation in the biological and behavioral control of alcohol-dependent subjects.** *Brain Behav Immun.* 2012;26(6):911-8. Leaky gut and inflammation were observed in non-cirrhotic alcohol-dependent subjects and inflammation was correlated to depression and alcohol-craving. This suggests that the gut-brain axis may play a role in the pathogenesis of alcohol-dependence.

Gecse K, et al. **Leaky gut in patients with diarrhea-predominant irritable bowel syndrome and inactive ulcerative colitis.** *Digestion* 2012;85(1):40-6. Elevated gut permeability is localized to the colon both in diarrhea predominant IBS and in inactive ulcerative colitis patients.

Zhang S, et al. [**The effects of milk and milk products on non-steroidal anti-inflammatory drug induced intestinal damage in rats**]. *Zhonghua Nei Ke Za Zhi* 2011;50(9):771-5. Bovine colostrum may have a beneficial effect in prevention of NSAIDs induced small intestinal injuries and preserve mechanical barrier of small intestinal mucosa which is probably relative to epidermal growth factor.

Marchbank T, et al. **The nutriceutical bovine colostrum truncates the increase in gut permeability caused by heavy exercise in athletes.** *American Journal of Physiology. Gastrointestinal and Liver Physiology* 2011;300(3):G477-84. Colostrum may have value in enhancing athletic performance and preventing heat stroke. **FULL TEXT.**


Mir R, et al. **The structural basis for the prevention of nonsteroidal antiinflammatory drug-induced gastrointestinal tract damage by the C-lobe of bovine colostrum lactoferrin.** *Biophysical Journal.* 2009 Dec 16;97(12):3178-86. Study indicates that C-terminal half of bovine lactoferrin (C-lobe) can be exploited for the prevention of NSAID-induced gastropathy. **FULL TEXT.**

Maes M, Leunis JC. **Normalization of leaky gut in chronic fatigue syndrome (CFS) is accompanied by a clinical improvement: effects of age, duration of illness and the translocation of LPS from gram-negative bacteria.** *Neuro Endocrinology Letters* 2008;29(6):902-10. Normalization of the IgA and IgM responses to translocated LPS may predict clinical outcome in Chronic Fatigue Syndrome. **FULL TEXT.**
weakened tight junction barrier with subsequent gut-derived inflammation is a novel pathway in Chronic Fatigue Syndrome. CFS patients with leaky gut can be treated with specific natural anti-inflammatory and anti-oxidative substances and a leaky gut diet.

Maes M, et al. **Normalization of the increased translocation of endotoxin from gram negative enterobacteria (leaky gut) is accompanied by a remission of chronic fatigue syndrome.** Neuro Endocrinology Letters 2007;28(6):739-44. Upon treatment with specific antioxidants and a "leaky gut diet", which both aim to treat increased gut permeability, and immunoglobins intravenously, the increased translocation of the LPS of gram negative enterobacteria normalized and this normalization was accompanied by a complete remission of the Chronic Fatigue Syndrome symptoms.

Liu Z, et al. **Tight junctions, leaky intestines, and pediatric diseases.** Acta Paediatr. 2005;94(4):386-93. Disruption of TJs leads to intestinal hyperpermeability (the so-called "leaky gut") and is implicated in the pathogenesis of several acute and chronic pediatric disease entities that are likely to have their origin during infancy, such as systemic inflammatory response syndrome (SIRS), inflammatory bowel disease, type 1 diabetes, allergies, asthma, and autism.


Kim JW, et al. **Combined effects of bovine colostrum and glutamine in diclofenac-induced bacterial translocation in rat.** Clinical Nutrition. 2005 Oct;24(5):785-93. The combined administration of bovine colostrum and glutamine was able to prevent the non-steroidal anti-inflammatory drug (NSAID)-induced gut damage and bacterial translocation in rats. A greater benefit was seen with the combination rather than colostrum or glutamine alone and no benefit was seen with low fat milk.


Gastrointestinal Inflammation and Repair Group, Imperial College, London (2003). Unpublished research. In an in vitro experimental study, colostrum stimulated intestinal cell growth and reestablished a healthy epithelial layer following injury. In an in vivo experimental study, colostrum powder was also shown to reduce gastric injury.


Blättler U, et al. **Feeding colostrum, its composition and feeding duration variably modify proliferation and morphology of the intestine and digestive enzyme activities of neonatal calves.** Journal of Nutrition 2001;131(4):1256-1263. A similar study done on calves either receiving or not
receiving colostrum. This study concentrated on the development and health of the gastrointestinal epithelium and found that the development and health of this epithelium was markedly superior in those receiving colostrum. Colostrum also influenced the production of lipase enzyme by the pancreas.

Playford RJ, et al. *Co-administration of the health food supplement, bovine colostrum, reduces the acute non-steroidal anti-inflammatory drug-induced increase in intestinal permeability*. *Clinical Science* 2001;100:627-633. This study showed that colostrum also prevents an increase in gastrointestinal permeability due to NSAID use, whereas NSAID use alone without colostrum causes an increase in permeability.


Sangild P, et al. *Intestinal Macromolecule Absorption in the Fetal Pig after Infusion of Colostrum in Utero*. *Pediatric Research* 1999;45:595-602. The prenatal pig intestine is similar to the neonatal pig intestine in that colostrum stimulates both the macromolecule absorption and the cessation of macromolecule uptake (intestinal closure).

Playford RJ, et al. *Bovine colostrum is a health food supplement which prevents NSAID induced gut damage*. *Gut* 1999;44:653-658. Although non-steroidal anti-inflammatory drugs (NSAIDs) are very effective in controlling joint pain in arthritis, their use also causes significant, and sometimes fatal, gastrointestinal damage. Supplementation with colostrum, however, significantly reduced and healed injury caused by NSAIDs. TGF stimulates new cell growth and a 20% increase in intestinal villi height. By repairing the intestinal mucosal barrier and increasing the surface area in the gut, more nutrients may be absorbed into the bloodstream.

Pluske JR, Morel PCH. *Increasing weaner pig productivity in New Zealand pig herds*. Unpublished research (1999). Piglets fed a liquid supplement with colostrum powder had a marked increase in villi height in the lumen of the small intestine, indicating greater digestion and absorption of nutrients. There were also an increased number of immune cells in the villi, indicating enhanced immune competency.

Bühler C, et al. *Small intestinal morphology in eight-day-old calves fed colostrum for different durations or only milk replacer and treated with long-R3-insulin-like growth factor I and growth hormone*. *Journal of Animal Science* 1998;76:758-765. The intestines of calves fed colostrum compared to those not fed colostrum revealed that those fed colostrum had significantly increased villus size and crypt depths. This translates into greater surface area and thus increased absorption of nutrients.

Carver JD, Barness LA. *Trophic factors for the gastrointestinal tract*. *Clinical Perinatology* 1996;23(2):265-285. Factors in colostrum which promote the development of the GI tract in newborn infants also help protect against such diseases as Crohn's disease, colitis, necrotizing enterocolitis and diarrhea.

nonsteroidal anti-inflammatory drugs (aspirin, ibuprofen, arthritis medications, and others), cytotoxic drugs used to treat cancer, corticosteroid drugs, and, by their action on bowel flora, antibiotics.

Lim SG, et al. *Intestinal permeability and function in patients infected with human immunodeficiency virus. A comparison with coeliac disease*. Scand J Gastroenterol. 1993;28(7):573-80. Abnormal permeability and reduced intestinal absorption capacity are common in HIV patients, occur at all stages of HIV disease, especially in the presence of diarrhoea, and with the exception of lactulose permeation, are relatively similar to the alterations seen in coeliac disease.


Meilants H. *Reflections on the link between intestinal permeability and inflammatory joint disease*. Clin Exp. Rheumatology 1990;8(5):523-524. The gastrointestinal tract is recognized as having important endocrine, metabolic, immunologic, and barrier functions, as well as its traditional role in nutrient absorption. There is a current resurgence of interest in the role of intestinal barrier failure in the development of systemic infection and multiple organ failure in the critically ill or injured patient.

Rooney PJ, et al. *A short review of the relationship between intestinal permeability and inflammatory joint disease*. Clinical and Experimental Rheumatology 1990;8(1):75-83. The connection between increased permeability of the intestines and inflammatory arthritis is examined. The gut is the likely source of the antigens which cause inflammatory arthritis.


Crissinger K, Kvietys P, Granger D. *Pathophysiology of gastrointestinal mucosal permeability*. Journal of Internal Medicine 1990;228:145-154. The concept of the plasma clearance method, methodological aspects of the technique, factors that influence plasma-to-lumen clearance measurements (e.g. solute size, blood flow, and permeability of the epithelial cell barrier), and advantages and disadvantages of the clearance method are discussed.

leukocyte (PMN)-derived oxidants may mediate the enhanced mucosal permeability, electrolyte transport, and epithelial cell injury associated with acute inflammation of the bowel.

Katz KD, Hollander D. *Intestinal mucosal permeability and rheumatological diseases*. *Baillere's Clinical Rheumatology* 1989;3(2):271-284. The inability of the intestinal lining to control the influx of antigens into the blood due to leaky gut or a dysfunctional immune system may represent the prime means by which the antigens which cause numerous diseases, including autoimmune diseases. Leaky gut has been linked to patients with ankylosing spondylitis, rheumatoid arthritis, Crohn's disease, and celiac sprue (a genetic autoimmune disease characterized by damage to the small intestine due to eating wheat gluten).

Katz KD, et al. *Intestinal permeability in patients with Crohn's disease and their healthy relatives*. *Gastroenterology* 1989;97:927-931. Intestinal permeability may be abnormal as a secondary result of inflammation, or as a result of a primary genetic abnormality.

Wood NC, et al. *Abnormal intestinal permeability. An aetiological factor in chronic psychiatric disorders?* *British Journal of Psychiatry* 1987;150:853-6. Chronic psychiatric in-patients showed abnormal intestinal permeability which could not be attributed to established bowel disease. Patients who were receiving neuroleptic but not anticholinergic drugs were those most often showing abnormal intestinal permeability.


Bjarnason I, Peters TJ, Wise RJ. *The leaky gut of alcoholism: possible route of entry for toxic compounds*. *The Lancet* 1984;1(8370):179-82. Increased intestinal permeability to toxic "non-absorbable" compounds of less than 5000 molecular weight may account for some of the extraintestinal tissue damage common in alcoholic patients.


Walker WA. *Antigen absorption from the small intestine and gastrointestinal disease*. *Pediatric Clinics of North America* 1975;22:731-746. When increased quantities of toxic or antigenic macromolecules gain access to the body because of a derangement in the intraluminal digestive process or because of a defect in the mucosal barrier, antigen absorption may be altered and result in either local intestinal or systemic disorders.

**Immune Health**

transient changes in NK cell numbers. Data suggest that upon consumption, interaction of CLMWF with immune cells in the gut mucosa triggers immediate events with systemic consequences.

Tokaev ÉS, et al. [Composition and clinical use of bovine colostrums]. Vopr Pitan. 2012;81(3):35-40. The critical analysis of the modern literature showed bovine colostrums is rich with immunoglobulins, antimicrobials and growth factors in comparison with nature milk. The positive effect of supplementation of bovine colostrums in diarrhea in persons with immune-deficiency syndromes, for treatment NSAID-induced gastrointestinal disturbances, at postoperative responses and in treatment of upper respiratory infection is supposed.

Thapa BR. Health factors in colostrum, Indian Journal of Pediatrics. 2005 Jul;72(7):579-81. Bovine colostrum can be obtained in large quantity and has properties similar to human colostrum. It has been used for various disorders of the body. It has properties to stimulate immune system, contains growth factors and many bioactive substances needed for the body to combat with wear and tear. Bovine colostrum has been used for various gastrointestinal disorders, respiratory tract infection, rheumatoid arthritis, healing injured tissues of body etc.

Solomons NW. Modulation of the immune system and the response against pathogens with bovine colostrum concentrates. European Journal of Clinical Nutrition 2002;56(Suppl.3):524-528. The ability of colostrum to protect infants against pathogens, specifically those which cause gastroenteritis and severe diarrhea, makes it an ideal, cheap, safe and effective means of protecting children in those parts of the world where medical assistance is lacking or substandard and could save thousands of lives each year.

Hagiwara K, et al. Oral administration of IL-1 beta enhanced the proliferation of lymphocytes and the O(2)(-)(-) production of neutrophil in newborn calf. Veterinary Immunology and Immunopathology 2001;81(1-2):59-69. Interleukin-1ß in colostrum stimulates the immune system by increasing the amount of peripheral white blood cells, especially monocytes.

van Hooijdonk AC, Kussendrager KD, Steijns JM. In vivo antimicrobial and antiviral activity of components in bovine milk and colostrum involved in non-specific defense. British Journal of Nutrition 2000;84(Suppl.1):S127-S134. Lactoferrin and lactoperoxidase, both present in colostrum in large amounts, provide non-specific defense against a broad spectrum of pathogens, including bacteria and viruses. This is significant both for the protection of commercially important animals as well as humans.


of natural killer cells, but the production of IL-2 reverses this effect. This is thought to be another way that colostrum modulates the immune system response.


Ebina T, et al. Passive immunizations of suckling mice and infants with bovine colostrum containing antibodies to human rotavirus. Journal of Medical Virology 1992;38:117-123. Study confirmed that oral immunization via colostrum or milk against rotavirus was possible, safe and effective.

Stephan W, et al. Antibodies from colostrum in oral immunotherapy. Journal of Clinical Chemistry and Clinical Biochemistry 1990;28:19-23. An immunoglobulin preparation from pooled bovine colostrum was found to be very effective in treating severe diarrhea, such as often found in AIDS patients.


Staroscik K, et al. Immunologically active nonapeptide fragment of a proline-rich polypeptide from bovine colostrum: amino acid sequence and immunoregulatory properties. Molecular Immunology 1983;20(12):1277-1282. Chain has the same ability to regulate the activity of the immune system as the hormones of the thymus gland; it activates an underactive immune system. PRP also suppresses an overactive immune system, such is often seen in autoimmune diseases. PRP is highly anti-inflammatory and appears to act on T-cell precursors to produce helper T-cells and suppressor T-cells.

Ogra PL, et al. Colostrum-derived immunity and maternal-neonatal interaction. Annals of the New York Academy of Sciences 1983;409:82-95. Peyer's patches are found throughout the intestinal tract, and groups of similar immunoactive cells are found in the bronchial mucosa. Both the intestinal and bronchial immunoactive cell groups respond to allergens, antigens and pathogens by neutralizing or destroying them. In newborns, these special cell groups are not immediately operative but protection is provided by a variety of immune factors from the mother's colostrum. Antibodies found in colostrum protect against Eschericia coli, Salmonella, Shigella, Vibrio cholera, Bacteriodes fragilis, Streptococcus pneumoniae, Bordtella pertussis, Clostridium diphtheria, Clostridium tetani, Streptococcus mutans and Candida albicans.
Hanson LA, Ahlstedt S, Andersson B, et al. Mucosal Immunity. Annals New York Academy of Sciences 1983;83:1-20. Oligosaccharides present in human milk seem to specifically prevent pneumococcal attachment to retropharyngeal cells. This anti-attachment capacity, in addition to that provided by milk and salivary IgA antibodies, may explain why breast-fed babies have less otitis media than formula-fed ones.


Swarbrick ET. The Handling of Ingested Antigens. In: The Immunology of Infant Feeding, 1981, Plenum Press, NY, Wilkinson AW, ed., pp. 13-20. During the first 24-36 hours after birth, a newborn's bowel wall has a large number of open pores through which large the immunoactive molecules found in colostrum can enter the body.


Sandholm M, Hankanen-Buzalski T. Colostral trypsin-inhibitor capacity in different animal species. Acta Vet Scand 1979;20(4):469-476. Bovine colostrum was found to contain a powerful trypsin-inhibitor which protects colostrum immunoglobulins from digestion. Demonstrated that colostrum from cows richer in immune factors and inhibitor than colostrum from humans.

Pineiro A, et al. Trypsin inhibitor from cow colostrum., Isolation, electrophoretic characterization and immunologic properties. Biochem Biophys Acta 1975;379(1): 201-206. Absence of crossed reactivity was observed between bovine colostral trypsin inhibitor and trypsin inhibitors of bovine serum. This strongly suggests the high specificity of this inhibitor as a colostral and milk constituent.


Sabin AB. Antipoliomyelitic substance in milk from human beings and certain cows. Journal of Diseases of Children 1950;80:866-870. Seminal study by Dr. Albert Sabin, inventor of the oral polio vaccine, in which he discovered antibodies against the polio virus in colostrum.
Bacterial Infections

Sponseller JK, et al. Hyperimmune bovine colostrum as a novel therapy to combat Clostridium difficile infection. *Journal of Infectious Diseases*. 2015 Apr 15;211(8):1334-41. Nonimmune colostrum-treated piglets developed moderate to severe diarrhea and colitis. In contrast, (HBC) hyperimmune bovine colostrum-treated piglets had mild or no diarrhea and mild or no colitis. HBC provides an oral, cost-effective, and safe alternative to antibiotic therapy for clostridium difficile. By preserving intestinal microbiota, HBC may be more efficacious than antibiotics.

Champagne CP, et al. Effect of bovine colostrum, cheese whey, and spray-dried porcine plasma on the in vitro growth of probiotic bacteria and *Escherichia coli*. *Canadian Journal of Microbiology*. 2014 May;60(5):287-95. In vitro data suggest that colostrum could be considered as supplements to animal feeds to improve intestinal health because of their potential to promote growth of probiotic bacteria and to inhibit growth of pathogenic bacteria such as *E. coli*.

Steele J, et al. Hyperimmune bovine colostrum for treatment of GI infections: A review and update on Clostridium difficile. *Hum Vaccin Immunother*. 2013;22;9(7). Hyperimmune bovine colostrum was efficacious in the treatment of *C. difficile* infection in the gnotobiotic piglet model, and may provide an effective treatment alternative to antibiotics, which can spare the normal gut microflora, and reduce rates of recurrence and antibiotic resistance.

Rabinovitz BC, et al. Vaccination of pregnant cows with EspA, EspB, γ-intimin, and Shiga toxin 2 proteins from *Escherichia coli* O157:H7 induces high levels of specific colostral antibodies that are transferred to newborn calves. *Journal of Dairy Science* 2012;95(6):3318-26. Bovine colostrum with increased levels of antibodies against EHEC O157:H7 may be obtained by systemic immunization of pregnant cows, and that these specific antibodies are efficiently transferred to newborn calves by feeding colostrum. Hyperimmune colostrum and milk may be an alternative to protect calves from early colonization by EHEC O157:H7 and a possible key source of antibodies to block colonization and toxic activity of this bacterium.

Otto W, et al. Randomized control trials using a tablet formulation of hyperimmune bovine colostrum to prevent diarrhea caused by enterotoxigenic *Escherichia coli* in volunteers. *Scandinavian Journal of Gastroenterology* 2011;46(7-8):862-8. Administration of a tablet formulation of hyperimmune bovine colostrum containing antibodies against ETEC strains may reduce the risk of travelers' diarrhea. Active tablet formulations were significantly more effective than placebo in protecting volunteers against the development of diarrhea caused by ETEC. **FULL TEXT**.

Møller HK, et al. Bovine colostrum is superior to enriched formulas in stimulating intestinal function and necrotising enterocolitis resistance in preterm pigs. *British Journal of Nutrition* 2011;105(1):44-53. Modulation of bacteria-stimulated murine bone marrow-derived dendritic cells (DC) cytokine response by bovine colostrum whey in vitro may be due to a synergistic action of various milk bioactives, and it may explain its beneficial effects on necrotising enterocolitis development and intestinal function in a piglet model of preterm infants.
Gao W, et al. **Specific IgG activity against diarrheagenic bacteria in bovine immune milk and effect of pH on its antigen-binding activity upon heating.** *Journal of Dairy Research* 2010;77(2):220-4. The specific IgG from milk antibodies of immunized lactating cows may be used as an abundant source of hyper-immune products for prevention of multibacteria-induced diarrhea, however, the effect of pH on its antigen-binding activity upon heating should be carefully considered and designed.

Rawal P, et al. **Role of colostrum in gastrointestinal infections.** *Indian Journal of Pediatrics* 2008;75(9):917-21. Colostrum has been found to be effective in infantile hemorrhagic diarehas, other diarehas and reduces the likelihood of disease progressing to hemolytic uremic syndrome. It has also been tested in H. pylori infection and diarrhea in immunodeficiency.

Huang XH, et al. **Specific IgG activity of bovine immune milk against diarrhea bacteria and its protective effects on pathogen-infected intestinal damages.** *Vaccine* 2008;26(47):5973-80. The specific IgG from milk antibodies of immunized lactating bovine prevented pathogen-infected intestinal damages, and potently inhibited pathogen-induced diarrhea in a study of 17 strains of pathogenic diarrhea bacteria.

Vilte DA, et al. **Bovine colostrum contains immunoglobulin G antibodies against intimin, EspA, and EspB and inhibits hemolytic activity mediated by the type three secretion system of attaching and effacing Escherichia coli.** *Clinical and Vaccine Immunology* 2008;15(8):1208-13. Early colostrum from cows contains antibodies, lactoferrin, and other unidentified substances that impair type three secretion system (TTSS) function in attaching and effacing E. coli strains. Bovine colostrum might act by reducing Enterohemorrhagic Escherichia coli (EHEC) colonization in newborn calves and could be used as a prophylactic measure to protect non-brest-fed children against EHEC infection in an area of endemcity. FULL TEXT.

Hammarstrom L, Weiner CK. **Targeted antibodies in dairy-based products.** *Advances in Experimental Medicine and Biology* 2008;606:321-43. Bovine colostrum-based immune milk products have proven efficacy in prophylaxis and treatment against various infectious diseases in humans such as diarrheal diseases caused by various pathogens like E. coli and rotavirus.

Rokka S, et al. **Effect of specific colostral antibodies and selected lactobacilli on the adhesion of Helicobacter pylori on AGS cells and the Helicobacter-induced IL-8 production.** *Scandinavian Journal of Immunology* 2008;68(3):280-6. Suppression of IL-8 production by lactic acid bacteria or colostral products could have a suppressive effect on inflammation in Helicobacter infection, the most common causes of gastritis, gastric ulcer and adenocarcinoma.

Biswa P, et al. **Immunomodulatory effects of bovine colostrum in human peripheral blood mononuclear cells.** *New Microbiology* 2007;30(4):447-54. The Th1-promoting activity of bovine colostrum (induced by IL-12) could contribute, together with the antibodies, to the protective effect of bovine colostrum on the offspring. Bovine colostrum could also represent an inexpensive therapeutic tool in prevention and treatment of several human microbial infections, including influenza. FULL TEXT.

Akisu C, et al. **Effect of human milk and colostrum on Entamoeba histolytica.** World Journal of Gastroenterology 2004;10(5):741-742. Colostrum was found to provide protection against Entamoeba histolytica, the cause of amoebiasis, a serious, chronic illness characterized by dysentery, gastrointestinal ulceration and abscess formation and intestinal blockage in infants particularly.


Casswall TH, et al. **Bovine anti-Helicobacter pylori antibodies for oral immunotherapy.** Scandinavian Journal of Gastroenterology 2002;37(12):1380-1385. Bovine colostrum with high titers against H. pylori was given to H. pylori infected mice. Comparison of treated mice with control mice showed a 50-66% cure rate for H. pylori infection in treated mice. Binding studies also showed that the colostrum prevented binding of the H. pylori.


Seifert J, et al. **Endotoxin inactivation by enterally applied colostrum of different composition.** Eur Surg Res. 2002;34(1-2):68-72. Not only gammaglobulin but especially lactoferrin seems to be responsible for the elimination of endotoxin with regard to enterally applied colostrum preparations.


Lilius EM, Marnila P. **The role of colostral antibodies in prevention of microbial infections.** Current Opinion in Infectious Diseases 2001;14(3): 295-300. Colostrum offers passive protection against a variety of microbial pathogens in the form of specific immunoglobulin A, G and M antibodies. It is especially effective in the prevention of various gastroenteric infections.

Graczyk TK, et al. **Successful hyperimmune bovine colostrum treatment of Savanna monitors (Varanus exanthematicus) infected with Cryptosporidium sp.** J Parasitol. 2000;86(3):631-2. Hyperimmune bovine colostrum therapy was efficacious in V. exanthematicus and is recommended for lizards with gastric cryptosporidiosis.
Korhonen H, et al. Milk immunoglobulins and complement factors. *British Journal of Nutrition* 2000;84(Suppl.1):S75-S80. Bovine colostrum contains three main classes of immunoglobulin IgG (IgG1 75% and IgG2), IgM and IgA, plus hemolytic and bactericidal complement. Complement is a complex group of proteins which act in concert with antibodies to inactivate and/or kill pathogens.

Gopal PK, Gill HS. Oligosaccharides and glycoconjugates in bovine milk and colostrum. *British Journal of Nutrition* 2000;84(Suppl.1):S69-S74. Another way colostrum helps protect against infections is through the oligosaccharides and glycoconjugates it contains. These are complex sugars which compete for binding sites in the GI tract with pathogens.

van Hooijdonk AC, Kussendrager KD, Steijns JM. In vivo antimicrobial and antiviral activity of components in bovine milk and colostrum involved in non-specific defence. *Br J Nutr.* 2000;84 Suppl 1:S127-34. Lactoferrin and lactoperoxidase, both present in colostrum in large amounts, provide non-specific defense against a broad spectrum of pathogens, including bacteria and viruses. This is significant both for the protection of commercially important animals as well as humans.

Wada T, et al. The therapeutic effect of bovine lactoferrin in the host infected with Helicobacter pylori. *Scandinavian Journal of Gastroenterology* 1999;34(3):238-243. Mice infected with *H. pylori* were given a daily dose of bovine lactoferrin for 2-4 weeks. Their intestines were then examined for bacterial content. Numbers of *H. pylori* were reduced to 10% of pre-lactoferrin levels and greatly decreased the numbers of *H. pylori* bound to the intestinal wall. Serum antibody titer to *H. pylori* were reduced to practically zero, indicating that the immune response of the host was no longer recognizing *H. pylori* infection. Therefore it was deduced that lactoferrin has a direct antibacterial effect on *H. pylori* infection and prevents binding of the pathogen to the intestinal lining.


Bitzan MM, et al. Inhibition of Helicobacter pylori and Helicobacter mustelae binding to lipid receptors by bovine colostrum. *The Journal of Infectious Diseases* 1998;177:955-961. *H. pylori* and *H. mustelae* (a gastric pathogen of ferrets) are both bound by lipid receptors (phosphatidylethanolamine, gangliotetraosylceramide and gangliotriaosyl-ceramide) in the gut, allowing them to carry out their pathogenic activities. Bovine colostrum, however, was shown to prevent binding of the pathogens to these lipid receptors even though there was no detectable anti-*H. pylori* antibody activity in the colostrum.

Korhonen H. **Bactericidal effect of bovine normal and immune serum, colostrum and milk against Helicobacter pylori.** *Journal of Applied Bacteriology* 1995;78:655-662. Helicobacter pylori is a major cause of gastritis and ulcers in humans. Serum and colostrum from non-immunized Friesian cows were found to be highly bactericidal against H. pylori. Post-colostral milk did not show any bactericidal effect against H. pylori.

Watzl B, et al. **Enhancement of resistance to Cryptosporidium parvum by pooled bovine colostrum during murine retroviral infection.** *Am. T. Trop. Med. Hyg.* 1993;48(4):519-523. Parasite colonization of intestinal villi was significantly reduced in immunosuppressed mice that received dietary supplemental pooled bovine colostrum compared with those that did not receive colostrum treatment. Since the nonimmune bovine colostrum contained no anti-Cryptosporidium antibodies, this suggests that passively transferred antibodies alone are unlikely to have provided the improved resistance.


Doyle PS. **Anti-Cryptosporidium parvum antibodies inhibit infectivity in vitro and in vivo.** *Infection and Immunity* 1993;61(10):4079-4084. Hyperimmune bovine colostral immunoglobulin inhibits C. parvum infectivity in a reproducible in vitro assay, and this inhibition was correlated with the protective capacity of the bovine colostrum in vivo.


Flanigan T, et al. **In vitro screening of therapeutic agents against Cryptosporidium: hyperimmune cow colostrum is highly inhibitory.** *J Protozool.* 1991;38(6):225S-227S. Hyperimmune bovine colostrum was highly inhibitory of Cryptosporidium infection in vitro and its soluble fraction remained significantly inhibitory while the soluble fraction of conventional colostrum did not.

Ellison RT III, Giehl TJ. **Killing of gram-negative bacteria by lactoferrin and lysozyme.** *Journal of Clinical Investigation* 1991;88(4):1080-1091. Lactoferrin and lysozyme act together to kill gram-negative bacteria, such as Vibrio cholerae (cholera), Salmonella typhimurium (food poisoning) and Eschericia coli. The lactoferrin attaches to and destroys the cell wall of the bacteria, allowing the lysozyme to enter and lyse (burst) the organisms.

Ushijima H, Dairaku M, Mukoyama A. [**Bacteriostatic activity of bovine colostrum**]. *Kansenshogaku Zasshi.* 1991;65(1):54-60. Lactoferrin and lactoferrin Fe were useful for the bacteriostatic reaction.

Stephan W, Dichtelmuller H, Lissner R. **Antibodies from colostrum in oral immunotherapy.** *J Clin Chem Clin Biochem.* 1990;28(1):19-23. An immunoglobulin preparation for oral use was prepared from pooled bovine colostrum from more than 100 animals. The preparation has high antibacterial antibody titres, and a high capacity for the neutralization of bacterial toxins. It is well tolerated and highly effective in the treatment of severe diarrhoea. The preparation is spray-dried and stable at 2-8 degrees C.
Heaton P. Cryptosporidiosis and acute leukemia. Arch Dis Child 1990;65(7):813-814. Paper presented at 6th annual Asian Pediatric Conference. Treatment of 3 year old with acute cryptosporidia caused diarrhea. Bovine colostrum 100 ml 3 x daily in form of milkshake. Within two weeks symptoms alleviated. Cryptosporidia tests negative. Bovine colostrum is a very rich source of immunoglobulins. Pooled colostrum from nonimmunized cows provides an effective method of controlling symptoms in immunodeficient patients. Immunoglobulin concentrated may provide an effective, convenient method by which immunology can be administered.

Fayer R, Perryman LE, Riggs MW. Hyperimmune bovine colostrum neutralizes Cryptosporidium sporozoites and protects mice against oocyst challenge. J Parasitol. 1989;75(1):151-3. Activity of colostral whey (produced by a cow immunized with oocysts of Cryptosporidium parvum and found to provide prophylaxis against cryptosporidiosis in calves) was given to mice who subsequently had fewer C. parvum.


Tzipori S, Roberton D, Chapman C. Remission of diarrhoea due to cryptosporidiosis in an immunodeficient child treated with hyperimmune bovine colostrum. Br Med J (Clin Res Ed). 1986;293(6557):1276-7. Infusion of hyperimmune bovine colostrum produced against parasite antigen, given by nasogastric tube, was started after symptoms had persisted for three weeks in 3 year old male. Vomiting and diarrhoea resolved within five days of treatment, and oocysts were no longer seen in the stools after eight days. Hyperimmune bovine colostrum may be useful in the treatment of many patients with immunodeficiency disorders.


Ogra PL, et al. **Colostrum derived immunity and maternal neonatal interaction**, *Annals of the New York Academy of Sciences* 1983;409: 82-92. Peyer's patches are found throughout the intestinal tract, and groups of similar immunoactive cells are found in the bronchial mucosa. Both the intestinal and bronchial immunoactive cell groups respond to allergens, antigens and pathogens by neutralizing or destroying them. In newborns, these special cell groups are not immediately operative but protection is provided by a variety of immune factors from the mother's colostrum. Antibodies found in colostrum protect against Eschericia coli, Salmonella, Shigella, Vibrio cholera, Bacteriodes fragilis, Streptococcus pneumoniae, Bordetella pertussis, Clostridium diphtheria, Clostridium tetani, Streptococcus mutans and Candida albicans.


Morris JA, et al. **Passive protection of lambs against enteropathogenic Escherichia coli: Role of antibodies in serum and colostrum of dams vaccinated with K99 antigen**, *J. Med. Microbiol*. 1980; 13(2):263-71. Mother sheep and cows given doses of E. coli orally developed antibodies for E. coli in their colostrum. When nursing offspring were then dosed with E. coli, immune factors from the mothers’ colostrum prevented the E. coli from attaching to the bowel wall and protection resulted.

Wada N, et al. **Neutralizing activity against Clostridium difficile toxins in the supernatants of cultured colostral cells**, *Infect. Immun*. 1980; 29(2):545-50. Aqueous phase of colostrum had a neutralizing effect against C. difficile toxin. Neutralizing activity against the toxin found in five supernatants of cultured colostral cells was completely abolished only by anti-human IgA antibody as assessed by immune precipitation.


Michalek SM, McGhee JR. **Effective immunity to dental caries: passive transfer to rats to antibodies to streptococcus mutans elicits protection**, *Infection and Immunity*. 1977;17:644-650. The presence of specific salivary immunoglobulin A antibodies in gnotobiotic rats correlated with a reduction in the level of plaque, numbers of viable S. mutans in plaque, and levels of S. mutans-induced dental caries. This paper discusses the importance of antigen dosage for induction of a secretory immune response that is protective against S. mutans-induced dental caries.


**Viral Infections**


van Hooijdonk AC, Kussendrager KD, Steijns JM. In vivo antimicrobial and antiviral activity of components in bovine milk and colostrum involved in non-specific defence. *Br J Nutr.* 2000;84 Suppl 1:S127-34. Lactoferrin and lactoperoxidase, both present in colostrum in large amounts, provide non-specific defense against a broad spectrum of pathogens, including bacteria and viruses. This is significant both for the protection of commercially important animals as well as humans.


Riddell SR, et al. Restoration of viral immunity in immunodeficient humans by the adoptive transfer of T cell clones. *Science* 1992;257(5067):238-41. The adoptive transfer of antigen-specific T cells to establish immunity is an effective therapy for viral infections and tumors in animal models. The application of this approach to human disease would require the isolation and in vitro expansion of human antigen-specific T cells and evidence that such T cells persist and function in vivo after transfer.

Ushijima H, et al.[Immunoglobulin components and anti-viral activities in bovine colostrum]. *Kansenshogaku Zasshi.* 1990;64(3):274-9. Lactoferrin and lactoferrin Fe were useful for the bacteriostatic reaction.

**Rotavirus**

Farthing MJ. *Treatment of gastrointestinal viruses*. *Novartis Found Symp*. 2001;238:289-300; discussion 300-5. Anti-diarrheal treatments, such as hyperimmune bovine colostrum, probiotics and antiviral agents are largely experimental and have not been introduced into routine clinical practice.


Superti F, et al. **Antirotaviral activity of milk proteins: lactoferrin prevents rotavirus infection in the enterocyte-like cell line HT-29.** *Medical Microbiology and Immunology (Berlin)* 1997;186(2-3):83-91. Beta-lactoglobulin, apo- and iron-saturated lactoferrin inhibit rotaviral infection in a dose-dependent manner. Apo-lactoferrin prevents both rotavirus hemagglutination and viral binding to susceptible cells. It also markedly inhibits rotavirus antigen synthesis when added during the virus adsorption step.

Mitra AK, et al. **Hyperimmune cow colostrum reduces diarrhoea due to rotavirus:** a double-blind, controlled clinical trial. *Acta Paediatr*. 1995;84(9):996-1001. Colostrum from cows immunized with rotavirus antigen is clinically effective in reducing the duration and severity of childhood diarrhoea due to rotavirus.


Davidson G, et al. **Passive immunisation of children with bovine colostrum containing antibodies to human rotavirus.** *Lancet* 1989;2(8665):709-12. In a 10-day controlled study, children fed bovine colostrum did not get rotavirus while 13.8% of those who were fed an artificial infant formula acquired the virus.

Brüssow H, et al. **Bovine milk immunoglobulins for passive immunity to infantile rotavirus gastroenteritis.** *Journal of Clinical Microbiology* 1987;25(6):982-986. Protection against rotavirus, a dangerous pathogen which can cause serious, even fatal diarrhea in infants, can be passed orally through milk or colostrum safely and effectively.

Yolken RH, et al. **Antibody to human rotavirus in cow's milk.** *The New England Journal of Medicine* 1985;312(10):605-610. Raw and pasteurized milk contained detectable levels of IgG1 antibody directed at rotavirus. Commercially available infant formulas had little or no anti-rotavirus antibody activity. The alteration of milk-processing procedures or the addition of effective antibodies to milk preparations commonly used in the nutrition of young children may alter the clinical course of rotavirus infection or decrease the transmission of rotavirus throughout susceptible populations.
Ebina T, et al. **Prevention of rotavirus infection by cow colostrum antibody against human rotavirus.** *Lancet.* 1983;29:1029-1030. Cattle were exposed to oral doses of rotavirus; colostrum from these cows contained antibodies which, when fed to humans, prevented them from getting rotavirus.

Askaa J, et al. **Rotavirus associated diarrhoea in nursing piglets and detection of antibody against rotavirus in colostrum, milk and serum.** *Nord Vet Med.* 1983;35(12):441-7. Antibody content in porcine milk samples showed a rapid decline during the first few days of the lactation periods. Rotavirus was excreted in periods ranging from 4 to 9 days.


**Influenza**

Wong EB, et al. **Bovine colostrum enhances natural killer cell activity and immune response in a mouse model of influenza infection and mediates intestinal immunity through toll-like receptors 2 and 4.** *Nutrition Research.* 2014 Apr;34(4):318-25. Colostrum-supplemented mice demonstrated less reduction in body weight after influenza infection, indicating a less severe infection, increased NK cell cytotoxicity, and less virus burden in the lungs compared with controls. Colostrum supplementation enhanced NK cell cytotoxicity and improved the immune response to primary influenza virus infection in mice.

Uchida K, et al. **Augmentation of cellular immunity and protection against influenza virus infection by bovine late colostrum in mice.** *Nutrition* 2012;28(4):442-6. Oral administration of skimmed and concentrated bovine late colostrum activates not only systemic cellular immunity but also local cellular immunity, such as in the respiratory tract, and that activation of cellular immunity is one of the mechanisms of amelioration of influenza virus infection.

Belcaro G, et al. **Prevention of flu episodes with colostrum and Bifivir compared with vaccination: an epidemiological, registry study.** *Panminerva Med.* 2010;52(4):269-75. The number of influenza episodes registered with the immunomodulators was significantly lower than those observed in patients using vaccination or no prevention. The number of days of disease was higher in untreated controls compared to the groups treated with immunomodulators and 2 times higher in the vaccination group compared to the same groups.

Ng WC, et al. **Prevention and treatment of influenza with hyperimmune bovine colostrum antibody.** *PLoS One* 2010;5(10):e13622. Bovine colostrum, containing approximately 500 g of IgG per milking per animal was investigated as a source of polyclonal antibody for delivery to the respiratory tract. Passive transfer of specific antibody may provide a useful means of preventing or treating influenza A/Puerto Rico/8/34.

Alisky, J. **Bovine and human-derived passive immunization could help slow a future avian influenza pandemic.** *Med. Hypotheses* 2009;72, 74–75. It is theoretically possible to quickly create and distribute large quantities of milk-based and serum-based passive immune globulin active against the strains of avian influenza present in a particular geographic area.
Cesarone MR, et al. **Prevention of influenza episodes with colostrum compared with vaccination in healthy and high-risk cardiovascular subjects: the epidemiologic study in San Valentino.** *Clin Appl Thromb Hemost.* 2007;13(2):130-6. The incidence of complications and hospital admission from influenza was higher in the group that received only a vaccination compared with the colostrum groups. Colostrum, both in healthy subjects and high-risk cardiovascular patients, is at least 3 times more effective than vaccination to prevent flu and is very cost-effective.

Kawasaki Y, et al. **Inhibition by kappa-casein glycomacropeptide and lactoferrin of influenza virus hemagglutination.** *Bioscience, Biotechnology, and Biochemistry* 1993;57(7):1214-1215. Lactoferrin inhibits the hemagglutination (clumping of blood cells) of the influenza virus. Hemagglutination inhibition is one of the tests which show the effectiveness of influenza vaccines.


**Poliovirus**

Sabin A, Fieldsteel AH. **Antipoliomyelitic activity of human and bovine colostrum and milk.** *Pediatrics* 1962; 29:105 -115. Dr. Albert Sabin isolated antipolio antibodies in bovine colostrum and a successful vaccine prepared.

Sabin, AB. **Anti-poliomyelitic substance in milk from human beings and certain cows.** *AMA Am J Dis Child.* 1950;80(5):866-7. Seminal study by Dr. Albert Sabin, inventor of the oral polio vaccine, in which he discovered antibodies against the polio virus in colostrum.

**Hepatitis**

Hara K, et al. **Lactoferrin inhibits hepatitis B virus infection in cultured human hepatocytes.** *Hepatology Research* 2002;24(3):228. Bovine lactoferrin prevents infection of cultured human liver cells with hepatitis B virus, while transferrin, casein and lactalbumin have no effect.


**Herpes**

Andersen JH, et al. Lactoferrin and lactoferricin inhibit Herpes simplex 1 and 2 infection and exhibit synergy when combined with acyclovir. *Antiviral Research* 2003;58(3):209-215. When used against HSV-1 and -2, the combination of lactoferrin or its peptide lactoferricin with acyclovir demonstrated good synergy. The effective dosage of both lactoferrin and acyclovir could be reduced 2-7 times.

Isaacs CE, et al. Reporting in Experimental Biology. *Science* 1995;231. Teams confirm colostrum delivers not just antibodies but a battery of infection fighting agents. Among them, retinoic acids, a vitamin A derivative. Retinoic acids conferred protection and reduced colonization if herpes-infected culture cells. Although not a cure, retinoic acids effectively reduced the herpes virus to levels where the body’s immune system could fight off an outbreak.

Raloff. More Ways Mother’s Milk Fights Disease. *Science News* 1995;147:231. Mother’s milk contains retinoic acid which helps baby fight herpes virus. The glycoprotein kappa casein protects against bacteria that causes stomach ulcers. Retinoic acid and kappa casein are also found in colostrum.


Kohl S, et al. Human colostral cytotoxicity: I. Antibody-dependent cellular cytotoxicity against Herpes simplex viral-infected cells mediated by colostral cells. *Journal of Clinical Laboratory Immunology* 1978;1(3):221-4. Colostral cells along with antibody were found to destroy herpes simplex-infected cells.


**HIV/AIDS**

Winnall WR, et al. The maturation of antibody technology for the HIV epidemic. *Immunology & Cell Biology.* 2014 Aug;92(7):570-7. Novel antibody production techniques have also been designed, allowing antibodies to be obtained from non-mammalian cells, bovine colostrum and the periplasm and cytoplasm of bacteria. These advances may allow large-scale production of HIV antibodies that are capable of protecting against HIV infection or serving as therapeutics that reduce the need for life-long antiretroviral treatment.
Kramski M, et al. **Anti-HIV-1 antibody-dependent cellular cytotoxicity mediated by hyperimmune bovine colostrum IgG.** *European Journal of Immunology* 2012;42(10):2771-81. HIV-specific IgG can be easily and inexpensively produced in large quantities using bovine colostrum. Antibody-dependent killing was observed in the presence of anti-HIV-1 colostrum IgG but not nonimmune colostrum IgG. Bovine anti-HIV colostrum IgG has robust HIV-1-specific antibody-dependent cellular cytotoxicity activity and therefore offers a useful source of antibodies able to provide a rapid and potent response against HIV-1 infection.

Kramski M, et al. **Hyperimmune bovine colostrum as a low-cost, large-scale source of antibodies with broad neutralizing activity for HIV-1 envelope with potential use in microbicides.** *Antimicrobial Agents and Chemotherapy* 2012;56(8):4310-9. Bovine colostrum-derived anti-HIV antibodies could be an option for preparing the substantial quantities of broadly neutralizing antibodies that would be needed in a low-cost topical combination HIV-1 microbicide. FULL TEXT.


Florén CH, et al. **ColoPlus, a new product based on bovine colostrum, alleviates HIV-associated diarrhea.** *Scand J Gastroenterol.* 2006;41(6):682-6. Patients with HIV-associated diarrhea experienced decrease in stool evacuations per day from 7.0+/-.2.7 to 1.3+/-.0.5, a substantial decrease in self-estimated fatigue of 81%, an increase in body-weight of 7.3 kg per patient and an increase in CD4+ count by 125% after taking a bovine colostrum supplement for four weeks.


Viani RM, et al. **Lactoferrin inhibits HIV-1 replication in vitro and exhibits synergy when combined with zidovudine.** *AIDS* 1999;13(10):1273-4. Human and bovine lactoferrin have anti-HIV-1 activity; when combined with zidovudine, they demonstrate synergism against SI and NSI HIV-1 clinical isolates, and may prove useful in decreasing the perinatal transmission of HIV-1.

Droge W, Holm E. **Role of cysteine and glutathione in HIV infection and other diseases associated with muscle wasting and immunological dysfunction.** *FASEB J* 1997;11(13):1077-1089. Abnormally low plasma cystine and glutamine levels, low natural killer cell activity, skeletal muscle wasting or muscle fatigue, and increased rates of urea production defines a complex of abnormalities that is tentatively called "low CG syndrome." And symptoms are seen in patients with HIV infection, cancer, major injuries, sepsis, Crohn's disease, ulcerative colitis, chronic fatigue syndrome, and to some extent in overtrained athletes. Cysteine supplementation may be a useful therapy if combined with disease-specific treatments. Cysteine is a precursor to glutathione, an important anti-oxidant in colostrum.
Greenberg PD, Cello JP. **Treatment of severe diarrhea caused by Cryptosporidium parvum with oral bovine immunoglobulin concentrate in patients with AIDS.** *J Acquir Immune Defic Syndr Hum Retrovirol.* 1996;13(4):348-54. Study which looked at the treatment of cryptosporidiosis diarrhea in AIDS patients with an immunoglobulin concentrate from bovine colostrum. Best results were found using a powdered form of the concentrate rather than in capsules.

Harmsen MC, et al. **Antiviral effects of plasma and milk proteins: lactoferrin shows potent activity against both human immunodeficiency virus and human cytomegalovirus replication in vitro.** *Journal of Infectious Diseases* 1995;172:380-8. Lactoferrin likely exerts its effect at the level of virus adsorption or penetration (or both), because after human cytomegalovirus penetrated fibroblasts, the ongoing infection could not be further inhibited.

Nowak MA, McMichael AJ. **How HIV defeats the immune system.** *Scientific American* 1995;273(2):58-65. Traditional disease fighting methods such as vaccines are not effective in fighting HIV. Viral load should be lessened so the immune system can do its job.

Richie DJ, Becker ES. **Update on the management of intestinal cryptosporidiosis in AIDS.** *Ann.Pharmacother* 1994;28:767-778. Despite the availability of some evolving and potentially promising treatment modalities, including hyperimmune bovine colostrum, further controlled clinical trials are necessary to evaluate the role of pharmacotherapy for intestinal cryptosporidiosis in patients with AIDS.

Anderson I. **Powdered milk cure for fatal diarrhoea.** *New Scientist* January 6, 1994. HIV patients receiving IGF-1 were less likely to develop full-blown AIDS than patients receiving other treatments.


Shield J, et al. **Bovine colostrum immunoglobulin concentrate for cryptosporidiosis in AIDS.** *Arch Dis Child.* 1993;69(4):451-3. Lactobin®, a commercial hyperimmune bovine colostrum with potent anticytosteporidial activity, was administered to a 4 year old child with AIDS and severe diarrhoea associated with cryptosporidiosis. There was significant clinical improvement in the diarrhoea and permanent elimination of the parasite from the gut.

Lim SG, et al. **Intestinal permeability and function in patients infected with human immunodeficiency virus. A comparison with coeliac disease.** *Scand J Gastroenterol.* 1993;28(7):573-80. Abnormal permeability and reduced intestinal absorption capacity are common in HIV patients, occur at all stages of HIV disease, especially in the presence of diarrhoea, and, with the exception of lactulose permeation, are relatively similar to the alterations seen in coeliac disease.

Rump JA, et al. Treatment of diarrhoea in human immunodeficiency virus-infected patients with immunoglobulins from bovine colostrum. Clin Invest. 1992;70(7):588-594. Immunoglobulins from bovine colostrum were very effective in treating chronic diarrhea in AIDS patients from a variety of causes. Colostral immunoglobulins are highly resistant to digestion in the gastrointestinal tract.


Ungar BL, et al. Cessation of Cryptosporidium-associated diarrhea in an acquired immunodeficiency syndrome patient after treatment with hyperimmune bovine colostrum. Gastroenterology 1990;98(2):486-9. Case study of patient receiving bovine colostrum hyperimmune to Cryptosporidium by direct duodenal infusion. In the 48 hours after treatment, stools were formed and oocysts to Cryptosporidium were absent. The patient remained asymptomatic for 3 months.

Keech A, et al. Peptide immunotherapy: a new direction in HIV/AIDS treatment. (Unpublished Research). Results of the studies showed increases in CD4+ T-cell counts to normal or near normal levels, reduction in viral loads, and the remission of HIV/AIDS related physical symptoms in most patients with days, reduction of clinical symptoms, as well as significant weight gains, within six to twelve weeks of treatment. This suggests that PRP spray may prove to be a useful, low cost, easy to use, and side effect-free adjunt therapy in the treatment of HIV/AIDS. PRPs are shown to be increasingly popular and well tolerated immune and cytokine modulators for both immune suppressed and autoimmune conditions.

Autoimmune Disorders


Feldmann M, et al. Cytokines in autoimmune disorders. International Review of Immunology 1998;17(1-4)217-228. Cytokines are important protein mediators of immunity, inflammation, cell proliferation, differentiation, fibrosis, and so forth, in other words, all the major biological processes which underlie autoimmune disorders. Modulating the effects of these cytokines, particularly TNF-α, can result in amelioration of the symptoms of the disorders.
Katz KD, Hollander D. **Intestinal mucosal permeability and rheumatological diseases.** *Baillere's Clinical Rheumatology* 1989;3(2):271-284. The inability of the intestinal lining to control the influx of antigens into the blood due to leaky gut or a dysfunctional immune system may represent the prime means by which the antigens which cause numerous diseases, including autoimmune diseases. Leaky gut has been linked to patients with ankylosing spondylitis, rheumatoid arthritis, Crohn's disease, and celiac sprue (a genetic autoimmune disease characterized by damage to the small intestine due to eating wheat gluten).

**Arthritis**

De Keyser F, et al. **Gut inflammation and spondyloarthropathies.** *Current Rheumatology Reports* 2002;4(6):525-532. Spondyloarthropathies (SpA) are a related group of arthritic conditions which include ankylosing spondylitis, reactive arthritis, psoriatic arthritis and arthritis associated with inflammatory bowel disease. SpA have been correlated with gut inflammation and are immunologically related Crohn's disease. Colostrum's ability to control gut inflammation and modulate the activity of TNF-a indicate that it may be of benefit in SpA treatment.


Jenkins RT, et al. **Increased intestinal permeability in patients with rheumatoid arthritis: a side-effect of oral nonsteroidal anti-inflammatory drug therapy?** *Br. J. Rheumatology* 1997;26(2):10-37. Patients with rheumatoid arthritis taking prescribed NSAIDs displayed increased intestinal permeability. It has not been determined beyond doubt whether this finding is due to disease process or therapy with oral NSAIDs.

Feldmann M, et al. **Role of cytokines in rheumatoid arthritis.** *Annual Review of Immunology* 1996;14:397-440. Several clinical trials using a chimeric anti-TNF alpha antibody have shown marked clinical benefit, verifying the hypothesis that TNF alpha is of major importance in rheumatoid arthritis. Overall, studies demonstrate that analysis of cytokine expression and regulation may yield effective therapeutic targets in inflammatory disease.


Zimecki M, et al. **Effect of a proline-rich polypeptide (PRP) on the development of hemolytic anemia and survival of New Zealand black (NZB) mice.** *Archivum Immunologiae et Therapiae*
Experimentalis 1991;39(5-6):461-467. Colostrinin (PRP) increased survival in mice susceptible to hemolytic anemia, an autoimmune disease. It is hypothesized the colostrinin induces suppressor cells which slow development of the disease. This suggests that colostrinin may have therapeutic value in treating autoimmune diseases such as juvenile arthritis.


**Asthma**


Rottem M, Shoenfeld Y. Asthma as a paradigm for autoimmune disease. Int Arch Allergy Immunol. 2003;132(3):210-4. The parallel appearance of asthma and autoimmune conditions in the same patients may reveal that such aberrations of the immune system have a common pathophysiologic mechanism. Mast cells, which play a key role in asthma, and the wealth of inflammatory mediators they express, make it likely that they have profound effects on many autoimmune processes. Activation of protein kinases by inflammatory cytokines and environmental stresses may contribute to both allergic and autoimmune diseases. The presence of autoantibodies in some allergic diseases suggests an autoimmune basis for these conditions. Because of the central role T cells play in immune reactivity, the T cell receptor loci have long been considered important candidates for a common disease susceptibility within the immune system such as asthma, atopy, and autoimmunity. Immunomodulation is the key to successful treatment of asthma and autoimmune conditions.


Elrod, KC, et al. Lactoferrin, a potent tryptase inhibitor, abolished late-phase airway responses in allergic sheep. American Journal of Respiratory Critical Care Medicine 1997;156:375-381. Tryptase, a digestive enzyme, has been implicated in various aspects of asthma, including bronchoconstriction and airway hyperreactivity. Lactoferrin has been shown to inhibit tryptase activity, thus relieving the symptoms of asthma.


**Inflammatory Bowel Disease**

Bodammer P, et al. *Alteration of DSS-mediated immune cell redistribution in murine colitis by oral colostral immunoglobulin.* *BMC Immunology* 2013;14:10. Colostrum has a potential use in disease recovery and epithelial homeostasis following intestinal injury. Colostral sIgA failed to improve acute disease activity but promoted weight gain and modulated immune cell responses that are involved in the genesis of colitis. [FULL TEXT](#).

Bodammer P, et al. *Bovine colostrum increases pore-forming claudin-2 protein expression but paradoxically not ion permeability possibly by a change of the intestinal cytokine milieu.* *Public Library of Science One* 2013;8(5):e64210. Bovine colostrum was shown to be a prophylactic agent with properties that strengthen barrier function and favor epithelial restitution in IBD. Modulation of the intestinal transforming growth factor-β expression might have compensated the claudin-2 increase and contributed to the observed barrier strengthening effects of colostrum in vivo and in vitro. [FULL TEXT](#).


Langmead L, Rampton DS. *Review article: complementary and alternative therapies for inflammatory bowel disease.* *Alimentary Pharmacology & Therapeutics* 2006;23(3):341-9. Patients with mild to moderately severe distal colitis received bovine colostrum enemas or placebo twice daily for 4 weeks, in addition to mesalazine. Colostrum improved symptom over placebo (-2.9 v. -0.3). [FULL TEXT](#).


De Keyser F, et al. Gut inflammation and spondyloarthropathies. Current Rheumatology Reports 2002;4(6):525-532. Spondyloarthropathies (SpA) are a related group of arthritic conditions which include ankylosing spondylitis, reactive arthritis, psoriatic arthritis and arthritis associated with inflammatory bowel disease. SpA have been correlated with gut inflammation and are immunologically related Crohn's disease. Colostrum's ability to control gut inflammation and modulate the activity of TNF-α indicate that it may be of benefit in SpA treatment.

Borody TJ, et al. Tunnel vision in the bowel. Center for Digestive Diseases (2001). Review of irritable bowel syndrome, including ulcerative colitis and Crohn's disease, and its etiology, including infective agents such as Shigella and Campylobacter. Infections of the gut are difficult to treat because no antimicrobial therapy is available that is effective against Clostridia spores. Only bovine colostrum has proven clinical efficacy in eradicating intestinal pathogens, such as rotavirus, and may help control the infections seen in chronic disorders such as irritable bowel syndrome due to the number of biologically active components in colostrum. The growth factors in colostrum help heal intestinal erosions and ulcerations. It also contains anti-inflammatory factors and is nutrient rich. Colostrum may be used alone or in combination with other anti-inflammatory and/or immune substances. Future research should focus on identifying immune strategies, novel delivery systems and identification of the bioactives in colostrum.


**Type 1 Diabetes**

Hwang KA, et al. Oral administration of insulin-like growth factor-I from colostral whey reduces blood glucose in streptozotocin-induced diabetic mice. British Journal of Nutrition 2012;108(1):39-45. Insulin-like growth factor-I-rich fraction (IGF-I-RF) obtained from Holstein colostrum could be a useful component for an alternative therapeutic modality for the treatment of diabetes in insulin-resistant patients. The blood glucose levels of STZ-induced diabetic mice fed with IGF-I-RF (50 μg/kg per d) were significantly reduced by 11 and 33 % at weeks 2 and 4, respectively.

Vaarala O. The gut immune system and type 1 diabetes. Annals of the New York Academy of Science 2002;958:39-46. There is increasing evidence that the gut immune system is important in the development of type 1 (autoimmune) diabetes. One of the causes of type diabetes in children may be too early introduction of cow’s milk to the diet in infants, which causes an autoimmune response to insulin.

Pennisi E. Immune therapy stems diabetes' progress. Science News 1995;145:37. Diabetic mice treated with a particular monoclonal antibody have regained the ability to regulate their blood sugar, leading researchers to hope that a similar treatment may one day stop insulin-dependent diabetes in humans.
**A New Way to Fight Diabetes.** Newsweek. November 15, 1993. Researchers at UCLA and Stanford say that diabetes is caused by an allergic reaction to GAD, a protein. The immune system in diabetics turns against other antigens. A single injection produced tolerance to GAD in mice, eliminating the disease process.


Francis GL, et al. *Insulin-like growth factors 1 and 2 in bovine colostrum. Sequences and biological activities compared with those of a potent truncated form.* Biochemistry Journal 1988;251(1):95-103. The sequence of bovine IGF-1 was found to be identical with that of human IGF-1.

**Type 2 Diabetes**

Jakubowicz D, Froy O. *Biochemical and metabolic mechanisms by which dietary whey protein may combat obesity and type 2 diabetes.* J Nutr Biochem. 2013;24(1):1-5. The amino acids and peptides in whey protein (found in colostrum) stimulate the release of several gut hormones that potentiate insulin secretion from β-cells and are associated with regulation of food intake.

Mizrahi M, et al. *Alleviation of insulin resistance and liver damage by oral administration of Imm124-E is mediated by increased Tregs and associated with increased serum GLP-1 and adiponectin: results of a phase I/II clinical trial in NASH.* Journal of Inflammatory Research 2012;5:141-50. In a small human trial, hyperimmune bovine colostrum supplementation caused a decrease in fasting glucose levels; improved oral glucose tolerance test and homeostatic model assessment insulin resistance scores; and alleviation in lipid profile. The effects were accompanied by increased serum levels of glucagon-like peptide 1 (GLP-1), adiponectin and T regulatory cells. Study concluded that hyperimmune bovine colostrum alleviates nonalcoholic steatohepatitis. **FULL TEXT**.

Adar T, et al. *Oral administration of immunoglobulin G-enhanced colostrum alleviates insulin resistance and liver injury and is associated with alterations in natural killer T cells.* Clinical Experimental Immunology 2012;167(2):252-60. Oral administration of hyperimmune bovine colostrum preparations can alleviate chronic inflammation, liver injury and insulin resistance associated with non-alcoholic steatohepatitis. Results showed decreased alanine aminotransferase (ALT) serum levels and serum triglycerides; improved glucose intolerance; and decreased serum tumour necrosis factor (TNF)-α levels.

Kim JH, et al. **Health-promoting effects of bovine colostrum in Type 2 diabetic patients can reduce blood glucose, cholesterol, triglyceride and ketones.** *Journal of Nutritional Biochemistry* 2009;20(4):298-303. Bovine colostrum can decrease levels of blood glucose and ketones, as well as reduce cholesterol and TGs, all of which may cause complications in Type 2 diabetic patients.

Dohm GL, et al. **IGF-I--stimulated glucose transport in human skeletal muscle and IGF-I resistance in obesity and NIDDM.** *Diabetes* 1990;39(9):1028-32. IGF-1 stimulates glucose transport by IGF-1 receptors in skeletal muscle, thus alleviating the hyperglycemia observed in non-insulin-dependent diabetes mellitus (NIDDM). Significantly, muscle from obese patients was resistant to this effect.

Francis GL, et al. **Insulin-like growth factors 1 and 2 in bovine colostrum. Sequences and biological activities compared with those of a potent truncated form.** *Biochemistry Journal* 1988;251(1):95-103. The sequence of bovine IGF-1 was found to be identical with that of human IGF-1.

### Multiple Sclerosis

Webster HD. **Growth factors and myelin regeneration in multiple sclerosis.** *Mult. Scler.* 1997;3(2):113-120. IGF-I treatment has been shown to reduce lesion severity and promote myelin regeneration in experimental autoimmune encephalomyelitis (EAE), an animal model of MS.


### Sjogren’s Syndrome


**Anti-Aging Benefits**


Boldogh I, Kruzel ML. *Colostrinin: an oxidative stress modulator for prevention and treatment of age-related disorders.* *Journal of Alzheimer's Disease* 2008;13(3):303-21. Colostrinin modulates intracellular levels of reactive oxygen species (ROS), via regulation of glutathione metabolism, activity of antioxidant enzymes and mitochondria function. Due to an improvement in senescence-associated mitochondrial dysfunction and a decrease in ROS generation, colostrinin decelerates the aging processes of both cultured cells and experimental animals. When given orally to mice, colostrinin increased their lifespan and improved various motor and sensory activities.

Thapa BR. *Therapeutic potentials of bovine colostrums.* *Indian Journal of Pediatrics* 2005;72(10):849-52. Bovine colostrum has properties to stimulate immune system, contains growth factors and many bioactive substances needed for the body to combat wear and tear.

Epel ES, et al. *Accelerated telomere shortening in response to life stress.* *Proc Natl Acad Sci U S A.* 2004;101(49):17312-5. Women with the highest levels of perceived stress have telomeres shorter on average by the equivalent of at least one decade of additional aging compared to low stress women. These findings have implications for understanding how, at the cellular level, stress may promote earlier onset of age-related diseases. Telomerase, found in colostrum, helps maintain chromosomal DNA.

Kurz DJ, et al. *Chronic oxidative stress compromises telomere integrity and accelerates the onset of senescence in human endothelial cells.* *Journal of Cell Science* 2004;117:2417-2426. Oxidative stress due to the buildup of oxidization by-products has been linked to the onset of cell senescence in blood vessel lining cells by disrupting telomere integrity. Telomeres are the "tails" of the chromosomes, the length of which determine the number of cell divisions a cell can undergo before reaching its limit. Glutathione, a powerful natural antioxidant, is crucial in maintaining telomere integrity.


Rudman D, et al. *Effects of Human Growth Hormone in Men over 60 Years Old*. *N Engl J Med*. 1990;323(1):1-6. The decline in activity of the growth hormone-IGF-1 system may be related to the loss of lean muscle mass and increase in fat mass with aging. Administration of growth hormone to men over 60 years of age resulted in increased IGF-1 levels in the blood similar to that found in much younger men, increase lean body mass, decreased fat mass and an increase in skin thickness.

**Alzheimer’s Disease**

Janusz M, Zablocka A. *Colostrinin: a proline-rich polypeptide complex of potential therapeutic interest*. *Cell Mol Biol (Noisy-le-grand)*. 2013 Nov 3;59(1):4-11. Beneficial effects of PRP/Colostrinin in the case of Alzheimer's disease were shown in double-blind placebo-controlled trials, in long-term open-label studies and in multicenter clinical trials. A very important property of PRP/Colostrinin and one of its components, a nonapeptide (NP), is the prevention of Aβ aggregation and the disruption of aggregates already formed. Moreover, PRP has been found to modulate neurite outgrowth, suppress uncontrolled activation of cells, and reduce 4-HNE-mediated cellular damage. Biological response modifying activity of PRP/Colostrinin can play an important role in its use in the treatment of Alzheimer’s disease and suggests its application beyond neurodegenerative disorders.


Janusz M, Zablocka A. *Colostral proline-rich polypeptides—immunoregulatory properties and prospects of therapeutic use in Alzheimer's disease*. *Current Alzheimer’s Research* 2010;7(4):323-33. PRP/Colostrinin benefits were shown for the first time in double-blind placebo-controlled, long-term open-label clinical trials. PRP/Colostrinin prevented amyloid-beta aggregation and disruption of existing aggregates. The same properties were expressed by one of PRP's components, a nonapeptide (NP). PRP also modulated neurite outgrowth; suppressed uncontrolled activation of cells; reduced 4-HNE-mediated cellular damage; and modulated expression in cellular redox regulation, cell proliferation, and differentiation. This activity may be significant in the treatment of Alzheimer’s.


Stewart MG. **Colostrinin: a naturally occurring compound derived from mammalian colostrum with efficacy in treatment of neurodegenerative diseases, including Alzheimer's.** *Expert Opin Pharmacother.* 2008;9(14):2553-9. Colostrinin reduces oxidative stress, prevents beta-amyloid aggregation and prolongs the lifespan in a laboratory model of premature ageing. An increasingly important application for colostrinin is as a nutraceutical product for use in the early stages of cognitive decline in humans and as a veterinary nutraceutical for companion animals.

Boldogh I, Kruzel ML. **Colostrinin: an oxidative stress modulator for prevention and treatment of age-related disorders.** *Journal of Alzheimer’s Disease* 2008;13(3):303-21. Colostrinin modulates intracellular levels of reactive oxygen species (ROS), via regulation of glutathione metabolism, activity of antioxidant enzymes and mitochondria function. Due to an improvement in senescence-associated mitochondrial dysfunction and a decrease in ROS generation, colostrinin decelerates the aging processes of both cultured cells and experimental animals. When given orally to mice, colostrinin increased their lifespan and improved various motor and sensory activities.

Stewart MG, Banks D. **Enhancement of long-term memory retention by Colostrinin in one-day-old chicks trained on a weak passive avoidance learning paradigm.** *Neurobiology of Learning & Memory* 2006;86(1):66-71. Colostrinin from mammals has efficacy as a cognitive enhancer (long-term memory).

Schuster D, et al. **Protective effect of colostrinin on neuroblastoma cell survival is due to reduced aggregation of beta-amyloid.** *Neuropeptides* 2005;39(4):419-26. The neuroprotective effects exerted by colostrinin are related to the reduction of beta-amyloid fibrils. Low doses of colostrinin attain cytotoxic protection levels similar to those of the highest doses.

Bilikiewicz A, Gaus W. **Colostrinin (a naturally occurring, proline-rich, polypeptide mixture) in the treatment of Alzheimer’s disease.** *Journal of Alzheimers Disease.* 2004 Feb;6(1):17-26. After 15 weeks of supplementation, results showed a stabilizing effect of Colostrinin on cognitive function in ADAS-cog (p = 0.02) and on daily function in IADL (p = 0.02). The overall patient response was also in favor of the active (p = 0.03). Patients graded as mild on entry also showed a superior response of ADAS-cog compared with more advanced cases (p = 0.01). Evidence from this study indicates an early beneficial effect on cognitive symptoms and daily function. Colostrinin has potential value in the treatment AD.
**Bone Health/Osteoporosis**

Włodarski KH, et al. [The importance of lactoferrin in bone regeneration]. *Polski Merkuryz Lekarski*. 2014 Jul;37(217):65-7. Lactoferrin is an iron-binding protein secreted by mammary gland, thus present in milk and in colostrum, which are a cheap and easy to obtain sources of this protein. Lactoferrin is also present in specific granules of neutrophils. Lactoferrin is a multifunctional agent involved, among others in the immune response and in the regulation of bone metabolism. Lactoferrin activates of osteoblast proliferation and bone matrix secretion, and inhibits apoptosis of osteoblast and osteoclastogenesis. Lactoferrin administered to rodents accelerates bone healing and prevents bone loss induced by ovariectomy. Therefore the use of lactoferrin or milk whey in osteoporosis treatment and prevention is postulated.


Du M, et al. Protective effects of bovine colostrum acid proteins on bone loss of ovariectomized rats and the ingredients identification. *Molecular Nutrition & Food Research* 2011;55(2):220-8. Bovine colostrum acidic proteins (BCAP) increased the bone mineral content and bone mineral density of the femur in a dose-dependent manner. These positive effects attribute to the fact that osteopontin, lactoferrin, epidermal growth factor and insulin-like growth factor-2 are the dominant proteins in BCAP.

Lee J, et al. Effect of a Growth Protein-Colostrum Fraction on bone development in juvenile rats. *Bioscience, Biotechnology, and Biochemistry* 2008;72(1):1-6. Growth Protein-Colostrum (GP-C), a fraction of bovine colostrum, enhanced the growth and mineralization of the femur as evidenced by increased serum osteocalcin and bone mineral density. GP-C was also found to increase osteoblast proliferation in vitro. FULL TEXT.

**Cardiovascular Disease**

Luque A, et al. Early atherosclerotic plaques show evidence of infection by Chlamydia pneumonia. *Front Biosci (Elite Ed)*. 2012;4:2423-32. Data showed that Chlamydia pneumoniae might play an important role in activation and development of the initial stages of atherosclerotic lesions.

Isenberg JS, et al. Thrombospondin-1 stimulates platelet aggregation by blocking the antithrombotic activity of nitric oxide/cGMP signaling. *Blood* 2008;111(2):613-23. The release of thrombospondin-1 from alpha-granules during activation provides positive feedback to promote efficient platelet aggregation and adhesion by overcoming the antithrombotic activity of physiologic levels of nitric oxide. FULL TEXT.
Hernández-Ledesma B, et al. **Beta-lactoglobulin as source of bioactive peptides.** *Amino Acids* 2008;35(2):257-65. Beta-lactoglobulin is currently an important source of biologically active peptides, which once released by enzymatic proteolysis, play important roles such as antihypertensive, antioxidant and antimicrobial activities as well as opioid-like features and ability to decrease the body-cholesterol levels.

Zimecki M, Kruzel ML. **Milk-derived proteins and peptides of potential therapeutic and nutritive value.** *Journal of Experimental Therapeutics & Oncology* 2007;6(2):89-106. Casein-derived peptides have been found to have antihypertensive effects. Glycomacropeptide (GMP)--a peptide derived from kappa casein, exhibits antibacterial and antithrombotic activities. Lysozyme is effective in treatment of periodontitis. Alpha lactalbumin lowered blood pressure in rats.

Virok D, et al. **Chlamydia pneumoniae and human cytomegalovirus in atherosclerotic carotid plaques—combined presence and possible interactions.** *Acta Microbiol Immunol Hung.* 2006;53(1):35-50. C. pneumoniae is often present in combination with HCMV in atherosclerotic carotid lesions. The in vitro coinfection model reveals that the doubly-infected monocytes are potent expressors of proatherosclerotic genes, suggesting that this coinfected population may accelerate the process of atherosclerosis.


Kleinz MJ, Davenport AP. **Emerging roles of apelin in biology and medicine.** *Pharmacology and Therapeutics* 107(2):198-211 (2005). Apelin has a hypotensive effect on blood pressure; promotes angiogenesis; stimulates cardiac contractility; plays a role in cardiac tissue remodeling; regulates fluid homeostasis.

FitzGerald RJ, et al. **Hypotensive peptides from milk proteins.** *Journal of Nutrition* 2004;134(4):980S-988S. Milk proteins, both caseins and whey proteins, are a rich source of ACE inhibitory peptides. Several studies in spontaneously hypertensive rats show that these casokinins and lactokinins can significantly reduce blood pressure. **FULL TEXT.**

Murakami M, et al. **Structural analysis of a new anti-hypertensive peptide (beta-lactosin B) isolated from a commercial whey product.** *Journal of Dairy Science* 2004;87(7):1967-74. Four peptide products derived from milk proteins showed strong anti-hypertensive activities (> −18.0 mm Hg). A sample of WE80BG derived from whey proteins showed the strongest anti-hypertensive activity (−21.2 +/- 16.9 mm Hg) with a medium level of ACE inhibitory activity (53.6%).
Juul A, et al. Low serum insulin-like growth factor I is associated with increased risk of ischemic heart disease: a population-based case-control study. Circulation 2002;106(8):939-44. Individuals without ischemic heart disease but with low circulating IGF-I levels and high IGFBP-3 levels have significantly increased risk of developing ischemic heart disease during a 15-year follow-up period. Findings suggest that IGF-I may be involved in the pathogenesis of ischemic heart disease.


FitzGerald RJ, Meisel H. Lactokinins: whey protein-derived ACE inhibitory peptides. Nahrung 1999;43(3):165-7. Peptides derived from the major whey proteins, i.e. alpha-lactalbumin and beta-lactoglobulin in addition to bovine serum albumin, inhibit ACE.


Friend T. Gum Disease Linked to Heart Illness. USA TODAY February 17, 1998. Mark Herzberg of the University of Minnesota said that the most common strain of bacteria in dental plaque can cause blood clots that induce heart attacks when they enter the bloodstream. Chronic inflammation of the gums due to plaque could also be involved in the inflammation of the lining of the blood vessels that is known to lead to the build-up of plaque in the arteries. Studies also show that dental plaque bacteria are linked to infective endocarditis and lung infections.
Lange LG, Schreiner GF. **Immune Mechanisms of Cardiac Disease.** *New England Journal of Medicine* 1994;330(16):1129-35. Many cardiac diseases are the result of immune sensitization to cardiac antigens. Such immune mediated injury results in the presence of inflammatory cells within the myocardium, leading to myocarditis. Cellular, rather than humoral, immunity has been the target of most of the research conducted on immune-related heart disease, with lymphocytes and macrophages being the predominant infiltrating cells. Cardiac disease associated with the immune mechanisms include giant-cell-associated cardiomyopathy and primary idiopathic myocarditis. Research aimed at discovering the mechanisms by which myocardium affect muscle cell functions and rearrange myocardial cell architecture has greatly increased the medical community’s knowledge of the immune mechanisms of heart disease. The development of successful drug therapy for such conditions is now considered possible.

Ohri SK, et al. *Cardiopulmonary bypass impairs small intestinal transport and increases gut permeability.* *Ann Thorac Surg.* 1993;55(5):1080-6. Gastrointestinal damage occurs in 0.6% to 2% of patients after cardiopulmonary bypass (CPB), and carries a mortality of 12% to 67%.

Robert L, et al. *The effect of procyanidolic oligomers on vascular permeability. A study using quantitative morphology.* *Pathol Biol.* 1990;38:608-616. In some pathological conditions, such as inflammation or diabetes, vascular permeability can be abnormally increased. Treatment of animals with procyanidolic oligomers prevented the permeability increase produced by i.v. collagenase injection.


**Brain Injury/Stroke**


Kim SE, et al. *Neuroprotective effects of bovine colostrum on intracerebral hemorrhage-induced apoptotic neuronal cell death in rats.* *Neural Regeneration Research.* 2012 Aug 5;7(22):1715-21. Results revealed that colostrum treatment significantly suppressed N-methyl-D-aspartic acid-induced neuronal cell death in the rat hippocampus. Moreover, colostrum treatment improved short-term memory by suppressing hemorrhage-induced apoptotic neuronal cell death and decreasing the volume of the lesion induced by intracerebral hemorrhage in the rat hippocampus. These results suggest that colostrum may have a beneficial role in recovering brain function following hemorrhagic stroke by suppressing apoptotic cell death. [FULL TEXT](#)


**Cancer**

Chen HY, et al. Potential clinical applications of multi-functional milk proteins and peptides in cancer management. *Current Medicinal Chemistry*. 2014;21(21):2424-37 Lactoferricin peptide analogs are in early clinical development as antimicrobial agents and cancer immunotherapies. In addition, milk proteins and peptides are well tolerated and many exhibit oral bioavailability; thus they may complement standard therapies to boost overall success in cancer treatments. Lactoferrin, colostrum, and specific milk-derived peptide fractions are currently being developed as clinical nutrition for cancer prevention and chemotherapy protection. This review highlights the potential applications of milk proteins and peptides as pharmaceutical drug candidates and clinical nutrition in the overall management of cancer.


Tung YT, et al. Bovine lactoferrin inhibits lung cancer growth through suppression of both inflammation and expression of vascular endothelial growth factor. *J Dairy Sci*. 2013;96(4):2095-106. Oral supplementation with bovine lactoferrin suppressed the formation of pulmonary tumors. It decreased the levels of proinflammatory cytokines, such as tumor necrosis factor-α, and antiinflammatory cytokines, resulting in limited inflammation, which then restricted growth of the lung cancer.

Artym, J. [Antitumor and chemopreventive activity of lactoferrin]. Postępy Higieny i Medycyny Doświadczalnej 2006;60:352-369. Lactoferrin provides anti-tumor protection through its immunomodulatory abilities, so it is of particular value in cancer patients with impaired immunity. Lactoferrin increases the number and the activity of T and B cells and NK cells, stimulates the release of a number of cytokines (IL-1, IL-6, IL-8, IL-18, IFN-γ, TNF-α), increases the phagocytic and cytotoxic activity of monocytes and macrophages, accelerates the maturation of T and B cells, and elevates the expression of several types of cellular receptors, including CD4, zeta chain of the CD3 complex, LFA-1, CD11, ICAM-1, and selectin P. In addition, it also exhibits chemopreventive properties, regulates the activity of Phase I and Phase II enzymes which participate in the activation and detoxification of carcinogens, and regulates the composition of the intestinal flora.


Tsuda H, et al. Cancer prevention by bovine lactoferrin and underlying mechanisms – A review of experimental and clinical studies. Biochemistry and Cell Biology 2002;80(1):131–136. Review article of studies which indicate that bovine lactoferrin is an effective anticancer agent in rat studies; capable of significantly inhibiting colon, esophagus, lung, bladder, and tongue carcinogenesis. Following the administration of lactoferrin to animals which had been exposed to a variety of carcinogenic chemicals, phase I enzymes (which seek out carcinogenic materials and “switch them on”) were inhibited in colon cancer test subjects while activity of phase II enzymes (which act to detoxify the carcinogens switched on by the phase I enzymes) was increased in the tongue cancer study. There was a marked increase in natural killer cell and cytotoxic T-lymphocyte activity in both the mucosal layer of the small intestine and peripheral blood cells, increasing the production of IL-18 and caspase-1 and the subsequent production of interferon-gamma cells. It was also found that lactoferrin has significant anti-Hepatitis C virus activity.

Tanaka T, et al. Chemopreventive effect of bovine lactoferrin on 4-nitroquinoline 1-oxide-induced tongue carcinogenesis in male F344 rats. *Japanese Journal of Cancer Research* 2000;91(1):25-33. A more detailed study of the effect of lactoferrin administration on chemically induced carcinomas of the tongue in rats. A 2% lactoferrin solution produced better protection against the development of carcinoma than the weaker 0.2% solution, though both provided more protection than the control group. With a 2% solution, only 20% of the rats developed cancer, and they showed 64% less multiple tumors than the control group. It was further determined that the method of action of the lactoferrin was through modification of cell proliferation and detoxifying enzymes, such as glutathione S-transferase and quinone reductase.

Kuhara T, et al. Orally administered lactoferrin exerts an anti-metastatic effect and enhances production of IL-18 in the intestinal epithelium. *Nutrition and Cancer* 2000;38(2):192–199. Oral administration of bovine lactoferrin or its hydrolyzed form caused an increase in CD4+ and CD8+ lymphocytes and asialoGM I+ (a specific type of natural killer cell) in the spleen and blood, and their cytotoxic activities against several types of cancer cell lines were increased. CD4+ and CD8+ lymphocytes were also increased in intestinal mucosa accompanied by a marked increase in IL-18 production. Using this model, the effects on metastasis of colon carcinoma to the lung was studied and significant inhibition of metastasis was found. The results suggest that the anti-metastatic effect of lactoferrin may be due to enhanced cellular immunity.


Damiens E, et al. Lactoferrin inhibits G1 cyclin-dependent kinases during growth arrest of human breast carcinoma cells. *Journal of Cell Biochemistry* 1999;74(3):486–498. It is known that lactoferrin inhibits cell proliferation and suppresses tumor growth. The mechanism of how it does this is unknown. However, in this study, lactoferrin applied to a breast carcinoma cell line arrests the growth of these cells at the G1 [growth and preparation of the chromosomes for replication] to S [DNA synthesis] transition of the cell cycle. The arrest is associated with a dramatic increase in the levels of Cdk2 [cyclin-dependent kinase 2] and cyclin E and an inhibition of Cdk2 kinase activity. Cdk4 activity is also decreased and Cdk inhibitor p21 (CIP I) expression is increased. Lactoferrin also maintains the cell cycle regulator retinoblastoma protein pRb in a hypophosphorylated form. Therefore, lactoferrin induces growth arrest by modulating the expression and activity of key G1 regulatory proteins.

Damiens E, et al. Effects of human lactoferrin on NK cell cytotoxicity against hematopoietic and epithelial tumor cells. *Biochimica et Biophysica Acta* 1998;1402(3):277–287. Human lactoferrin applied at levels found in inflammation was found to boost the cytotoxic activity of natural killer (NK) cells against hematopoietic and breast epithelial tumor cell lines. It also significantly increases the susceptibility to lysis of breast and colon epithelial tumor cell lines but not the hematopoietic tumor cells. Lactoferrin is shown to inhibit epithelial cell proliferation by blocking cell cycle progression.
Sekine K, et al. Inhibition of azoxymethane-initiated colon tumor by bovine lactoferrin administration in F344 rats. Japanese Journal of Cancer Research 1997;88(6):523–526. Rats were treated with azoxymethane, a chemical which induces colon cancer in rats. They were then given bovine lactoferrin orally for 36 weeks. 57.5% of the rats in the control group that received no lactoferrin developed carcinomas, while only 25% of the rats that received 0.2% lactoferrin solutions developed carcinomas. Rats that received a stronger dose of lactoferrin, 2%, had only a 15% rate of tumor development.

Ushida Y, et al. Inhibitory effects of bovine lactoferrin on intestinal polyposis in the Apc(Min) mouse. Cancer Lett. 1998;134(2):141-5. An overall tendency for a reduction in the total number of polyps in the small intestine was evident in the bovine lactoferrin-treated animals, along with significant suppression in the jejunum at the 2% dose. Additionally, body growth suppression, presumed to be due to anemia and/or intussusception as a consequence of numerous polyps in the intestine, was alleviated. No toxic effects were observed in the intestinal epithelium, and the data suggest that bovine lactoferrin may be a chemopreventor of intestinal polyposis.

Blach-Olszewska Z, Janusz M. Stimulatory effect of ovine colostrinine (a proline-rich polypeptide) on interferons and tumor necrosis factor product by murine resident peritoneal cells. Arch Immunol Ther Exp (Warsz) 1997;45(1):43-47. Colostrinin stimulates the production of tumor necrosis factor-alpha (TNF-a) and interferon-beta (INF-β), both important cytokines in the inflammatory response.

Inglot AD, et al. Colostrinine: a proline-rich polypeptide from ovine colostrum is a modest cytokine inducer in human leukocytes. Arch Immunol Ther Exp (Warsz) 1996;44(4):215-224. PRP-treated volunteers showed signs of psycho-stimulation. Observations suggest that ovine PRP is active in humans and may have therapeutic value as an immunostimulant and/or neurotropic cytokine.


Kroning R, et al. Enhancement of drug sensitivity of human malignancies by epidermal growth factor. British Journal of Cancer 1995;72(3):615–619. Study shows that a number of human cancers become more sensitive to chemotherapeutic agents in the presence of epidermal growth factor. Cancers showing increased sensitivity include ovarian carcinoma, cancers of the head, neck, cervix, colon, prostate, and pancreas, and non-small-cell lung cancer. Drugs to which the cancers became more sensitized include most common chemotherapeutic agents, such as cisplatin, carboplatin, tetraplatin, taxol, melphalan and 5-fluorouracil.


Watzl B, et al. **Enhancement of resistance to Cryptosporidium parvum by pooled bovine colostrum during murine retroviral infection.** *Am. J. Trop. Med. Hyg.* 1993;48(4): 519-523. Parasite colonization of intestinal villi was significantly reduced in immunosuppressed mice that received dietary supplemental pooled bovine colostrum compared with to those that did not receive colostrum treatment. Since the nonimmune bovine colostrum contained no anti-Cryptosporidium antibodies, this suggests that passively transferred antibodies alone are unlikely to have provided the improved resistance.

Lidbeck A, et al. **Lactobacilli, anticarcinogenic activities and human intestinal microflora.** *European Journal of Cancer Prevention* 1992;1:341–353. Recent studies in humans have shown that intake of L. acidophilus significantly reduced the mutagen excretion after consumption of fried meat. Several mechanisms by which lactobacilli might exert anticarcinogenic effects are discussed. Certain strains of lactobacilli might lower the colon cancer risk in humans.

Neely EK, et al. **Insulin-like growth factors are mitogenic for human keratinocytes and a squamous cell carcinoma.** *J Invest Dermatol.* 1991;96(1):104-10. IGF-1 and IGF-2 are mitogens for normal and transformed human keratinocytes and that their actions are primarily mediated through the type I IGF receptor, whereas insulin is a mitogen through both the IGF-1 receptor and the insulin receptor.

Flanigan T, et al. **In vitro screening of therapeutic agents against Cryptosporidium: hyperimmune cow colostrum is highly inhibitory.** *J Protozool.* 1991;38(6):225S-227S. Hyperimmune bovine colostrum was highly inhibitory of Cryptosporidium infection in vitro and its soluble fraction remained significantly inhibitory while the soluble fraction of conventional colostrum did not.


Heaton P. **Cryptosporidiosis and acute leukemia.** *Arch Dis Child* 1990;65(7):813-814. Paper presented at 6th annual Asian Pediatric Conference. Treatment of 3 year old with acute cryptosporidia caused diarrhea. Bovine colostrum 100 ml 3 x daily in form of milkshake. Within two weeks symptoms alleviated. Cryptosporidia tests negative. Bovine colostrum is a very rich source of immunoglobulins. Pooled colostrum from nonimmunized cows provides an effective method of controlling symptoms in immunodeficient patients. Immunoglobulin concentrated may provide an effective, convenient method by which immunology can be administered.

Fayer R, Perryman LE, Riggs MW. **Hyperimmune bovine colostrum neutralizes Cryptosporidium sporozoites and protects mice against oocyst challenge.** *J Parasitol.* 1989;75(1):151-3. Activity of colostral whey (produced by a cow immunized with oocysts of Cryptosporidium parvum and found to provide prophylaxis against cryptosporidiosis in calves) was given to mice who subsequently had fewer C. parvum.

Moro I, et al. **Natural killer cells in human colostrum**, *Cell Immunol*. 1985;93(2):467-74. Approximately 0.5% of colostral cells were identified as natural killer cells of two morphological types.

**Athletic Performance**

Jones AW, et al. **Effects of bovine colostrum supplementation on upper respiratory illness in active males**, *Brain Behavior & Immunity*. 2014 Jul;39:194-203. Study demonstrated that bovine colostrum supplementation of 20 grams limits the increased salivary bacterial load in physically active males during the winter months. This may provide a novel mechanism of immune-modulation with colostrum and a relevant marker of in vivo (innate) immunity and risk of upper respiratory infections.


Appukutty M, et al. **Colostrum supplementation protects against exercise-induced oxidative stress in skeletal muscle in mice**, *BMC Research Notes* 2012;5:649. Daily bovine colostrum supplementation was beneficial to skeletal muscle to reduce the oxidant-induced damage during muscular exercise. **FULL TEXT**.

Davison G. **Bovine colostrum and immune function after exercise**, *Medicine & Sport Science*. 2012;59:62-9. Although mechanisms are not fully understood, existing evidence does support the notion that bovine colostrum is beneficial for certain groups of athletes, such as those involved in strenuous training (e.g. endurance athletes), in terms of immunity and resistance to upper respiratory tract infection.


Davison G, Diment BC. **Bovine colostrum supplementation attenuates the decrease of salivary lysozyme and enhances the recovery of neutrophil function after prolonged exercise**, *British Journal of Nutrition* 2010;103(10):1425-32. Bovine colostrum supplementation either speeded the recovery (neutrophil function) or prevented the decrease (salivary lysozyme) in these measures of innate immunity. These results suggest that 4 weeks of bovine colostrum supplementation limits the immunodepressive effects induced by an acute prolonged physical stressor, such as exercise, which may confer some benefits to host defense. **FULL TEXT**.
Shing CM, et al. The influence of bovine colostrum supplementation on exercise performance in highly trained cyclists. *British Journal of Sports Medicine* 2006;40(9):797-801. Low dose bovine colostrum protein concentrate supplementation elicited improvements in 40km time trial performance during a high intensity training period and maintained ventilatory threshold following five consecutive days of high intensity training. FULL TEXT.

Brinkworth GD, et al. Effect of bovine colostrum supplementation on the composition of resistance trained and untrained limbs in healthy young men. *European Journal of Applied Physiology* 2004;9(11):53-60. Either bovine colostrum or whey protein was given to young men who were either in training or not in training. Those in the training group who received colostrum showed a significantly greater increase in both upper arm circumference and cross-sectional area compared to those receiving whey, while those who were not in training showed no change.

Buckley JD, et al. Effect of bovine colostrum on anaerobic exercise performance and plasma insulin-like growth factor I. *Journal of Sports Science* 2003;21(7):577-588. Athletes in training were given either bovine colostrum or placebo for 8 weeks. Those receiving colostrum showed a significant increase in peak anaerobic power over placebo.


Molloy T, et al. The roles of growth factors in tendon and ligament healing. *Sports Medicine* 2003;33(5):381-394. The roles of five different growth factors, IGF-1, TGF-β, vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF) and basic fibroblast growth factor (bFGF), in healing tendon and ligament injuries is explored. Each plays a different but vital role in the process.


Coombes JS, et al. Dose effects of oral bovine colostrum on physical work capacity in cyclists. *Medicine and Science in Sports and Exercise* 2002;34(7):1184-1188. Dosage studies done on training cyclists showed a small but significant improvement in time trials at doses of 20 g or 60 g/day.


Crooks C, et al. **Bovine colostrum supplementation increases levels of s-IGA in distance runners: a study based on athletes in training for the 2002 Rotorua marathon.** Unpublished research. Marathon runners in training were given bovine colostrum or placebo for 12 weeks in a double blind study. Those in the colostrum group showed significantly more secretory IgA (s-IgA) in their saliva than either the placebo group or sedentary controls. The colostrum group also reported a significantly lower rate of upper respiratory infections (URI) during this period.


Kuipers H, et al. **Effects of oral bovine colostrum supplementation on serum insulin-like growth factor-I levels.** *Nutrition* 2002;18(7-8):165-172. A study for the International Olympic Committee showed no increase in blood IGF-1 or IGF-bp3 levels after 4 weeks time.

Antonio J, et al. **The effects of bovine colostrum supplementation on body composition and exercise performance in active men and women.** *Nutrition* 2001;17(3):243-247. Actively training male and female athletes were given colostrum supplementation or placebo for a period of 8 weeks. Subjects receiving colostrum but not placebo showed an increase in lean body mass.

Kasemkijwattana C, et al. **Use of growth factors to improve muscle healing after strain injury.** *Clinical Orthopedics* 2000;370:272-285. Muscle injuries, such as strains, are common in athletes. The use of growth factors, such as IGF-1, in treating such injuries is explored.


Hwa V, Oh Y, Rosenfeld RG. **The insulin-like growth factor binding protein (IGFBP) superfamily.** *Endocr Rev.* 1999; 20(6):761-87. The IGFBPs are known to mediate biological functions mainly through IGF-dependent mechanisms and also through IGF-independent mechanisms.


Spagnoli A, Rosenfeld RG. **The mechanisms by which growth hormone brings about growth. The relative contributions of growth hormone and insulin-like growth factors.** *Endocrinol Metab Clin North Am.* 1996;(3):615-31. Growth hormone may have specific growth-related actions in addition to stimulating IGF production, including promoting differentiation of prechondrocytes at the growth plate and stimulation of synthesis of proteins involved in IGF transport and clearance.

Burke ER. **Colostrum as an Athletic Enhancer and Help for AIDS.** *Nutrition Science News* 1996;5:30-32. While leaky gut is of concern to everyone, it is particularly so for athletes who need to utilize all the nutrients they take in and prevent infection when their immune systems are impaired following exercise. Many athletes suffer irritable bowel syndrome as a result of incomplete digestion of protein supplements. The role of colostrum-derived insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), platelet-derived growth factor (PDGF) and transforming growth factor-beta (TGF-ß) in healing leaky gut are explored.

Sparling PB, et al. **Selected scientific aspects of marathon racing. An update on fluid replacement, immune function, psychological factors and the gender difference.** *Sports Medicine* 1993;15(2):116-132. Negative changes to the immune system during long distance running increase the chances of upper respiratory infections in these athletes for a period following exercise. Proper nutrition, adequate rest and appropriate recover between workouts as well as other measures can lessen the risk.


Schwade S. **Insulin-like growth factors.** *Muscle & Fitness,* May 1992. Human muscle cells have a high affinity for IGF-1. Bovine colostrum has a higher concentration of IGF-1 than human colostrum, and its structure is virtually identical to human IGF-1. Colostrum slows protein breakdown, and stimulates glucose transport in muscle, which allows muscle tissue to efficiently use the available fuel.

Wu AH, Perryman MB. **Clinical applications of muscle enzymes and proteins.** *Curr Opin Rheumatol.* 1992;4(6):815-820. New enzyme and protein markers (troponin and carbonic anhydrase III) are being investigated, which are more specific than creatine kinase toward particular tissues. Measurement of creatine kinase isoforms may provide information about whether muscle turnover is acute or chronic.

Berk LS, et al. **The effect of long endurance running on natural killer cells in marathoners.** *Medicine and Science in Sports and Exercise* 1990;22(2):207-212. A significant decrease in natural killer cell populations were seen in marathon runners following three hours of maximal exercise with full recovery of pre-exercise levels by 21 hours. This correlated with increases in cortisol levels during exercise.


**Mental Health / Psychiatric Disorders**


Wood NC, et al. Abnormal intestinal permeability. An aetiological factor in chronic psychiatric disorders? British Journal of Psychiatry 1987;150:853-6. Chronic psychiatric in-patients showed abnormal intestinal permeability which could not be attributed to established bowel disease. Patients who were receiving neuroleptic but not anticholinergic drugs were those most often showing abnormal intestinal permeability.

Dohan FC, et al. Is schizophrenia rare if grain is rare? Biol Psychiatry. 1984;19(3):385-99. Grain glutens are harmful to schizophrenics; leaky gut may be involved.

**Autism**

Al-Farsi YM, et al. Effect of suboptimal breast-feeding on occurrence of autism: a case-control study. Nutrition 2012;28(7-8):e27-32. Autism spectrum disorders (ASD) was found to be associated with the late initiation of breast-feeding, a non-intake of colostrum, prelacteal feeding, and bottle-feeding. The risk of ASD was found to decrease in a dose-response fashion over increasing periods of exclusive breast-feeding and continued breast-feeding.

Brown CM, Austin DW. Autistic disorder and phospholipids: A review. Prostaglandins Leukot Essent Fatty Acids 2011;84(1-2):25-30. Study suggests that more research is needed to ascertain whether breastfeeding, and specifically, the administration of colostrum or an adequate substitute can play a preventative role by supplying the neonate with essential fatty acids at a critical juncture in their development.
Mostafa GA, et al. Serum anti-myelin-associated glycoprotein antibodies in Egyptian autistic children. J Child Neurol. 2008;23(12):1413-8. Anti-myelin-associated glycoprotein serum levels were significantly higher in autistic children with than those without such history. Autism could be, in part, one of the pediatric autoimmune neuropsychiatric disorders. Further studies are warranted to shed light on the etiopathogenic role of anti-myelin-associated glycoprotein antibodies and the role of immunotherapy in autism.


Singh VK. Autism, autoimmunity and immunotherapy: a commentary. The Autism Autoimmunity Project Newsletter 1999;1. Author makes a compelling argument for autism being considered an autoimmune disorder. The mechanism by which a developing brain might be affected would likely be an immune response resulting in antibodies against the brain or neurological tissue.


Wound Healing & Tissue Repair

Kshirsagar AY, et al. A comparative study of colostrum dressing versus conventional dressing in deep wounds. Journal of Clinical & Diagnostic Research. 2015 Apr;9(4):PC01-4. Colostrum powder dressings are safe, promotor of wound healing, more patient compliance in terms of less pain, less number of dressing required. FULL TEXT.


Kovacs D, et al. Bovine colostrum promotes growth and migration of the human keratinocyte HaCaT cell line. Growth Factors 2009;27(6):448-55. The biological activities of bovine colostrum are specifically mediated by the growth factor-induced activation of tyrosine kinase receptors. This underlines the relevance of the synergistic action exerted by the growth factors in stimulating keratinocyte proliferation and migration essential for tissue repair.


IGF-2 binds directly to vitronectin, a component of the extracellular skin matrix, to enhance protein synthesis and migration by skin cells in wound healing and skin regeneration.

El Ghalbzouri A, et al. **Fibroblasts facilitate re-epithelialization in wounded human skin equivalents.** *Laboratory Investigation* 2004;84(1):102-112. Re-epithelialization of wounds begins with the migration of keratinocytes (skin cells) from the edges of the wound. This migration is dependent on the interaction of the keratinocytes with dermal fibroblasts and extracellular matrix. This migration is accelerated by EGF and keratinocyte growth factor.

Bhora FY, et al. **Effect of growth factors on cell proliferation and epithelialization in human skin equivalents.** *Laboratory Investigation* 2004;84(1):102-112. Re-epithelialization of wounds begins with the migration of keratinocytes (skin cells) from the edges of the wound. This migration is dependent on the interaction of the keratinocytes with dermal fibroblasts and extracellular matrix. This migration is accelerated by EGF and keratinocyte growth factor.

Bibel DJ, et al. **Effect of growth factors on cell proliferation and epithelialization in human skin equivalents.** *Laboratory Investigation* 2004;84(1):102-112. Re-epithelialization of wounds begins with the migration of keratinocytes (skin cells) from the edges of the wound. This migration is dependent on the interaction of the keratinocytes with dermal fibroblasts and extracellular matrix. This migration is accelerated by EGF and keratinocyte growth factor.

Bhoro FY, et al. **Effect of growth factors on cell proliferation and epithelialization in human skin equivalents.** *Laboratory Investigation* 2004;84(1):102-112. Re-epithelialization of wounds begins with the migration of keratinocytes (skin cells) from the edges of the wound. This migration is dependent on the interaction of the keratinocytes with dermal fibroblasts and extracellular matrix. This migration is accelerated by EGF and keratinocyte growth factor.

Bibel DJ, et al. **Topical sphingolipids in antisepsis and antifungal therapy.** *Clinical and Experimental Dermatology* 1995;20(5):395-400. The sphingolipids sphingosine and sphinganine, both of which are strongly inhibitory effects for both bacteria and fungi in the stratum corneum of the skin, were used as topical antiseptics against Staphylococcus aureus and Candida albicans, as a restorative antiseptic against expanded normal skin flora, and as therapy for Candida albicans and Trichophyton mentagrophytes infections with very good results and low toxicity.

Bibel DJ, et al. **Sphingosines: antimicrobial barriers of the skin.** *Acta Dermato-Venereologica* 1993;73(6):407-411. One of the main functions of the skin is to prevent microbial infections. Skin lipids, particularly sphingosines, which are also derived from sphingomyelin, found in the stratum corneum of the skin. Sphingosines were found to have bactericidal, bacteriostatic or fungistatic effects on Staphylococcus aureus, Candida albicans, Trichophyton mentagrophytes, Trichophyton tonsurans and Epidermatophyton floccosum, common microbes found on the skin.

Tavakkol A, et al. **Expression of growth hormone receptor, insulin-like growth factor 1 (IGF-1) and IGF-1 receptor mRNA and proteins in human skin.** *Journal of Investigative Dermatology* 1992;99(3):343–349. Receptors for growth hormone and IGF-1 were isolated from human skin, indicating that skin cells may have the ability to react directly to growth hormone stimulation.


Imokawa G, et al. **Decreased level of ceramides in stratum corneum of atopic dermatitis: an etiologic factor in atopic dry skin?** *Journal of Investigative Dermatitis* 1991;96(4):523-526. The lipids found in the stratum corneum, particularly the ceramides (metabolic products of sphingomyelin), are important in maintaining the water retention and permeability barrier functions of the skin. Skin diseases marked by a breakdown in these functions, such as atopic dermatitis, are characterized by decreased levels of ceramides in the stratum corneum. Ceramide levels also decrease with age. Thus it is concluded that ceramide insufficiency is a factor in dry skin conditions.
Neely EK, et al. Insulin-like growth factors are mitogenic for human keratinocytes and a squamous cell carcinoma. *J Invest Dermatol.* 1991;96(1):104-10. IGF-1 and IGF-2 are mitogens for normal and transformed human keratinocytes and that their actions are primarily mediated through the type I IGF receptor, whereas insulin is a mitogen through both the IGF-1 receptor and the insulin receptor.


Sporn MB, et al. Polypeptide transforming growth factors isolated from bovine sources and used for wound healing in vivo. *Science* 1983;219, 1329-1331. Growth factors in bovine colostrum were found to be very effective in promoting wound healing; implications for trauma and surgical healing. TGF accelerated the healing of experimental wounds in rats by increasing the accumulation of protein, collagen and DNA in the affected area.


Wieczorek Z, et al. Proline-rich polypeptide from ovine colostrum: its effect on skin permeability and on the immune response. *Immunology* 1979;36(4):875-881. A proline-rich polypeptide from ovine colostrum had a regulatory activity stimulating or suppressing the immune response. The proline-rich polypeptide also increased the permeability of skin vessels in guinea-pigs.

**Pain Management**


Goebel A, et al. Intravenous immunoglobulin in the treatment of primary trigeminal neuralgia refractory to carbamazepine: a study protocol. *BMC Neurology* 2003;3(1):1. Patients with resistant trigeminal neuralgia, which is characterized by severe pain that is unresponsive to traditional pain management, participated in a double-blind study using intravenous immunoglobulin treatment compared to placebo. While pain management did not follow simple dose-response rules, intravenous IgG treatment did produce results ranging from full remission of pain to no effect.
Goebel A, et al. Human pooled immunoglobulin in the treatment of chronic pain syndromes. *Pain Medicine* 2002;3(2):119-127. Intravenous treatment with pooled IgG from colostrum was shown to be of benefit to patients suffering chronic pain due to fibromyalgia, spinal pain, complex regional pain syndrome (CRPS), peripheral neuropathic pain, and atypical odontalgia or facial pain without serious side effects. All patients had failed to respond to established pain treatment protocols.


**Sexual Health**


**Colostrum Supplementation in Infants & Children**

Derscheid RJ, Ackermann MR. The innate immune system of the perinatal lung and responses to respiratory syncytial virus infection. *Veterinary Pathology* 2013;50(5):827-41. For viral infections such as respiratory syncytial virus (RSV), the pulmonary innate immune responses has an essential role in defense as there are no fully effective vaccines or therapies for RSV infections of humans and reinfections are common. Lactoferrin, among other substances that have antimicrobial activity, may lead to an more effective therapeutic therapy.


Immunoglobulin A (IgA)-deficient children were supplemented with bovine colostrum three times daily for one week. These children had a lower infection severity score than the placebo group.

Pammi M, Abrams SA. Oral lactoferrin for the prevention of sepsis and necrotizing enterocolitis in preterm infants. *Cochrane Database Syst Rev*. 2011;(10):CD007137. Oral lactoferrin prophylaxis reduces the incidence of late-onset sepsis in infants weighing less than 1500 g and most effective in infants weighing less than 1000 g.

Panahi Y, et al. Bovine colostrum in the management of nonorganic failure to thrive: a randomized clinical trial. *Journal of Pediatric Gastroenterology and Nutrition* 2010;50(5):551-4. Bovine colostrum supplementation for a 3-month period is a useful method without any side effects, in addition to known medical and psychological treatments, to increase the weight of children with nonorganic failure to thrive.
Elizabeth KE. Bovine colostrum in those with immunodeficiency. Indian Pediatrics. 2009 Sep;46(9):817-8. The use of bovine colostrum rich in IgA is being advised in children for prevention and treatment of various conditions. The rationale behind this is the fact that secretory IgA (SIgA) can resist proteolytic degradation and can survive in the harsh environments of digestive and respiratory tracts. As it is abundant in secretions like tears, saliva and mucosal linings, it is also the first antibody to come in contact with different antigens. Bovine and human SIgA is found to be homologous and colostrum have identified as a rich source of SIgA.

Zimecki M, Artym J. [Therapeutic properties of proteins and peptides from colostrum and milk]. Postepy Hig Med Dosw (online). 2005;59:309-323. Lysozyme can be used in infant formulas for the treatment of periodontitis and the prevention of tooth decay. Antibacterial properties were exhibited by lactoperoxidase. Both lysozyme and lactoperoxidase required cooperative action with lactoferrin in combating bacteria.

Artym J, Zimecki M. [The role of lactoferrin in the proper development of newborns]. Postepy Hig Med Dosw (online). 2005;59:421-32. Oral lactoferrin stimulates both local and systemic immune response. Lactoferrin plays a role in the absorption of nutrients. The protein can deliver such metal ions as iron, manganese, and zinc and facilitate the absorption of sugars. Lactoferrin stimulates the proliferation of gut endothelial cells and the growth of gut-associated lymphatic follicles, which suggests the possibility of applying Lactoferrin in premature infants and patients with damaged intestinal mucus. Lactoferrin controls the proper composition of the gut microflora by suppressing the growth of pathogenic bacteria while promoting the multiplication of nonpathogenic Lactobacillus and Bifidobacterium.


Solomons NW. Modulation of the immune system and the response against pathogens with bovine colostrum concentrates. European Journal of Clinical Nutrition 2002;56(Suppl.3):524-528. Colostrum protects infants against gastrointestinal pathogens and authors of this study encourage further research into employing seasonal or chronic bovine colostrum feeding in populations of deprived infantile populations to reduce the rates of recurrent gastroenteritis and decrease immunostimulation to improve vitality and nutritional status in early life.

van der Strate BW, et al. Antiviral activities of lactoferrin. Antiviral Research 2001;52(3):225-39. Lactoferrin displays antiviral activity against both DNA- and RNA-viruses, including rotavirus, respiratory syncytial virus, herpes viruses and HIV. The antiviral effect of LF lies in the early phase of infection. Lactoferrin prevents entry of virus in the host cell, either by blocking cellular receptors, or by direct binding to the virus particles.
Satué-Gracia MT, et al. Lactoferrin in infant formulas: effect on oxidation. J Agric Food Chem. 2000;48(10):4984-90. Lactoferrin has bacteriostatic and bactericidal activities. Lactoferrin inhibited oxidation in a concentration-dependent manner even at concentrations beyond its capacity to bind iron at its two high affinity binding sites. Lactoferrin can be used as a dual purpose additive in infant formulas and similar food products for its antioxidant and its antimicrobial properties.


Buescher ES, McWilliams-Koeppen P. Soluble tumor necrosis factor-alpha (TNF-alpha) receptors in human colostrum and milk bind to TNF-alpha and neutralize TNF-alpha bioactivity. Pediatric Research 1998;44(1):37-42. Soluble tumor necrosis factor-alpha I and II from human colostrum and milk bind to TNF-alpha, that both colostrum and milk interfere with the bioactivity of TNF-alpha, and that affinity-purified sTNFRI from human milk blocks the bioactivity of TNF-alpha. These effects may contribute to the anti-inflammatory character of human colostrum and milk.


Carver JD, Barness LA. Trophic factors for the gastrointestinal tract. Perinatology 1996;23(2):265-285. GI trophic factors in colostrum and human milk can initiate cellular growth and expression of differentiated function, and they are important in adaptation and repair following injury in infants.

Bessler H, et al. Human colostrum stimulates cytokine production. Biol Neonate. 1996;69(6):376-82. Breast feeding is not only important for a well-balanced nutrient supply but also as a source for growth-promoting factors. It is suggested that the enhanced secretion of IL-1, IL-3 and IL-6 induced by human colostrum may compensate for the lower capacity of neonatal peripheral blood mononuclear cells to produce these cytokines. By stimulating the secretion of these cytokines, breast feeding may provide an additional mechanism for the regulation of the neonatal immune system and hematopoiesis.


Shield J, et al. Bovine colostrum immunoglobulin concentrate for cryptosporidiosis in AIDS. Arch Dis Child. 1993;69(4):451-3. Lactobin®, a commercial hyperimmune bovine colostrum with potent anticryptosporidial activity, was administered to a 4 year old child with AIDS and severe diarrhoea associated with cryptosporidiosis. There was significant clinical improvement in the diarrhoea and permanent elimination of the parasite from the gut.
Buescher ES, McIlheran SM. Colostral antioxidants: separation and characterization of two activities in human colostrum. *J Pediatr Gastroenterol Nutr.* 1992;14(1):47-56. Colostrum contains at least two separate antioxidants, one of which is ascorbate-like and the other is uric acid. Authors speculate that these antioxidants may function in human colostrum as traps for neutrophil-generated reactive oxygen metabolites.

Ebina T, et al. Passive immunizations of suckling mice and infants with bovine colostrum containing antibodies to human rotavirus. *Journal of Medical Virology* 1992;38:117-123. Study confirmed that oral immunization via colostrum or milk against rotavirus was possible, safe and effective.

Savilahti E, et al. Low colostral IgA associated with cow's milk allergy. *Acta Pediatr Scan.* 1991;80:1207-1213. An infant is more likely to develop cow's milk allergy if the mother's colostrum had a low total IgA content. (Bovine colostrum contains IgA.)


Heaton P. Cryptosporidiosis and acute leukemia. *Arch Dis Child* 1990;65(7):813-814. Paper presented at 6th annual Asian Pediatric Conference. Treatment of 3 year old with acute cryptosporidia caused diarrhea. Bovine colostrum 100 ml 3 x daily in form of milkshake. Within two weeks symptoms alleviated. Cryptosporidia tests negative. Bovine colostrum is a very rich source of immunoglobulins. Pooled colostrum from nonimmunized cows provides an effective method of controlling symptoms in immunodeficient patients. Immunoglobulin concentrated may provide an effective, convenient method by which immunology can be administered.

Davidson GP, et al. Passive immunisation of children with bovine colostrum containing antibodies to human rotavirus. *Lancet* 1989;2(8665):709-12. A 10-day course of bovine colostrum with high antibody titre against the four known human rotavirus serotypes in protecting children against rotavirus infection was examined in children 3-15 months admitted to hospital. The allocation to treatment or control (an artificial infant formula) was randomised. 9 of 65 control children but none of 55 treated children acquired rotavirus infection during the treatment period.


Brüssow H, et al. Bovine milk immunoglobulins for passive immunity to infantile rotavirus gastroenteritis. *Journal of Clinical Microbiology* 1987;25(6):982-986. Protection against rotavirus, a dangerous pathogen which can cause serious, even fatal diarrhea in infants, can be passed orally through milk or colostrum safely and effectively.
Use of bovine milk concentrate containing antibody to rotavirus to treat rotavirus gastroenteritis in infants. *J Infect Dis*. 1987;156(1):158-66. The use of a concentrate containing milk immunoglobulins prepared from rotavirus-hyperimmunized cows to treat infants hospitalized for acute rotavirus gastroenteritis resulted in a significant reduction in the duration of excretion of virus.

Tzipori S, Roberton D, Chapman C. Remission of diarrhoea due to cryptosporidiosis in an immunodeficient child treated with hyperimmune bovine colostrum. *Br Med J (Clin Res Ed)*. 1986;293(6557):1276-7. Infusion of hyperimmune bovine colostrum produced against parasite antigen, given by nasogastric tube, was started after symptoms had persisted for three weeks in a 3 year old male. Vomiting and diarrhoea resolved within five days of treatment, and oocysts were no longer seen in the stools after eight days. Hyperimmune bovine colostrum may be useful in the treatment of many patients with immunodeficiency disorders.

Antibody to human rotavirus in cow's milk. *The New England Journal of Medicine* 1985;312(10):605-610. Raw and pasteurized milk contained detectable levels of IgG1 antibody directed at rotavirus. Commercially available infant formulas had little or no anti-rotavirus antibody activity. The alteration of milk-processing procedures or the addition of effective antibodies to milk preparations commonly used in the nutrition of young children may alter the clinical course of rotavirus infection or decrease the transmission of rotavirus throughout susceptible populations.

Colostrum-derived immunity and maternal-neonatal interaction. *Annals of the New York Academy of Sciences* 1983;409:82-95. Peyer's patches are found throughout the intestinal tract, and groups of similar immunoactive cells are found in the bronchial mucosa. Both the intestinal and bronchial immunoactive cell groups respond to allergens, antigens and pathogens by neutralizing or destroying them. In newborns, these special cell groups are not immediately operative but protection is provided by a variety of immune factors from the mother's colostrum. Antibodies found in colostrum protect against *Eschericia coli*, *Salmonella*, *Shigella*, *Vibrio cholera*, *Bacteriodes fragilis*, *Streptococcus pneumoniae*, *Bordetella pertussis*, *Clostridium diphtheria*, *Clostridium tetani*, *Streptococcus mutans* and *Candida albicans*.

Interferon synthesis by human colostral leucocytes. *Arch Dis Child*. 1979;54(2):127-30. The antiviral potential of human colostral leucocytes was assessed by their capacity to produce interferon. Leucocytes cultured from colostrum were stimulated by mitogens or Newcastle disease virus to produce interferon which, by metabolic and physicochemical criteria, corresponded to normal human leucocyte interferon. Prepartum cells produced higher levels than postpartum cells.

Human colostral cells: Phagocytosis and killing of *E. Coli* and *C. Albicans*. *The Journal of Pediatrics* 1978;93(6):910-915. Cells found in colostrum are able to ingest and kill both *E. coli* and *Candida albicans*.


Antibodies in milk for protection against human disease. *Milchwissenschaft* 1959;14:469-473. Antirotavirus antibodies from colostrum of immunized cows were effective in ameliorating rotavirus gastroenteritis in children.

**Colostrum Supplementation in Dogs & Cats**

Satyaraj E, et al. *Supplementation of diets with bovine colostrum influences immune function in dogs, British Journal of Nutrition* 2013;18:1-6. Dogs fed the bovine colostrum-supplemented diet demonstrated a significantly higher vaccine response (canine distemper virus) and higher levels of fecal IgA when compared with the control group. Supplementing diets with bovine colostrum also resulted in significantly increased gut microbiota diversity and stability. Diets supplemented with bovine colostrum significantly influence the immune response in dogs.

Kuribayashi T, et al. *Bovine colostral antibody against verotoxin 2 derived from Escherichia coli O157:H7: resistance to proteases and effects in beagle dogs, Comparative Medicine* 2009;59(2):163-7. A bovine colostral antibody against verotoxin (VT) 2 of Escherichia coli O157:H7 was administered orally to beagles and compared with beagles given bovine plasma antibody or saline. The amount of VT2 in feces decreased significantly more rapidly after administration of bovine colostral antibody than after administration of bovine plasma antibody or saline. FULL TEXT.

Giffard CJ, et al. *Benefits of bovine colostrum on fecal quality in recently weaned puppies, Journal of Nutrition* 2004;134(8 Suppl):2126S-2127S. Oral supplementation with bovine colostrum improves fecal quality in puppies subject to the stresses of diet and environmental changes. Bovine colostrum supplementation may be an aid in reducing the rates of recurrent gastroenteritis and improving the vitality of puppies in early life. FULL TEXT.


Beaumont SL, et al. *Effects of bovine lactoferrin on in vitro replication of feline herpes virus, Veterinary Ophthalmology* 2003;6(3):245-250. Bovine lactoferrin has a notable inhibitory effect on the in vitro replication of feline herpes virus prior to and during viral adsorption, but not after. It appears that the lactoferrin blocks adsorption to the cell surface and/or penetration of the virus into the cell.