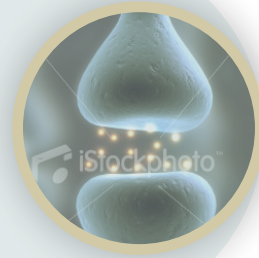


CHAPTER 8

WHAT ARE PROLINE-RICH POLYPEPTIDES?

Proline-rich polypeptides (PRPs) are one of the components of colostrum, as discussed in Part I. They function as signaling peptides that control the production of specific proteins, such as immunoglobulins, in cells of the immune system. Such signaling peptides are found throughout the body and are the main regulators of protein synthesis in cells for those proteins which are involved in extracellular functions, such as immunoglobulins.

Signaling peptides function as messengers in the body. They are how a cell keeps up with the latest news and events occurring in other parts of the body. If an infection of cold viruses is discovered in the lungs, for example, the cells of the immune system need to be informed of this so that they can join in the defense. So in this case the signaling peptides are like the alarm box in the firehouse. They warn the cells of the immune system that there is a problem and that they are needed to help fix it.

PRPs have the unique ability to modulate the immune system, increasing its activity level in the case of a challenge, such as an infection or a wound, and decreasing its activity level when the challenge is controlled. When an infection is detected by scout immune cells, chemical signals go out to mobilize other cells to come to the defense and fight off the infection. PRPs are one of the primary signals to go out at this time. And later, when the infection has been contained, PRPs are again one of the primary signals to call down the inflammatory response to the infection.

Thymocytes—lymphocytes which develop in the thymus gland in the neck—have PRP receptors on their surface membranes.[383] These thymocytes are stimulated by PRPs to either differentiate into helper T cells,[384] which are part of the inflammatory response to infection, or suppressor T cells[385] which inhibit the inflammatory response. PRPs regulate the differentiation and maturation of monocytes and macrophages, cells normally found in the bloodstream and connective tissue which are involved inflammation.[386] PRPs also induce resting B lymphocytes—lymphocytes that develop in the bone marrow—to differentiate and form mature B cells.[387] B cells are the only cells which produce immunoglobulins (antibodies).[388]

PRPs regulate the production of various cytokines, which are signaling molecules that regulate the immune response. These include IL-6 (interleukin-6), IL-10, INFγ (gamma interferon) and TNF-α (tumor necrosis factor-alpha).[389] This is one of the ways in which PRPs regulate the inflammatory response to infection. Both IL-6 and IL-10 are anti-inflammatory cytokines, but TNF-α is the main cytokine controlling the entire inflammatory cascade of cytokines. INF-γ is an inflammatory cytokine as well. It is particularly effective against viruses as it interferes with the genetic ability of viruses to replicate.

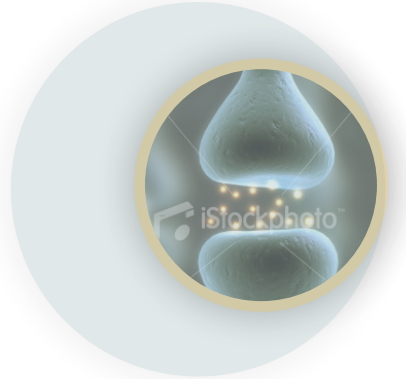
The inflammatory response consists of a complex series of events in which the body mobilizes its defenses to the site of the infection. PRPs are involved in that mobilization effort as well as controlling the production of immune proteins by immune cells. PRPs stimulate the production of leukocytes (white blood cells) which are a principal component of the inflammatory response.[390] PRPs increase the permeability of the blood vessels in the skin allowing immune cells and antibodies to enter the tissue space to fight off the infection.[391] PRPs stimulate natural killer (NK) cells, which are a specialized type of hunter-killer lymphocytes. They are the first responders in case of an infection and will attack and destroy anything they encounter that is not identified as "self."

PRP has been shown to be a potent stimulator of NK cell activity. Dr. Daryl See, MD, Director of the Bioassay Laboratory at the Institute of Longevity Medicine, conducted a comparative study of 196 dietary supplements that claimed immune

system enhancement, broad-spectrum antimicrobial activity and antioxidant action. Bovine colostrum was shown to promote significant NK cytotoxicity.[392] Later studies by Dr. See showed that transfer factor (PRPs) increased NK cell cytotoxicity by up to 400%. Among other natural products that increase NK cell cytotoxicity, none exceeded a 50% increase.[393] Another study by Dr. See showed that a combination of nutraceutical products, including transfer factor (PRPs), increased the cytotoxic activity of NK cells in patients with late-stage cancer.[394]

PRPs are immunoregulatory, however, so their function is not limited to calling out the troops in case of infection. They also come into play when it is time for the troops to stand down. If the inflammatory response to infection were allowed to continue once the infection has been controlled or isolated, then normal tissues would come under attack by the activated immune cells. Antibodies would be produced against proteins of the body rather than foreign proteins. This is exactly what happens in autoimmune conditions when the body begins attacking its own proteins, causing serious consequences. Thus the immunoregulatory effect of PRPs is just as important as their ability to mobilize the immune system to fight an infection. Due to this ability to both stimulate and dampen the immune response, PRPs have shown a great deal of promise in treating autoimmune conditions such as lupus, rheumatoid arthritis and Type 1 diabetes.

However, before we examine the benefits of PRPs in greater detail, let's take a look at the structure of PRPs and how signaling peptides actually work in the cell in order to give us a better idea of the process.



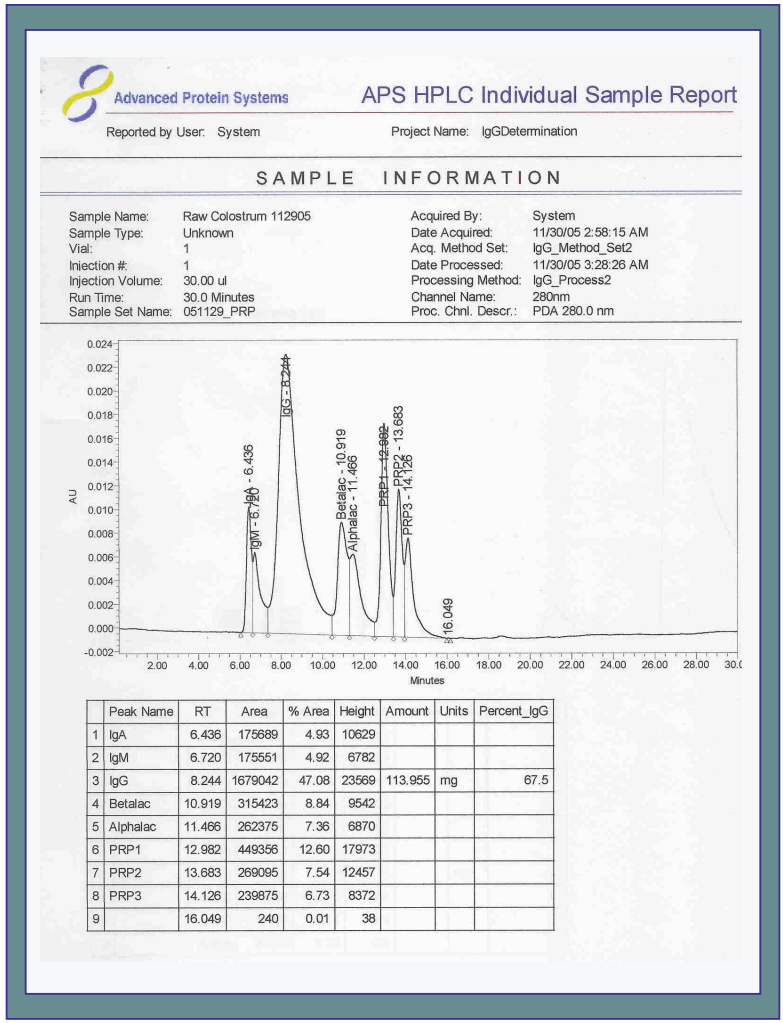
CHAPTER 9

STRUCTURE OF PRPS

A size exclusion ion-exchange column in a High Performance Chromatography Unit effectively separates the aqueous proteins in a liquid colostrum sample. The following pages in this chapter illustrate this peptide separation. Figure 1 shows an HPLC IX printout of a raw bovine liquid colostrum sample. Figure 2 shows the same colostrum sample, a liquid PRPS isolate, that has had the major colostrum components removed, leaving only the PRPs. By removing the other components of the beginning colostrum liquid, as shown in Figure 2, the peptides are now able to move more freely in the aqueous water solution, increasing the PRPs mass transfer coefficient, and thus transfer faster to our immune cells in our body, reducing molecular steric hindrance.

From Figure 2, the PRPs can be grouped by size into PRPS1 (larger, 2,500–5,000 molecular weight), PRPS2 (1,000–2,500 molecular weight), and PRPS3 (500–1,000 molecular weight). PRPS1 are the non-protein nitrogen component of colostrum, also seen in mammalian milk, and is biologically inactive. Figure 3 is a close-up of Figure 2 PRPs.

Using Proteomics (Gas Chromatography/Mass Spectrometry combined with an extensive peptide database) there have been many PRPs identified in colostrum. Figure 3 shows the molecular appearance of PRPS2 and PRPS3 peptides.



Advanced Protein Systems

APS HPLC Individual Sample Report

Reported by User: System

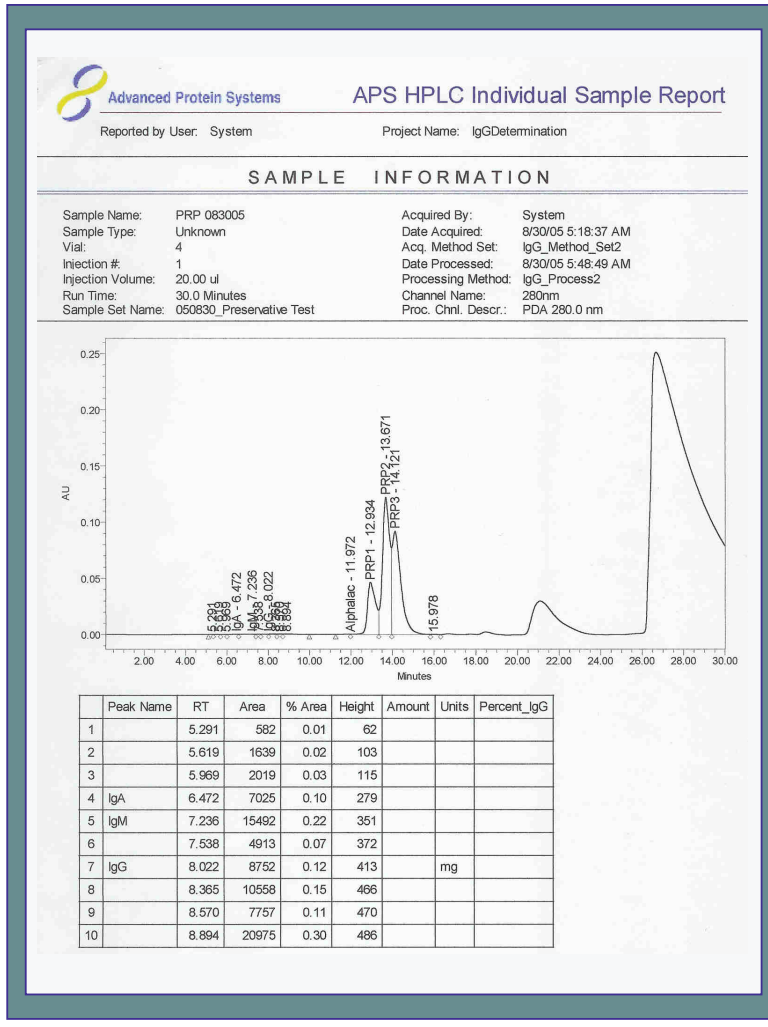
Project Name: IgGDetermination

SAMPLE INFORMATION

Sample Name:	Raw Colostrum 112905	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	11/30/05 2:58:15 AM
Vial:	1	Acq. Method Set:	IgG_Method_Set2
Injection #:	1	Date Processed:	11/30/05 3:28:26 AM
Injection Volume:	30.00 ul	Processing Method:	IgG_Process2
Run Time:	30.0 Minutes	Channel Name:	280nm
Sample Set Name:	051129_PRP	Proc. Chnl. Descr.:	PDA 280.0 nm

	Peak Name	RT	Area	% Area	Height	Amount	Units	Percent_IgG
1	IgA	6.436	175689	4.93	10629			
2	IgM	6.720	175551	4.92	6782			
3	IgG	8.244	1679042	47.08	23569	113.955	mg	67.5
4	Betalac	10.919	315423	8.84	9542			
5	Alphalac	11.466	262375	7.36	6870			
6	PRP1	12.982	449356	12.60	17973			
7	PRP2	13.683	269095	7.54	12457			
8	PRP3	14.126	239875	6.73	8372			
9		16.049	240	0.01	38			

Figure 1. HPLC of raw colostrum



	Peak Name	RT	Area	% Area	Height	Amount	Units	Percent_IgG
1		5.291	582	0.01	62			
2		5.619	1639	0.02	103			
3		5.969	2019	0.03	115			
4	IgA	6.472	7025	0.10	279			
5	IgM	7.236	15492	0.22	351			
6		7.538	4913	0.07	372			
7	IgG	8.022	8752	0.12	413		mg	
8		8.365	10558	0.15	466			
9		8.570	7757	0.11	470			
10		8.894	20975	0.30	486			

Figure 2. HPLC of PRPS liquid isolate

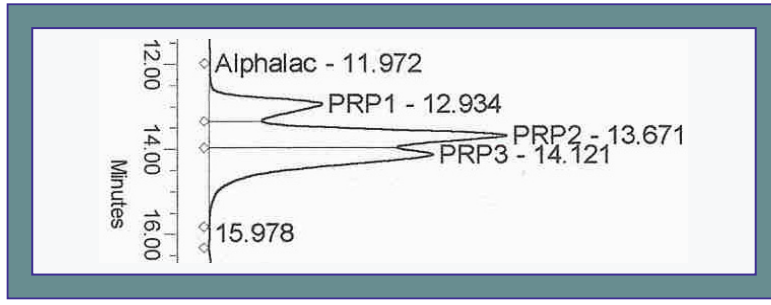


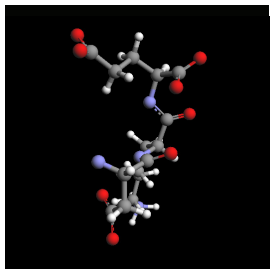
Figure 3. Close-up of PRPS1, PRPS2 and PRPS3 peaks.

	MW	Class	Approx. Volume	Amino Acid
				A= Ala= Alanine
Asp - Lys - Glu	390	PRP3	472	T = Thr Threonine
Leu - Asn - Phe	392	PRP3	474	V = Val= Valine
Ser - Glu - Gln - Pro	459	PRP3	555	C = Cys = Cysteine
Val - Val - Met - Glu - Val	576	PRP3	697	L = Leu = Leucine
Phe - Pro - Pro - Pro - Lys	585	PRP3	708	Y = Tyr = Tyrosine
Ser - Glu - Glu - Met - Pro	592	PRP3	716	I = Ile = Isoleucine
Pro - Gln - Ser - Val - Leu - Ser	630	PRP3	762	N = Asn = Asparagine
Asp - Ser - Gln - Pro - Pro - Val	642	PRP3	777	P = Pro = Proline
Val - Leu - Pro - Pro - Asn - Val - Gly	695	PRP3	841	Q = Gln = Glutamine
Asp - Pro - Pro - Pro - Pro - Gln - Ser	737	PRP3	892	F = Phe = Phenylalanine
Met - Gln - Pro - Pro - Pro - Leu - Pro	779	PRP3	943	D = Asp = Aspartic Acid
Ser - Trp - Met - His - Gln - Pro - Pro	882	PRP3	1067	W = Trp = Tryptophan
Ala - Phe - Leu - Leu - Tyr - Gln - Glu	883	PRP3	1068	E = Glu = Glutamic Acid
Arg - Gly - Pro - Phe - Pro - Ile - Leu - Val	898	PRP3	1087	M = Met = Methionine
Lys - Tyr - Lys - Leu - Gln - Pro - Glu	905	PRP3	1095	K = Lys = Lysine
Ser - Leu - Pro - Gln - Asn - Ile - Leu - Pro - Leu	994	PRP3	1203	G = Gly = Glycine
Val - Glu - Ser - Tyr - Val - Pro - Leu - Phe - Pro	1050	PRP3	1271	R = Arg = Arginine
Thr - Gln - Thr - Pro - Val - Val - Val - Pro - Pro - Phe	1084	PRP3	1312	S = Ser = Serine
Val - Tyr - Pro - Phe - Thr - Gly - Pro - Ile - Pro - Asn	1104	PRP2	1336	H = His = Histidine
Gln - Pro - Leu - Pro - Pro - Thr - Val - Met - Phe - Pro	1126	PRP2	1362	
Met - Pro - Gln - Asn - Phe - Tyr - Lys - Leu - Pro - Gln - Met	1397	PRP2	1690	
Leu - Phe - Phe - Phe - Leu - Pro - Val - Val - Asn - Val - Leu - Pro	1405	PRP2	1700	
Phe - Leu - Leu - Tyr - Gln - Glu - Pro - Val - Leu - Gly - Pro - Val - Arg	1531	PRP2	1853	
Val - Leu - Glu - Met - Lys - Phe - Pro - Pro - Pro - Pro - Gln - Glu - Thr - Val - Thr	1713	PRP2	2073	
Met - His - Gln - Pro - Pro - Gln - Pro - Leu - Pro - Pro - Thr - Val - Met - Phe - Pro	1717	PRP2	2078	
Asp - Leu - Glu - Met - Pro - Val - Leu - Pro - Val - Glu - Pro - Phe - Pro - Phe - Val	1729	PRP2	2092	
Leu - Lys - Pro - Phe - Pro - Lys - Leu - Lys - Val - Glu - Val - Phe - Pro - Phe - Pro	1786	PRP2	2161	
Leu - Gln - Thr - Pro - Gln - Pro - Leu - Leu - Gln - Val - Met - Met - Glu - Pro - Gln - Gly - Asp	1925	PRP2	2329	
Ser - Leu - Thr - Leu - Thr - Asp - Val - Glu - Lys - Leu - His - Leu - Pro - Leu - Pro - Leu - Val - Gln	2016	PRP2	2439	
Leu - Gln - Pro - Glu - Ile - Met - Gly - Val - Pro - Lys - Val - Lys - Glu - Thr - Met - Val - Pro - Lys	2024	PRP2	2449	
Asp - Gln - Pro - Pro - Asp - Val - Glu - Lys - Pro - Asp - Leu - Gln - Pro - Phe - Gln - Val - Gln - Ser	2067	PRP2	2501	
Ala - Thr - Phe - Asn - Arg - Tyr - Gln - Asp - Asp - His - Gly - Glu - Glu - Ile - Leu - Lys - Ser - Leu	2136	PRP2	2585	
His - Lys - Glu - Met - Pro - Phe - Pro - Lys - Tyr - Pro - Val - Glu - Pro - Phe - Thr - Glu - Ser - Gln	2191	PRP2	2651	
Leu - Ser - Gln - Pro - Lys - Val - Leu - Pro - Val - Pro - Gln - Lys - Ala - Val - Pro - Gln - Arg - Asp - Met - Pro - Ile - Gln	2470	PRP2	2989	

Table 1. Amino Acid Sequence of PRPS2 and PRPS3s.

Using Proteomics (Gas Chromatography/Mass Spectrometry combined with an extensive peptide database) there have been many PRPs identified in colostrum.

Figure 3 shows the molecular appearance of PRPS2 and PRPS3 peptides.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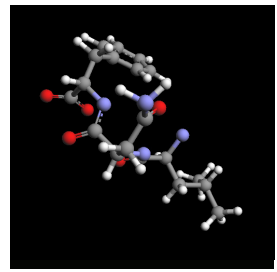
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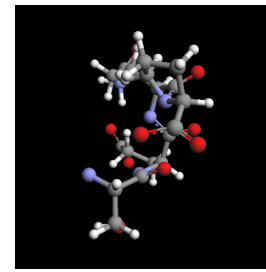
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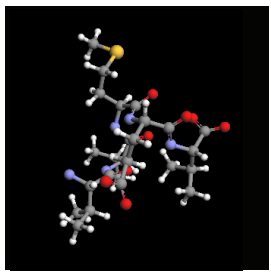
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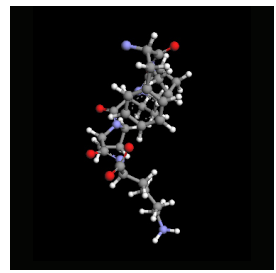
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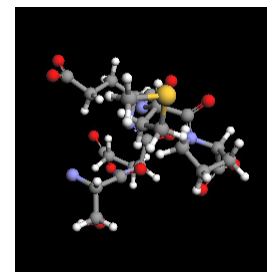
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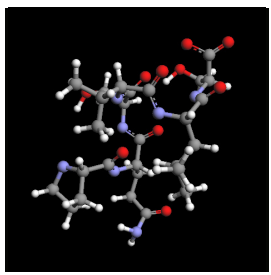
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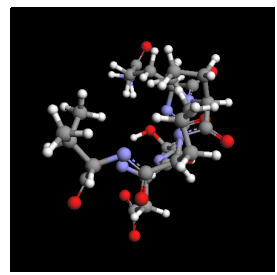
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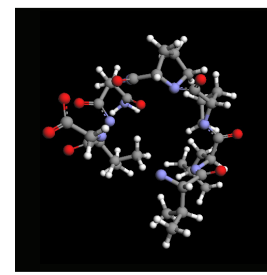
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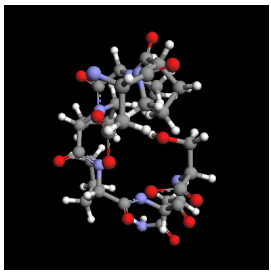

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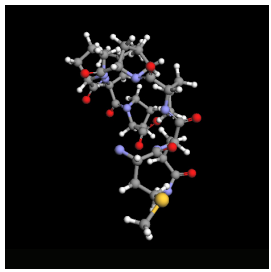

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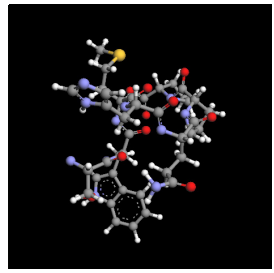

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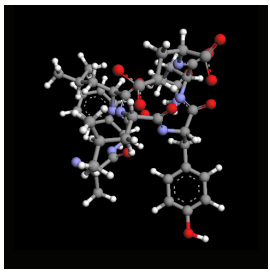

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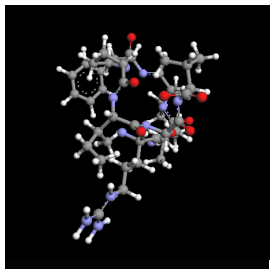

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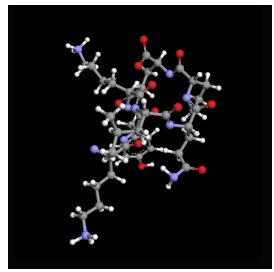

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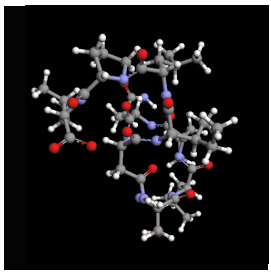

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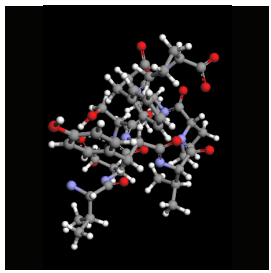

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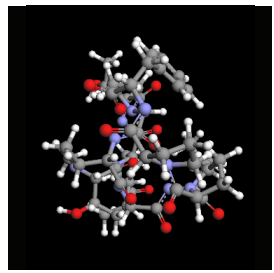

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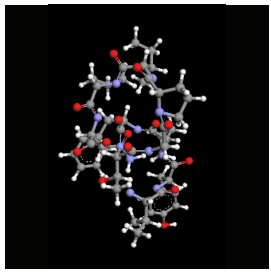

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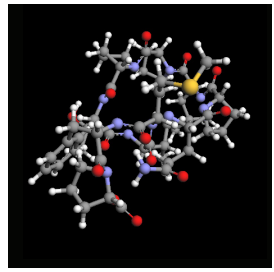

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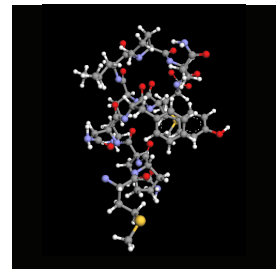

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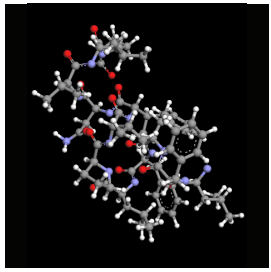

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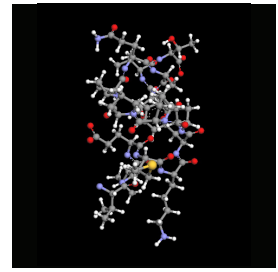

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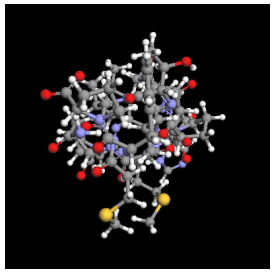

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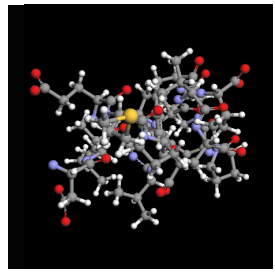

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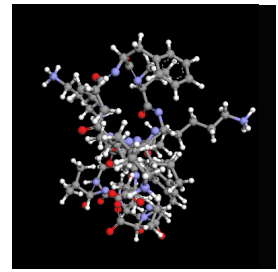

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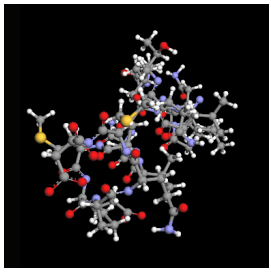

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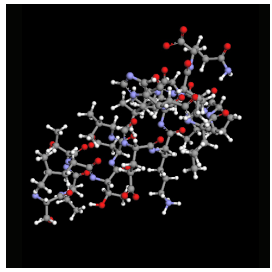

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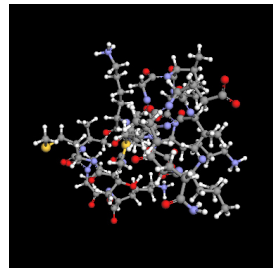

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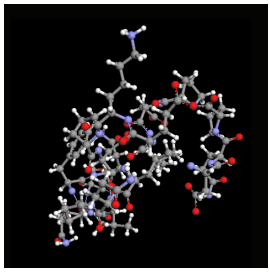

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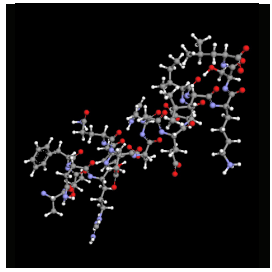

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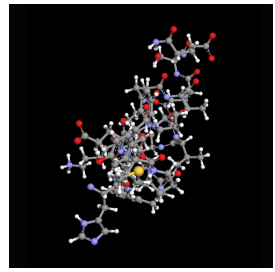

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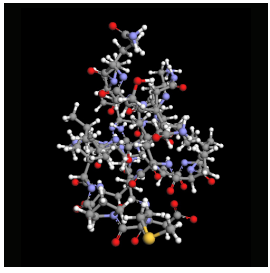
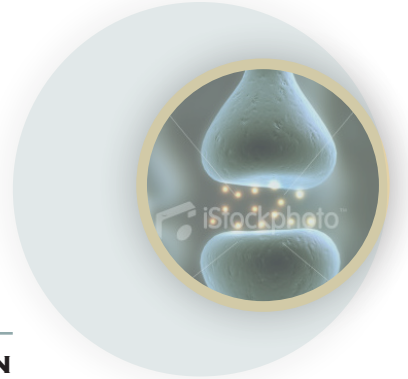


LSQPKVPVQKAVPQRDMPIQ

Figure 3. Molecular appearances of PRPS2 and PRPS3 peptides.



CHAPTER 10

SIGNAL TRANSDUCTION

When a peptide messenger attaches to a receptor on the surface of a cell, a series of biochemical reactions take place that result in some action occurring in the cell, such as a specific protein being produced by the cell. This process is called signal transduction. It may be worthwhile to take a look at how this process takes place to understand how PRPs and other signaling peptides function in the body.

The membranes that surround all cells in the body are composed of phospholipids—long fatty acid chains with hydrophilic (water-loving) and hydrophobic (water-fearing) areas that when assembled into a bilayered membrane form a selectively permeable barrier. The membrane is also composed of proteins that are embedded in the phospholipid and that function as receptors, channels and structural components of the cell. The receptors for PRPs and other signaling peptides are found in this pospholipid bilayer.

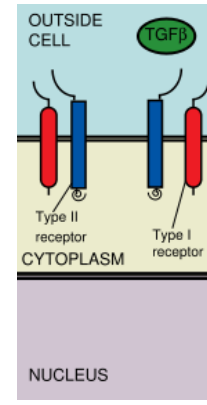


FIGURE 1 TGF-β AND ITS RECEPTORS IN THE CELL MEMBRANE. (DRAWINGS BY JEROME WALKER)

For an example of how signal transduction works, let us look at the signal transduction pathway that transforming growth factor-beta (TGF-β) activates.[395] First, the TGF-β molecule, known as a ligand (or binder), binds to the TGF-β receptor in the cell membrane of the target cell (re-

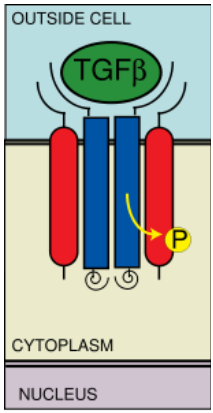


Figure 2
The ligand-receptor Complex.

ceptors for TGF-β are found on virtually every cell in the body), as shown in Figure 1. The Type 2 receptor shown is the TGF-β-specific receptor. The TGF-β molecule binds to two Type 2 receptors, and this action recruits two Type 1 receptors, which are not specific to TGF-β. These all bind together with the TGF-β molecule to form a complex (Figure 2).

The binding of these molecules together causes the Type 2 receptors to rotate to expose the enzymatically active portion of the receptor. When this happens, the Type 2 receptor phosphorylates (donates a phosphorus atom) the Type 1 receptor. This activates the Type 1 receptor protein. Meanwhile a protein in the cytoplasm of the cell, called SARA (SMAD anchor for receptor activation), brings another protein called RSMAD to the Type 1 receptor and facilitates its binding to the receptor (Figure 3). The phosphorus atom the Type I receptor received from the Type II receptor is then passed to the RSMAD. The result of this

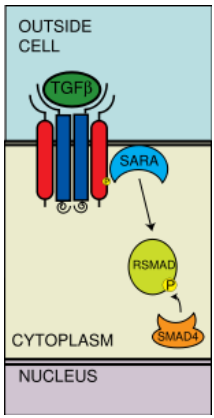


Figure 4
RSMAD release from receptor complex

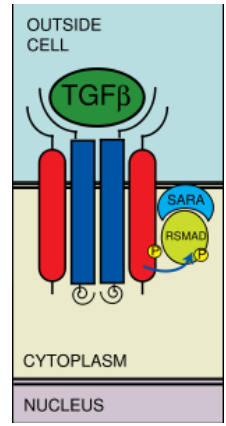


Figure 3
Phosphorylation of RSMAD

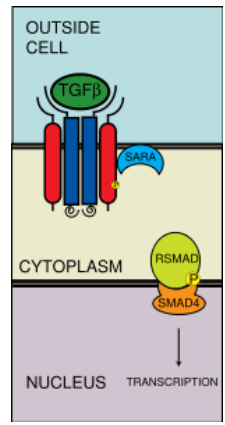
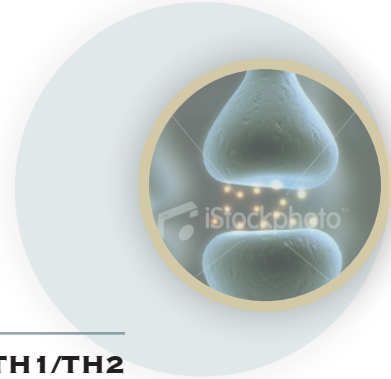


Figure 5
RSMAD-SMAD4 complex enters cell nucleus to initiate mRNA transcription

phosphorylation of the RSMAD is that it changes conformation and is released from the TGF-β-receptor complex (Figure 4). The RSMAD moves through the cytoplasm of the cell and binds to a coSMAD, in this case SMAD4. The combination of the RSMAD and coSMAD enter the nucleus of the cell (Figure 5) where it binds with transcription promoters and cofactors to cause the transcription of mRNA (messenger RNA), which then is used to synthesize the protein in the ribosomes of the cell. In the case of TGF-β, the protein would be one of several that TGF-β initiates, including proteins involved in apoptosis (programmed cell death), extracellular matrix formation, and immunosuppression.

This brief (and simplified) description of how signal transduction works inside the cell illustrates what a complex process is involved. With so many different steps and proteins involved, there are many places where regulation of the process can—and does—take place. This is how PRPs are able to modulate the immune response, by the action of regulatory proteins at different stages of the signal transduction cascade of events.

Now that we have some idea of how PRPs work, let us explore further the benefits of PRPs.



CHAPTER 11

THE ROLE OF PRPS IN TH1/TH2 CYTOKINE BALANCE

Role of Th1, Th2

Before one can understand the usefulness of PRPs, it is helpful to have an understanding of the Th1 helper/Th2 helper paradigm.[396] T helper lymphocytes develop along two lines of cell populations. Th1 cells, which modulate cell-mediated immunity, produce the cytokines IL-2, IFN-gamma, and TNF-alpha. Th2 cells, which modulate humoral immunity, or antibody production, produce IL-4, IL-5, IL-6, IL-10, and IL-13. Once you're familiar with the particular Th1/Th2 predominant phenotypes in a patient, you can more easily identify certain constellations of diseases or conditions and tailor your therapies.

Cell-mediated, or Th1 helper responses, are important in the body's ability to defend itself against viruses, fungi, parasites, cancer, and intracellular organisms. Cell-mediated immunity can be tested by:

1. Skin tests–delayed hypersensitivity skin testing;
2. Response to non-specific mitogens, such as phytohemagglutinin (PHA), concavalina, or pokeweed mitogens;
3. Response to specific mitogens, such as diphtheria, tetanus, or candida;
4. Response to alloantigens—mixed lymphocyte reaction;
5. T cell subsets;

6. IL-2R;
7. NK cell level;
8. NK cell activity;
9. IL-1 assay; and
10. IL-2 and interferon gamma, and other cytokines.

If one has a Th2-dominated condition with decreased cellular immunity and heightened humoral immunity, the conditions that tend to prevail are:

1. Allergies
2. Chronic sinusitis
3. Atopic eczema
4. Asthma
5. Systemic autoimmune conditions such as lupus erythematosus and mercury-induced autoimmunity
6. Vaccination-induced state
7. Certain cases of autism
8. Hyperinsulinism
9. Pertussis vaccination
10. Malaria
11. Helminth infection
12. Hepatitis C
13. Chronic giardiasis
14. Hypercortisolism
15. Chronic candidiasis
16. Cancer
17. Viral infections
18. Ulcerative colitis

A Th1-dominated picture would include the following medical states:

1. Diabetes Type 1
2. Multiple sclerosis
3. Rheumatoid arthritis

4. Uveitis
5. Crohn's disease
6. Hashimoto's disease
7. Sjögren's syndrome
8. Psoriasis
9. Sarcoidosis
10. Chronic Lyme disease
11. Helicobacter pylori infections
12. Entamoeba histolytica

Pregnancy is a Th2-dominant state. This is an advantage during pregnancy, since a Th1-dominant state, or cell-mediated immune response, would induce rejection of the fetus and placenta. Because it stimulates a Th1 response in most cases, PRPs should not be used in pregnancy. Certain autoimmune conditions, such as multiple sclerosis and rheumatoid arthritis, which are Th1-dominant states, are ameliorated during pregnancy.

Th1-dominant states are generally not helped by PRPs, and could be exacerbated. Many of them, such as rheumatoid arthritis, multiple sclerosis, and Crohn's disease, are thought to be possibly caused by an infection or reaction to a pathogen. If the Th1 response is an inadequate attempt of the immune system to fight off a microbe, then PRPs would augment that process and be effective in certain cases. Clinically, this is seen in certain cases, e.g., Crohn's disease, multiple sclerosis, and chronic Lyme disease, where PRPs help a Th1-dominant condition.
PRPs augment cell-mediated immunity or push a Th2 to a Th1 state. This is useful in Th2-dominated conditions. Normally, on exposure to gut-related microbes and childhood infections, a child's Th2-dominated immune system is subject to Th1 stimulation and Th1/Th2 balance ensues.[399] If TH2 dominance remains, this can lead to atopic (allergic) states. We see this in the increased incidence of allergic symptoms, postnasal drip, asthma, etc, in clinical practice.

The other side of this Th2 state is a decreased Th1 or cell-mediated immunity. With this, we see an increased incidence of viral infection, fungal infection, and cancer. Vaccinations tend to push the immune system toward a Th2-dominant state.

To help overcome this tendency, we can use PRPs pre- and post-immunization.

Cancer, Cell-mediated Immunity, and PRPs

Since cancer can be associated with a Th1-deficient state, use of PRPs should be considered as part of immune augmentation therapy. Factors that decrease cell-mediated immunity and increase Th2 dominance are age, cytotoxic cancer treatments, post-surgery stress, metastatic disease, etc.[400] Cell-mediated immunity (CMI) can be a predictor of morbidity and mortality over the age of sixty. In patients with liver metastases or colon rectal carcinoma, CMI is predictive of survival.[401] Decrease in cell-mediated immunity, along with an increase in circulating immune complexes, indicates unfavorable prognosis in cancer patients.[402] Studies show that patients who have multiple skin cancers had impaired CMI.[403] In a study of gynecological cancer patients compared to control groups, those on chemotherapy had a decrease in immune parameters (i.e., refractory decreased cell-mediated immunity), whereas the group getting immunotherapy (in this case, thymopeptin) maintained their immune parameters at normal levels.[404,405] Immunologically deficient cancer patients are susceptible to infection by viral pathogens, such as herpes zoster and cytomegalovirus (CMV). Infection occurs as a result of cytotoxic therapy and deficiency of cell-mediated immunity.[406] Th1-dominant states, characterized by increased amounts of IL-2 and IFN-γ, are immuno-stimulatory and limit tumor growth. In contrast, Th2-predominant patterns, characterized by IL-4 and IL-10 cytokines, are immuno-inhibiting and stimulate tumor growth. HIV progression to HHV-8 infection with Kaposi's sarcoma, ulcerative colitis, progression to colon cancer, and obesity with increased incidence of carcinoma are all associated with the increased Th2 state (and decreased cell-mediated immunity). Studies suggest that this shift to Th2 dominance precedes the cancerous transformation. As the cancer grows, it becomes increasingly hypoxic. This leads to further suppression of cell-mediated immunity, allowing decreased immune surveillance. Studies show that a Th2 immune response is associated with a proangiogenesis state, which facilitates cancer growth.[407]

PRPs have been shown to improve cellular immunity in patients with immune defects.[408] Since they augment Th1 or cell-mediated immunity, PRPs are helpful in

these situations. For example, by conveying cell-mediated immunity against bladder and prostate tissue-specific antigen, PRPs were efficacious in the treatment of stage D3 hormone-unresponsive metastatic prostate cancer. Follow-up showed increased survival rates in fifty patients, with complete remission in two, possible remission in six, and no progression of metastatic disease in fifty-eight.[409] PRPs were shown to improve survival as an adjunct to resection in non-small cell lung carcinoma.[410]

Before PRPs were derived from colostrum, it was obtained from dialyzed leukocyte extract (DLE). The literature has many citations of DLE of an antigen-specific nature being used for various viral conditions, autoimmune conditions, and certain cancers. It has been found that DLE facilitated immunity to tumor-associated antigen. Fudenburg showed that PRPs could, from selected donors, increase the cell-mediated responses to tumor-associated antigens in human osteogenic sarcoma patients.

One of the compromises on our cell-mediated immunity is environmental stress (e.g., chemical or heavy metal pollution). It has been shown that long-term exposure to polychlorinated hydrocarbons suppresses phagocytosis, decreases NK cell activity, and reduces lymphocyte response to mitogens in mice.[411] Alterations in immune dysregulation, with a predominantly Th2 response, occurs with lead and mercury exposure. This leads to impaired cell-mediated immunity, increased incidence of infectious disease or cancer, and can end with an autoimmune disease.[412]

Viral Infections

Currently in medicine, we are seeing increased problems with viral infections, such as otitis media, measles, chronic fatigue, Epstein-Barr virus (EBV), cytomegalovirus (CMV), acquired immunodeficiency syndrome (AIDS) due to human immunodeficiency virus (HIV), hepatitis, and West Nile virus. Treatment regimens range from interferon to azidothymidine (AZT), ribavirin, and relenza. However, even with all the high-tech immune weapons available, we are still losing the battle.

In the treatment of viral infections, PRPs provide a modality that works at a fundamental level. They have been shown to induce interferon in patients with viral infections.[413]

Viral infections tend to have increased Th2 and decreased Th1. This is also seen with fungal infections, parasitic diseases, and cancer. Bacterial infections are associated with decreased Th2-dominant states.

By stimulating Th1, PRPs may be advantageous in the treatment of hepatitis. In hepatitis C, the activation of the Th2 dominance plays a role in the development of chronic hepatitis changes. Th1 stimulation may result in clearance of viral particles and improvement in the hepatitis.[414,415] Studies show that severe complicated measles has been treated successfully with non-specific PRPs. Symptoms were ameliorated within 24 hours, without side effects.[416]

One theory claims that one of the mechanisms involved in autistic spectrum disorders is an immune imbalance toward a dominant Th2 pattern, resulting from measles, mumps, and rubella (MMR) vaccination. Currently, a study is ongoing to test the efficacy of PRPs to act as an immune modulator in this disorder.

It is well-known that viruses play an important role in the etiology of acute otitis media (AOM) in children. In a study of AOM, 75% of the children were positive for viruses such as respiratory syncytial virus (RSV), parainfluenza, and influenza, and 48% had the causal viruses in the middle ear effusion.[417] These viruses probably act as antecedents to the bacterial infections typical of AOM.[418] This could account for the excellent results seen in early treatment and prevention of otitis media using PRPs.

A certain percentage of asthmatics have their symptoms precipitated by respiratory infection, most of these secondary to viral infections. A study conducted with PRPs and asthmatic patients showed that approximately 50% discontinued their steroid medication and the other half decreased their steroid use. Overall, there was a decrease in hospital admissions. Administration of PRPs improved cellular immunity. No adverse effects or allergic reactions were observed.[419]

An increased incidence of infection, such as parainfluenza virus, syncytial virus, adenovirus, etc, may be precipitating factors in children who have asthma. It was also found that children with asthma have a propensity toward frequent infection.[420] Twelve of fifteen children exhibited defects in T cell immunity, many of which were not drastic[421]. This should emphasize that functional, suboptimal defects in cell-mediated immune function can be a factor in viral illnesses, as measured with sensitive immunological testing. Once again, we see that PRPs can help in conditions with increased susceptibility to viruses, a dominant Th2 (decreased cell-mediated) profile.

It was found that women with extended human papilloma virus (HPV) infections have defective protective mechanisms of cell-mediated immunity.[422] A pronounced shift from Th1 to Th2 cytokine pattern is associated with more extensive HPV infection. Increased gynecological problems are found secondary to HPV. The potential of PRPs in HPV infections needs to be further explored.

Chronic Infection

The addition of PRPs can help an impaired immune system that is subject to chronic infections. How many practitioners see this scenario? A child comes down with recurrent bronchitis or tonsillitis, starting shortly after birth, necessitating frequent courses of antibiotics. This can then lead to symptoms of chronic candidiasis. A history of chronic eczema or allergic diathesis can also be found. Immunological or skin testing shows a mild defect in cell-mediated immunity, but no abnormalities. Grohn reported on several similar cases and obtained successful treatment with administration of PRPs.[423] Here we see that PRPs are helpful for elevated Th2 states, allergy, chronic candidiasis, and eczema.

PRPs have ameliorated cases of recurrent, non-bacterial cystitis (NBRC) when treatment with antibiotics and nonsteroidal drugs was unsuccessful, and cell-mediated immunity to herpes simplex and candida was decreased.[424] Various studies show positive results with PRPs in chronic mucocutaneous candidiasis.[425]

In Lyme disease, cytotoxic production of a Th2 phenotype is correlated to resis-

tance, while that of a Th1 phenotype is correlated to susceptibility.[426] This suggests that certain people have an immune glitch that makes their immune system prone to either the Th1 or Th2 pattern, and therefore more susceptible to different diseases. This may be precisely where PRPs, having immunomodulating activity, can be helpful. For instance, in Lyme patients we usually see a Th1 dominated pattern, but PRPs work very well for certain subsets of Lyme patients.

Chronic Fatigue

PRPs have been used in chronic fatigue immune dysfunction syndrome, especially if a viral etiology can be found. It has had varied success, although one may need to use increased dosages. If polyvalent PRPs are not successful, the use of antigen- or disease-specific PRPs may need to be explored.[427]

In elderly patients with cellular immunodeficiency and chronic fatigue syndrome, age-related decrease in recovery occurred after treatment with PRPs[428]. Success with PRPs in chronic fatigue syndrome secondary to human herpes virus-6 (HHV-6), genital or labial herpes, and recurrent ocular herpes has been well-documented.[429,430,431] A study on the effect of PRPs on the course of multiple sclerosis showed that it retarded the progression of the disease in mild to moderate cases.[432]

The Treatment

Treatment with PRPs is dose-dependent. In viral infections, one usually starts with three sprays three times a day. The dose is then tapered down to one spray three times a day. That dose is maintained in cases of chronic viruses, chronic herpes infection, chronic fatigue secondary to CMV or EBV, chronic colds and impaired resistance. If there is any flare-up in viral infections, the dose can be increased to three sprays three times a day. Usually patients report decreased susceptibility to colds and decreased nasal symptoms (for instance, postnasal drip and chronic sinus symptoms). In allergic conditions, an adult starts with two sprays three times a day, increasing to three sprays three times a day if symptoms worsen. Again, the dose is tapered to a maintenance level with amelioration of allergic symptoms.

In cases of chronic fatigue syndrome, patients start on three sprays three times a day. One may need to increase the dose depending on the response. Doses of four to five sprays three times daily can be used as an adjunct cancer treatment for patients undergoing chemotherapy and/or radiation therapy, with a resulting decrease in cellular immune function.

Various immune function tests, especially those measuring CMI, can be done to gauge maintenance dosage. One can also perform a cytokine panel, measuring IL-2, IL-4, IFN-γ, IL-10, etc. An elevated IL-2 and IFN-γ would indicate a TH1-predominant state, while an elevated IL-4 and IL-10 would point to a TH2-dominated state. NK cell activity, which is usually decreased in cases of cancer, is increased secondarily to PRP administration and can be periodically measured.

Occasionally when a patient starts PRPs, he or she may experience flu-like symptoms, nausea or gastrointestinal symptoms. Since PRPs are small peptides and do not contain milk protein, allergic reactions are rare. These symptoms are usually classified as Jarisch-Herxheimer reactions, and they probably signify a direct reaction of PRPs on gut or systemic pathogens. If patients are informed of these possible mild adverse reactions, they are more likely to continue treatment.

PRPs and Other Alternative Therapies

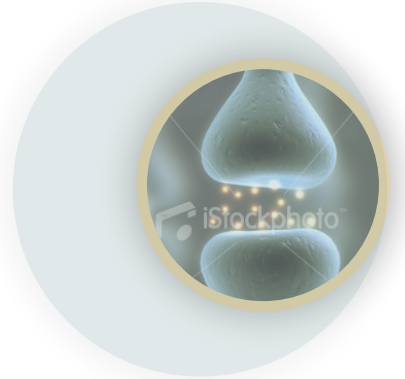
In complicated immune cases or in adjunct cancer treatment, it is advantageous to add complementary classes of herbs and nutrients to augment the immune-stimulatory effects. These auxiliary factors boost natural killer cell activity, increase phagocytosis, increase maturation of T cells, enhance general immunity, and trigger the complement cascade, helping cytotoxicity. Compounds that act synergistically with PRPs include thymic protein factors, Chinese herbs (such as astragalus, cordyceps, shiitake, maitake, and reishi mushrooms), inositol hexaphosphate, melatonin, 1-3 beta glucan, glutathione, and associated antioxidants. Vitamins A D, and B_6 promote the Th2 pattern, while vitamins E, C and folate support the production of a Th1 response.[433] Vitamin B_{12} suppresses the Th1 response.[434] In addition, acupuncture has been found to increase the immune perimeters of CMI. Levels of CD3+, CD4+, CD4+/CD8+ and beta-endorphins were found to be increased in patients with malignant tumors after a course of acupuncture treatment.[435]

Thymic factors cause maturation of naïve T cells and increase cell-mediated immunity. It is known that PRPs are more effective in post-thymic cells. Therefore both thymic factors and PRPs are recommended for mild thymic primary immunodeficiency.[436,437] A recent study by Dr. Daryl See showed that PRPs enhanced natural killer cell cytotoxic activity. The effect of PRPs was greater than that observed with other well-known NK cell activity enhancers, such as echinacea, acemannan, 1-3 beta glucan, IP-6, and certain Chinese mushrooms. Colostrum had one-quarter the potency. Other immune parameters, such as T cell function and test of cellular immunity, were not done in this particular study.[438]

Conclusion

Immune system functioning is at the heart of the increasing infectious and immunologic disorders seen in clinical practices. Through its unique properties and activities, PRPs are an extremely useful, relatively risk-free alternative and adjunctive therapy for treatment of cell-mediated or Th1-deficient conditions. Think of its potential use in illnesses such as cancer, chronic fatigue, viral infections, allergies, fungal infections, chronic infections, and autoimmune conditions.

[The Role of PRPs in TH1/TH2 Cytokine Balance, courtesy of Dr Steven J. Bock. Dr. Bock has been practicing alternative and integrative medicine for over 20 years. He has extensive experience in the integrative treatment of Lyme disease. Dr. Bock is a certified acupuncturist. He is medical director of The Rhinebeck Health Center, The Center for Progressive Medicine, and PatientsAmerica.com. He is the author of Natural Relief for Your Child's Asthma ***and*** Staying Young the Melatonin Way *(New York: Plume Books, 1996).]*



CHAPTER 12

BENEFITS OF PRPS

So far we have talked about how PRPs work in the body and how they affect the immune system. Now let us look more closely at the benefits PRPs provide.

PRPs are potent antivirals. Viruses are immune to antibiotics as antibiotics attack bacteria but not viruses. Going to the doctor to get antibiotics for a viral infection, such as a bad cold or the flu, is actually worse than counterproductive. Taking antibiotics unnecessarily kills off the flora in the intestines, which can lead to overgrowth by harmful bacteria or fungus, such as ***Candida***. This leads to leaky gut syndrome, poor nutrition and more disease. Furthermore overuse of antibiotics results in resistant strains of dangerous bacteria which no longer are susceptible to antibiotics. This can have fatal results. And you still have the viruses to contend with.

PRPs are known to provide immunity to a number of dangerous viruses.[439] These include all types of herpes viruses,[440,441,442,443,444,445,446] which are notoriously difficult to treat with standard pharmaceutical means. They are also effective against HIV,[447] measles,[448] and other viruses. Epstein-Barr virus (EBV) is a form of herpes virus that has been associated with infectious mononucleosis, Burkitt's lymphoma, nasopharyngeal cancer and autoimmune conditions, including chronic fatigue syndrome and multiple sclerosis. Anti-Human Herpes Virus-6 (HHV-6) PRPs have shown some promise in the treatment of multiple sclerosis, while both anti-HHV-6 and anti-EBV demonstrated some efficacy in the treatment of chronic fatigue syn-

drome.[449] PRPs have been used in the treatment of hepatitis B,[450] which is caused by the hepatitis B virus. PRPs are effective in the treatment of epidermodysplasia verruciformis (EV), a chronic viral infection of the skin caused by a variety of human papilloma viruses that is very resistant to standard treatments.[451]

There are also clinical reports of PRPs being used successfully against difficult bacterial and fungal infections. These include lung infections with ***Mycobacterium fortuitum***[452] and ***Mycobacterium tuberculosis***[453] (the causative agent of tuberculosis), cryptosporidiosis diarrhea in AIDS patients,[454,455] typhoid fever,[456] and melioidosis, a tropical infection found in immunocompromised individuals caused by ***Pseudomonas pseudomallei.***[457] PRPs are particularly effective against ***Candida*** fungal infections.[458,459,460]

PRPs have shown promise in the treatment of some cancers, though these studies are still in the early stages. These include mycosis fungoides[461] (lymphoma of the skin), nasopharyngeal carcinoma, renal cancer,[462] prostate cancer,[463] non-small cell lung cancer,[464,465] Hodgkin's disease,[466] melanoma metastatic to lung,[467] and osteogenic sarcoma.[468]

As part of their function to balance the immune system, PRPs have also been shown to prevent allergic responses to common indoor and outdoor allergens, including ragweed pollen and dust mites. PRPs decreased IgE and IgG1 production, significantly decreased airway eosinophilia (the accumulation of eosinophils, a type of white blood cell associated with inflammation, in the airway), and decreased mucous production and hypersensitivity to allergens.[469]

Oral supplementation of PRPs quickly modulate or balance the body's cytokine panel, particularly IL-4, IL-10 and IL-14. By down regulating these pro-inflammatory cytokines, food, airborne, and environmental allergens are then not recognized as allergies by the body's immune system. Thus the cytokine cascade immune response to these allergens does not result in the production of IgE antibodies.[470]

Atopic dermatitis, an allergic skin condition, responds favorably to treatment with PRPs, resulting in statistical improvement in all four clinical parameters (erythema,

eczema, pruritus, and papulae).[471] PRPs have also proven effective in the treatment of asthma,[472,473] again by the down regulation of particular cytokines, e.g., IL-5 and IL-9.

It is this property of modulating the immune system that can be used to advantage in the treatment of autoimmune disorders with PRPs.[474] Autoimmunity occurs when the body makes antibodies against its own proteins. There are many autoimmune conditions, such as rheumatoid arthritis, diabetes type 1, lupus erythematosus, multiple sclerosis, Sjögren's syndrome, pernicious anemia, Addison's disease, and so forth. PRPs have shown promise in treating these conditions by turning down the immune response to normal levels.[475,476] Laboratory trials in an experimental system using mice with induced hemolytic anemia showed that supplementation with PRPs resulted in longer lives and less evidence of the disease. Those mice started on treatment earlier in the progression of the disease had better results, suggesting that PRPs may induce suppressor T lymphocytes that control the development of the disease.[477] In another experimental trial, PRPs restored normal immune functioning.[478] Moderate success was found in treating multiple sclerosis.[479] PRPs were used successfully in a clinical trial with rheumatoid arthritis.[480] PRPs produced a "dramatic clinical and immunologic response" in lupus.[481] They have shown benefit in the treatment of Behçet's syndrome[482,483] as well as chronic fatigue syndrome.[484] An autoimmune-like disease called sarcoidosis, characterized by the formation of granular inflammatory nodules in various organs and thought to be caused by an alteration in immune function, also responds to treatment with PRPs.[485]

PRPs have shown great promise in slowing and even reversing the effects of Alzheimer's disease and other neurodegenerative disorders. There is some indication that some such disorders have a basis that resembles autoimmunity as there are remarkable similarities between the central nervous system and the immune system. A chemical that stimulates B cell replication and function in the immune system was tried in patients with Alzheimer's who had atrophy of the frontal lobe and immune dysfunction with dramatic response both immunologically and clinically.[486] Later studies have confirmed that PRPs significantly improved the condition or stabilized the progression of the disease.[487,488,489] PRPs have been

successfully used in the treatment of epilepsy[490,491] as well, indicating that they may potentially be of benefit in a variety of neurological conditions.

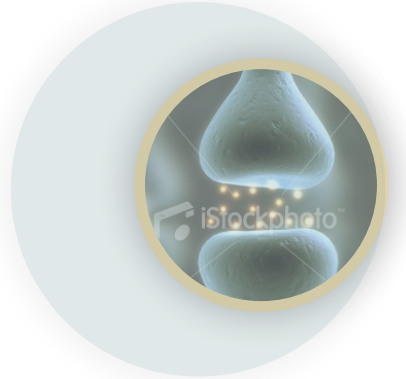
PRPs are an immune modulator, that is, a substance that produces differential responses in different classes of immune cells. This is different from strict immune stimulants and suppressors. Strict immune stimulation can lead to immune system exhaustion and can lead to immune compromise and ineffectiveness. PRPs are a true immune modulator since they also contain inducer and suppressor fractions and demonstrate different effects on various immune cell populations. This is in keeping with the differential functions of PRPs.

It is important to point out that PRPs appear to produce immunity by stimulating cell-mediated immunity rather than by transferring immunity, say, from a cow to a man as was originally believed. This was discussed in detail in Chapter 8. The fact that PRPs provide immunity to certain viruses, such as herpes and HIV, does not mean that they will not stimulate immunity to other types of viruses as they are doing so by stimulating the immune system to develop immunity, not "transferring" immunity from one organism to another.[492] It is also important to note that in all of these studies no side effects, adverse reactions or drug interactions were noted. PRPs are safe to use.

The immunomodulatory effect of PRPs may prove lifesaving if the threat of avian influenza ("bird flu," the H5N1 strain of influenza virus) becomes a reality. Health authorities are concerned that this deadly strain of flu could make the jump from birds to humans with deadly results—a global pandemic similar to the one in 1918 that killed millions. The bird flu virus kills by short-circuiting the immune system, disabling the feedback system that turns the immune response off before it can damage the body. The inflammatory response remains turned on, pumping out pro-inflammatory cytokines. The lungs become filled with fluid from the inflammatory process. The result is that the patient dies, not from the flu, but by literally drowning in his or her own fluids.[493] By modulating the immune system to normal levels, PRPs may be able to prevent this result, allowing the flu virus to be handled normally by the immune system.[494]

PRPs are also cytokine modulators. Cytokines are a diverse group of soluble proteins and peptides that act as humoral regulators at nanomolar to picomolar concentrations and which, either under normal or pathological conditions, modulate the functional activities of individual cells and tissues. These proteins also mediate interactions between cells directly and regulate processes taking place in the extracellular environment. Cytokines IL-1 and -6, interferon-γ and lymphokines have been shown to stimulate the lymph glands and are thought to be highly effective antiviral immune substances. Interleukins regulate the duration and intensity of the immune response and are responsible for cell-to-cell communication as well as boosting T cell activity and the production of immunoglobulins.

In summary, PRPs present an alternative to standard, pharmaceutical drug-based medicine and offer hope against otherwise difficult to treat or untreatable conditions. They are safe and come from a trusted source—cow's colostrum. Now we shall explore a real-life trial of PRPs in the fight against AIDS.



CHAPTER 13

PRPS AND AIDS

Since AIDS first appeared in the early 1980s, over 25 million people have died from the disease and an estimated 33.2 million people are infected with the HIV virus, according to WHO. In 2007 alone, approximately 2.1 million people died from the disease, including around 330,000 children under fifteen. Hardest hit of all is sub-Saharan Africa. Over three-quarters of all deaths from AIDS in 2007 occurred in this region.[495] Whole areas of some countries have been emptied of inhabitants, and the number of orphaned children continues to skyrocket. It is estimated that one in three people in Botswana are infected and life expectancy has declined from 65 pre-AIDS to only 40 today.[496]

While more effective remedies for treating AIDS have become available, the high cost of such remedies effectively prevents the people of so-called Third World countries from receiving these remedies. If an effective alternative could be found to the high-priced pharmaceutical drugs currently being used in the West, many lives could be saved which might otherwise be lost.

AIDS is an unusual viral infection in that the virus, a retrovirus known as Human Immunodeficiency Virus (HIV), attacks the very cells that normally would protect the body against a viral attack, the CD4+ lymphocytes (T cells), macrophages, and dendritic cells of the immune system. Infection by the virus kills cells in three ways: direct viral killing of the cells when the virus replicates; increased rates of apoptosis (programmed cell death) of infected cells; and targeting by CD8 cyto-

toxic lymphocytes that recognize infected cells and kill them. Eventually the T cell levels degrade to such low levels that cell-mediated immune function is lost. This leaves the body open to opportunistic infections, such as ***Pneumocystis pneumonia*** or Kaposi's sarcoma. These secondary infections are what eventually kill the victim. As PRPs are known to be immunomodulatory, up-regulating the immune system when it is underperforming and down-regulating it when it is hyperactive, it was hypothesized that giving AIDS patients a PRP supplement might counteract the effect of the HIV and restore T cell levels.

Synthetic peptides can also be used to help with HIV infection. Researchers developed Peptide T. Peptide T is a synthetically produced protein derived from gp120—the protein on the surface of HIV particles that binds to the CD4 molecule on the surface of some human cells. Peptide T was discovered in 1986 when scientists were screening for gp120 derived peptides which might block HIV infection. However, using synthetic peptides does not work as effectively as natural peptides because the synthetic peptides often do not fit into natural human cell receptors.

Based on the premise of using a PRP supplement to combat AIDS, a Phase I trial was carried out with several AIDS patients at the Infectious Disease Clinic in Dayton, Ohio, in 1996. A spray PRP preparation called PRPS™ was given to AIDS patients in a dosage of three sprays every four hours. Patients were initially assessed as to severity of the disease and clinical symptoms, such as diarrhea, nausea, vomiting, fever, cough, and so forth. Based on the success of these initial trials, two Phase II trials were carried out at the University of Nairobi, Nairobi, Kenya, in 2000.[497]

Results of these trials were very encouraging. All participants in the study experienced a rise in T cell levels. None had levels below 300 at the end of the study, while at the beginning of the study levels were well below normal (median 275). Over half of the patients had CD4+ levels in normal ranges (500–1500) by the end of the study (Tables 1–4).

	Before		After	
	No.	%	No.	%
150-200	17	29%	0	0%
201-250	10	17%	0	0%
251-300	21	36%	0	0%
301-400	4	7%	8	14%
401-500	4	7%	19	33%
501-600	2	3%	12	21%
601-1000	0	0%	19	33%
Totals	58		58	

Table 1 . CD4+ counts in 58 experimental subjects before and after application of oral PRPS spray.

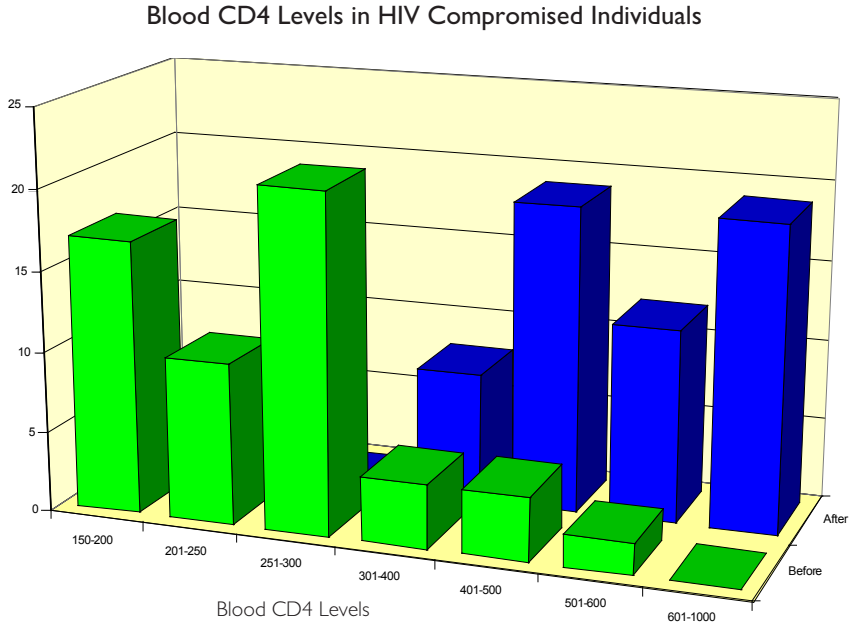


Table 2. CD4+ lymphocyte levels in HIV compromised individuals before and after treatment with PRPS oral spray. This bar graph clearly illustrates the marked increase in CD4+ lymphocyte counts in patients with long-term HIV/AIDS and severely depleted CD4+ counts after administration of oral PRPS spray. Results from trial 1 held in Nigeria.

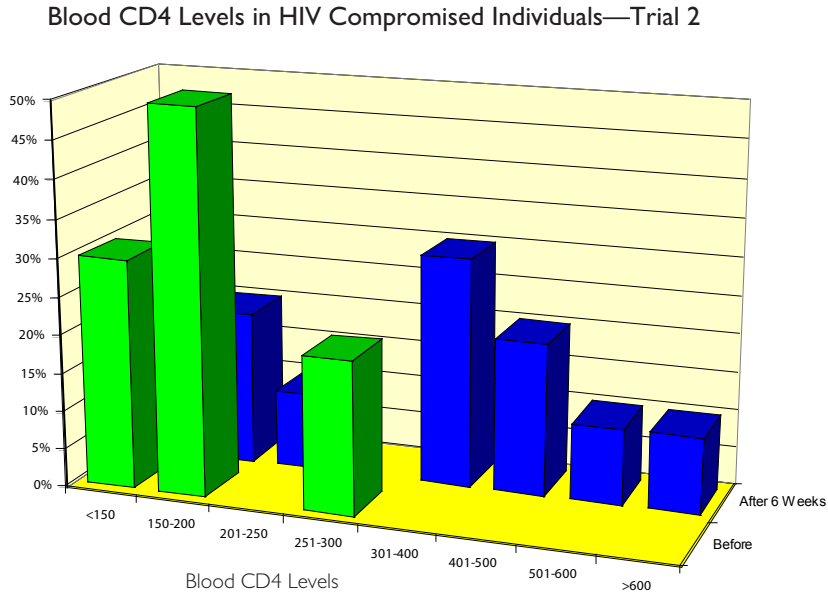


Table 3. CD4+ lymphocyte levels in HIV compromised individuals before and after treatment with PRPS oral spray. These results are from trial 2 held in Kenya.

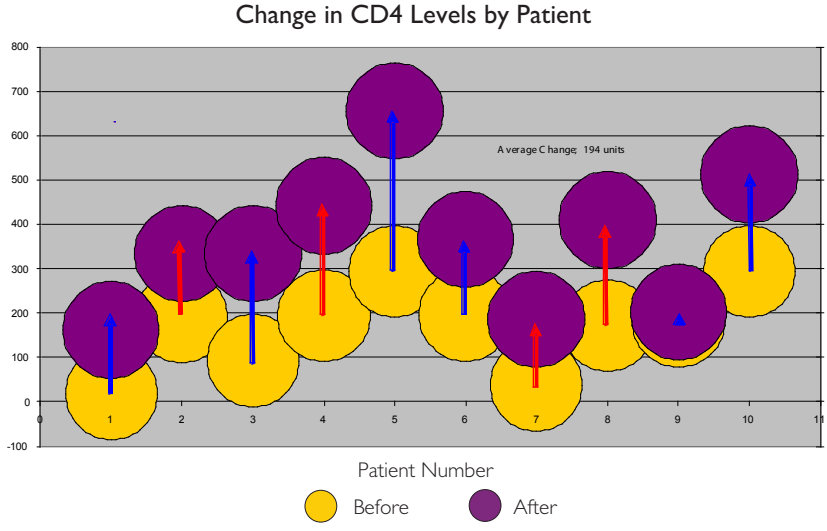


Table 4. A graphical representation of changes in CD4+ lymphocyte levels in patients participating in trial 2. While levels for some increased over 100% in some cases, what is particularly significant is that levels increased for all participants in the study.

Clinical symptoms also showed dramatic improvement over the course of the studies. All clinical parameters improved dramatically or were eliminated in the participants. These results are summarized in Tables 5 and 6.

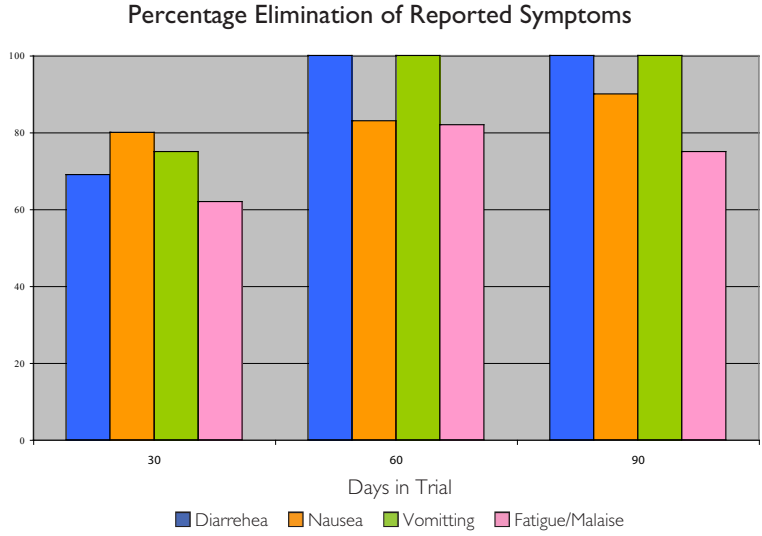


Table 5. Relief of diarrhea, nausea, vomiting, and fatigue/malaise in trial participants over the 90 days of the study

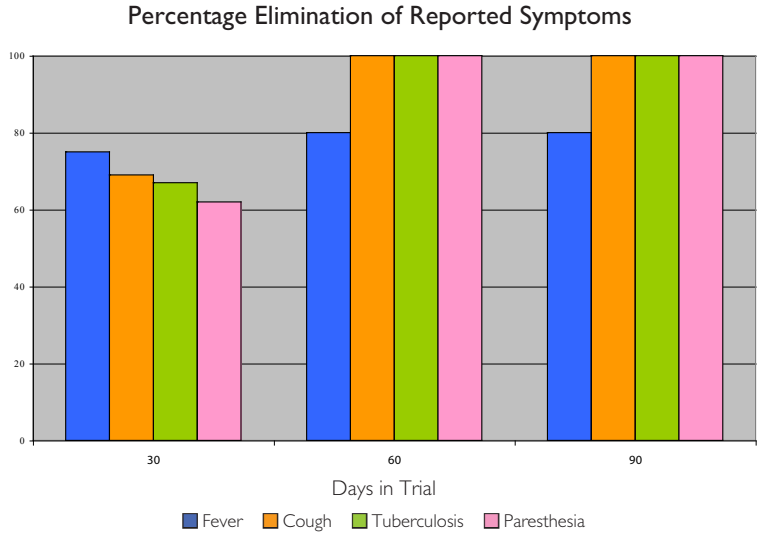


Table 6. Relief of fever, cough, tuberculosis and paresthesia in trial participants over the 90 days of the study.

Viral load also decreased dramatically in study participants, most likely as a result of the increase in T cells. These data are presented in Table 7.

	Initial Total	30 Day Total	60 Day Total
	92,448	9,755	445
	28,049	625	n/a
	33,093	239	n/a
	439	n/a	175
	59,821	n/a	320
	40,381	180	n/a
Expected Phase III % Reduction		<1,000	<500 (<250 at 90 days)

Table 7. Viral Load. Viral load counts in six patients from the Phase II trial.

Patients in the studies also experienced significant weight gain, another marker of improved health (Table 8). Patients receiving PRPs showed an average weight gain of 3.4 kg over the course of the study, while those receiving anti-retrovirus therapy (ART) averaged only a 0.3 kg weight gain.

These results show that supplementation with PRPs can significantly affect the course of viral disease, in particular one caused by a deadly virus like HIV. They also indicate that PRPs can be a valuable adjunct therapy for AIDS patients, greatly increasing quality of life, reversing the progress of the disease, and presumably increasing life expectancy. Phase III trials of this product are currently underway.

A recent study indicated an increase in lytic readings in 10 women and 10 men by an average of 248%[498] when given dialyzable leukocyte extract, a form of PRP. Lytic readings are an indication of the function of the body's natural killer cell activity. This may explain why PRPs are so successful against viral infections. However, much work remains to determine the actual mechanisms of action. A discussion of natural killer cell function follows.

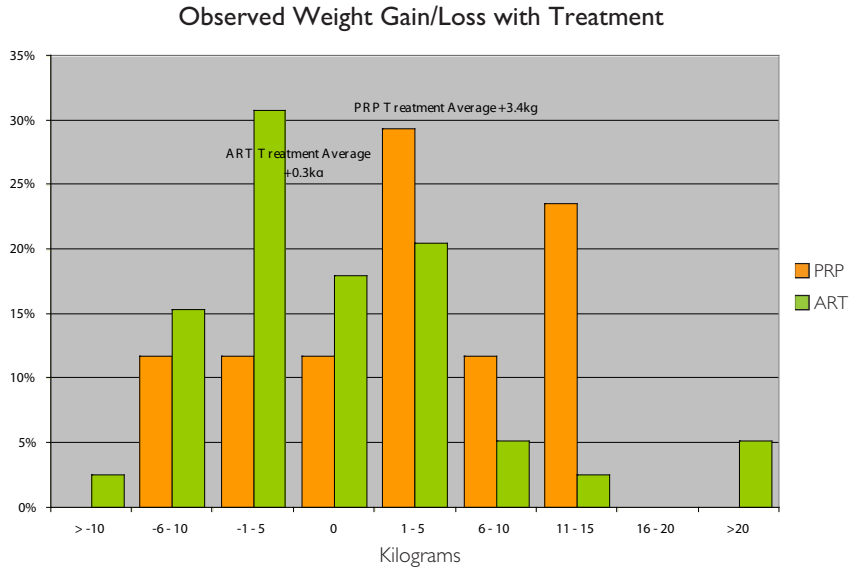
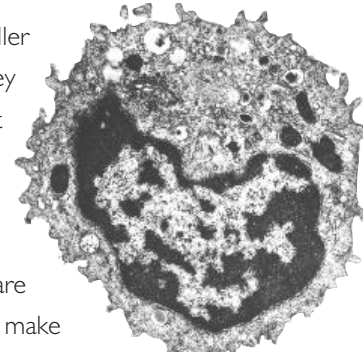


Table 8. Weight loss/gain for patients on oral PRPs or anti-retrovirus therapy (ART).

What Are Natural Killer Cells?



Of all the immune system's soldiers, natural killer cells (NK cells) are the most aggressive. They are the first line of defense against mutant and virus infected cells like Severe Acute Respiratory Syndrome (SARS) or West Nile that are a health threat. They are lymphocytes with no immunological memory and are part of the innate immune system. NK cells make up about 5–16% of the total lymphocyte population. Their specific function is to destroy infected and cancerous cells.

NK cells do not kill indiscriminately. They look for an IFF (Identification: Friend or Foe) banner flown by normal cells. If the NK cell sees this banner, it receives a signal to spare that cell. This signal overrides the NK cell's urge to kill. If this banner is absent on the target cell, the NK cell proceeds with its attack. It attaches

to the target and releases a lethal burst of chemicals that penetrate the cell wall. Fluids begin to leak in and out and eventually the cell explodes (lyses).

In addition to their role in the control of infections, NK cells help in the regulation of other aspects of the immune system that affect our overall health. Immunotherapy to help increase NK cell activity is becoming available and will become more widely used as knowledge of the immune system increases.[499]

FREQUENTLY ASKED QUESTIONS ABOUT PROLINE-RICH POLYPEPTIDES

PRPs contain tiny peptide molecules produced by immune T cells that play a central part in promoting immune system strength and effectiveness.

PRPs contain a set of messaging molecules that convey immune information within an individual's immune system. Nature also uses PRPs to carry immune information from one individual's immune system to another individual. PRPs are signaling peptides or **Proline-Rich Polypeptides (PRPs)** that have the ability to transfer immunity from one person to another. This immune information is vital to our health.

PRPs are the most exciting health discovery in recent decades.

PRPs are small immune messenger molecules that are produced by higher organisms. Their role is to transfer immune recognition signals between immune cells and thereby assist in educating naïve immune cells about a present or potential danger. PRPs are natural, microscopic molecules that are found in all animals. They are messenger molecules, passing information about the presence of an immune threat—whether external or internal—and how to properly respond, from immune cell to immune cell.

In the harsh and hostile environment in which a baby suddenly finds itself, invading microorganisms could rapidly overcome and destroy the new life. Nature has provided a procedure to rapidly educate the infant's naïve immune system. Prior to delivering a baby, the expectant mother prepares a natural immunizing cocktail that she includes in the first milk (colostrum) she provides to her new baby. PRPs provide a key part of this process.

Dr. CH Kirkpatrick determined that blood contains small peptides of about eight amino acid residues.[500] Eighteen different amino acids have been represented which may combine to create billions of different PRPs. These very small PRP molecules contain the essence of the immunological message.

PRPs do not elicit an allergic response and are not species-specific. What this means is that PRPs peptides produced by a cow are just as effective in humans as they would be in another cow. This exciting ability could spark a revolution in medicine and has prompted the following statement: "PRPs [have] an important role to play in modern medicine which, from AIDS to Ebola, faces the emergence of new viruses or the resurfacing of old pathologies such as tuberculosis"[501] PRPs have been successfully used to treat the following conditions: viral, fungal, neurological and parasitic infections, malignancies challenges, and autoimmune conditions.

How do PRPs work?

PRPs directly support the natural killer (NK) cells of the immune system. Natural killer (NK) cells provide the front line of defense specially equipped to locate and kill disease cells. NK cells attach to the surfaces of foreign substances or their outer cell wall and inject a chemical "grenade" (granule) into the interior. Once inside, the granules explode and destroy the foreign invader within five minutes. The NK cell itself remains intact and moves on to destroy the next immune attacker. Many doctors and clinics are finding PRPs helpful in promoting NK function and activity as well as supporting a healthy immune system for all patients.

The immune system plays a vital role in the quality of our health. Strong, active and optimally functioning NK cells promote optimal health and deter foreign substances from affecting immune function.

How was the active component (PRPs) discovered?

In 1949 Dr. H. Sherwood Lawrence was working on the problem of tuberculosis, which was a major health concern of the time. What he was trying to discover was if any component of the blood could convey a tubercular sensitivity from an exposed recovered donor to a naive recipient. Whole blood transfusions could be used but only between people of the same blood type. Lawrence first separated the blood's immune cells, the lymphocytes or white blood cells, from the whole blood. Then he broke open the lymphocytes and separated the contents of the cells into various size fractions. What he found was that a fraction of small molecules was able to transfer tuberculin sensitivity to a naive recipient. This is

what Dr. Lawrence called Proline-Rich Polypeptides (PRPs)—the active peptides in PRPs.

Is blood the only source of PRPs?

Originally it was. It was not until the mid-1980s that two researchers came up with the idea that PRPs or infopeptides may also be present in colostrum. The confirmation of this discovery was awarded a patent in 1989. Bovine (cow) colostrum is now the best source of PRPs.

What is the actual definition of infopeptides?

The term applies to a class of small peptides or proteins that circulate in the blood of mammals and accumulate or concentrate in their colostrum, in their milk, and in their blood sera. Infopeptides appear to convey information necessary for appropriate cellular function.

What prompted these scientists to look for PRPs in colostrum?

Those who have worked with cattle know that if a calf is not allowed to nurse from its mother it will most often die within a short time. The calves would die in spite of an abundance of food. Death in these cases was cause by infections brought on by the most common organisms. For whatever reason the immune systems of these calves were not working. Seeing this suggests that there is some kind of immune information being transferred from the mother to her infant. The logical question then became: was it PRPs? The answer was a resounding YES! How does PRPS™ liquid compare with whole colostrum supplements?

Comparing PRPs liquid to a whole colostrum supplement would be like comparing a precious metal to the ore from which it is derived. It is composed of highly concentrated PRPs which offer maximum immune benefit. Whole colostrum contains a much smaller concentration of PRPs.

Can these infopeptides be as effective for adults as for a newborn infant?

Infopeptides need to be processed to be effective for adults. The polypeptides from colostrum are not absorbable (or more properly, not "readable") by adults

unless separated and broken up into smaller sizes. One company has successfully accomplished this goal, and refers to its product as PRPS™.

Can we get enough human colostrum to provide enough of the infopeptides?

Bovine colostrum—that is, from cows—provides infopeptides that are fully effective in humans. Good thing, otherwise they would be prohibitively expensive. But does the bovine source of infopeptides really work as well as human?

This answer is a very definite yes. Whereas bovine colostrum and lactoferrin are close but not precise matches of their human counterparts, infopeptides from cows may be even closer. Dr. Stephen Levine, a biochemist, says that these polypeptides are so important to animal survival that they may have been genetically conserved through the evolutionary process with virtually no change from species to species, much like vitamin C or melatonin.

The clinical experience with bovine products is sufficiently compelling to imply that the bovine immune system is every bit as "smart" as the human one.

What is meant by the phrase, "No clear relationship between dose and benefit"?

In the studies done to date, it has been noted that the administration of PRPs above the minimum levels necessary for response does not enhance or intensify the benefit.

What do these infopeptides do for adults, anyway?

Early studies suggest that Infopeptides are extremely effective as anti-inflammatory agents as well as immune modulators.

What specific types of conditions are likely to respond to PRPs?

A variety of conditions have been helped, including infectious diseases, progressive degenerative disorders, allergic disorders, and even a dozen or so rare diseases. What types of conditions are least likely to respond to PRPs?

Those least likely to respond are those suffering from the effects of permanent tissue damage or environmental toxins.

How are PRPs administered?

In most cases, oral administration is preferred. Amounts from 1/4 to 1 teaspoon are placed in the mouth, or sprayed in the mouth and held or circulated for a few seconds prior to swallowing.

Topical application is also effective for burns, sutures, and other healing skin conditions.

How much is needed to be effective?

Again, small doses are effective. The usual mode of administration is a teaspoon of liquid or spray in the mouth, for example 2 mls or 3 sprays, held in contact with oral mucosa for a few minutes and then swallowed.

Are PRPs safe?

The safety of PRPs has been demonstrated in physician-monitored safety studies, and in normal use. As with any food, should evidence of intolerance develop, it is recommended that the use of PRPs be discontinued until an adequate assessment of the circumstances can be made. But in all of my research, talking at length to physicians and patients, no one has reported any deleterious side effects.

Should I take PRPs as a preventive?

Not necessarily, but if you feel you have been exposed or may be exposed to unhealthful surroundings, that's the time to take it. The developer of the product explains: "If I take PRPs in the morning, before going to work, and my coworkers are sneezing and coughing, I will be protected for six hours. Six hours later, another dose will protect me for the next six hours."

Interesting stuff! Interesting concept! You should know that I have been tracking the progress of PRPs with its history of success for problems ranging from acute viral attacks to serious chronic and even life-threatening disorders for a few years.

PRPs appears to have the potential to revolutionize at least three major areas of treatment. PRPSs are helpful for:

- Immune dysfunction, including underactive and overactive immune system, from minor to major, including AIDS and autoimmune disorders
- Childhood diarrhea
- Myalgias and muscle pains, including arthritis and fibromyalgia

Keep in mind that PRPs are not a magic bullet against a specific organism or disease. It appears to stimulate your immune system to action. In other words, it is a health maintenance product rather than a medicine.

Although its ability to conquer the first two areas of very serious afflictions is thrilling, I must admit that it is the third that has me reeling with excitement. Is there any among us who doesn't know at least one person suffering from fibromyalgia? At last, I now have a more positive response when so many of you come up to me at meetings, pleading for help because of this debilitating disorder.

Homeostasis requires the coordinated functioning of trillions of cells. Some influence on our cells inclines us toward wellness. This would require communication or advice and perhaps some form of informational media. It just may be that infopeptides are that media, advising every function of every well cell!

There's so much we have yet to understand. No matter. I don't know what the pistons or spark plugs do in my car, but that's no deterrent for me to drive.

Since PRPs are isolated from colostrum, what about milk allergies and lactose intolerance?

Milk allergies are caused by the large milk proteins, primarily casein, and to a lesser extent the immunoglobulins. These proteins are completely removed from the PRPs. Lactose intolerance is most common in Oriental populations; much less so in those of European or African decent. We are conscious of this, but we have noticed that the dose of lactose that a person receives is only 70mg, less than

the 80mg needed to promote an allergic result from taking lactose in lactose-intolerant people. Lactose intolerance itself is a food allergen, and because PRPs help modulate the Interleukin levels in the body, this reduces the probability of an allergic response.

How do PRPs compare to the colostrum products that are on the market now?

We looked seriously at hyperimmunized colostrum and eggs. These products are good, but certain issues must be addressed. First, the milk allergy and lactose intolerance issues as we discussed above. Second, the issue of immunoglobulin or antibody effectiveness. The use of cross-species antibody therapy can be effective in the short run. Long-term use, however, is ineffective since the recipient develops antibodies to the foreign antibody thus destroying its effectiveness. Antibody therapy is given intravenously since oral consumption leads to degradation of the antibodies in the stomach.

Are PRPs only good for newborns?

PRPs are good for everyone who has an immune imbalance. The three groups who are most in need of immune modulation are the young, the old, and anyone under stress. Almost all of us fall into one of these categories. We often talk of the baby boom generation. Most of these people are at an age where their immune systems are already becoming weaker. PRPs are a way to boost a lagging immune system and greatly improve one's health. However, pregnant woman or those trying to get pregnant should not take PRPs as this may interfere with the TH1/TH2 cytokine balance.

Have PRPs been scientifically validated?

Since Lawrence's discovery of PRPs in blood in 1949 (which he called transfer factor), there have been over 3000 scientific studies published on PRPs.

What conditions are responsive to PRPs?

PRP preparations have been used to effectively help with a wide range of diseases. These include bacterial, mycobacterial, fungal, parasitic, viral, and cancerous conditions. It is in part because of AIDS, or more specifically our frustration in

treating AIDS, that PRPs are experiencing a resurgence of research interest. In fact, a recent international symposium held in Italy was titled: PRPs in the Era of AIDS.

If PRPs are so effective, why hasn't the pharmaceutical industry jumped on PRPs?

I think that is exactly what we are seeing in many foreign countries, notably China, Czech Republic, Germany, Hungary, Poland, and Japan. In the US, PRPs have had an interesting history. The idea of PRPs flies in the face of conventional immunology. In the '50s antibiotics were the golden child of medicine followed in the '60s by steroids, such as cortisone, for inflammation and the synthetic steroid hormones like ethinyl estrogen and progestin that were used to create the birth control pill.

After an initial delay, PRPs (then known mainly as transfer factor) hit their heyday in the 70s and early 80s. Results, however, were inconsistent as researchers dove in sometimes with more enthusiasm than skill. The key feature that was missing in these investigations was a dependable assay technique for quality control of the product. The quality control issue was not resolved until the mid 1980s. Given that PRPs are not a single entity, pharmaceutical companies had fits trying to purify the material without losing efficacy. This forced fit into the single-entity, single-function drug dogma was disastrous.

The next issue that slowed PRP research is the age-old issue of funding. When AIDS hit the popular press, politicians shifted funding into AIDS research but with the focus on finding the cause and then finding a drug that would cure AIDS. The work of a few dedicated, but underfunded, researchers and the inability of the mainstream medical-pharmaceutical industry have combined to again focus attention on PRPs as one of the few modalities that is effective against diseases of viral origin.

Are there reasons why we haven't seen PRPs as a dietary supplement before now?

Yes, there are two doors that recently have opened that allow PRPs to be effec-

tively marketed now. The first door to open was the passage of DSHEA (Dietary Supplement Health and Education Act) in 1994. The provision for structure-functions claims allows the story of PRPs to be told without jeopardizing its status as a nutritional supplement. The second is technical. PRPs was definitely an idea way ahead of its time, and it had to wait for technology to catch up. The processing methods that allow for large-scale extraction of PRPs have only recently been perfected, and a commercial product has only been available for the past few years.

How does one discuss PRPs in terms of structure-function claims?
Simplistically, PRPs strengthen the immune system. But that is overly simplistic and could be used to describe a number of herbal products and other supplements. Let me answer the question by first reiterating that PRPs are not just a single entity. PRPs are in fact a complex mixture containing three separate fractions. These three fractions are an INDUCER fraction, an ANTIGEN-SPECIFIC fraction, and a SUPPRESSOR fraction.

Since our immune systems fight the microbe wars for us, let me use a military analogy to explain these three functions. The inducer fraction serves as the drill sergeant of basic training, whipping the immune system into shape but not telling them who to go out and attack. The antigen-specific fraction is like a set of wanted posters identifying critical features of the bad guys. If we were microbes, these specific identifiers would be our fingerprints, mug shots, etc. Similarly a whole set of PRPs are made against a single microbe type. Finally, the suppressor fraction is like the politicians who declare an end to the war and demobilize the troops. Without this final action, a lot of collateral damage would be done, whether in war or within ourselves.

When our immune system does not demobilize or overreacts, we suffer from autoimmune conditions such as multiple sclerosis and allergies. Unlike most immune supplements that provide the building blocks for proper immune function, PRPs function as an immune intelligence network. They pass on immune information and education that focuses the immune system, keeping it on task and effective. This is a whole new concept in immune system strengthening.

Are PRPs FDA approved?

It is approved as a dietary supplement, but not as a drug, according to Dr. Fudenburg (Progress in Drug Research, 1994, 42:378). Foods and dietary supplements are not approved per se by the FDA, and food supplements derived from milk would certainly fall under the category of GRAS (Generally Recognized As Safe).

Are PRPs safe?

YES! Researchers have given huge doses of PRPs to volunteers in an attempt to trigger some sort of adverse reaction. No harmful negative side effects were observed even when massive doses were used. Consuming several glasses of PRPs liquid may promote symptoms associated with lactose intolerance. Also, one should not consume large quantities of anything, even water because it may cause brain swelling and other health problems.

Are there any reports about PRPs helping people with cancer?

Radiation, chemotherapy, and surgery are the commonly used conventional cancer treatments. Both radiation and chemotherapy are highly damaging to fast growing cells in the body, such as intestinal lining cells, the cells of bone marrow, and the cells of the immune system. After such treatments, persons often have to be on very strong antibiotics in order to prevent infections, which presents a whole new set of problems.

The use of PRPs in combination with radiation or chemotherapy protects the immune system by some mechanism which we do not fully understand at the present. In cases of surgical removal of certain tumors the use of PRPs as an adjuvant therapy results in a higher survival rate.

What about colds?

Colds are viral diseases, and PRPs are used most commonly against viral conditions. Studies of PRPs and colds have not been officially done but interestingly, cold relief is a commonly reported side effect of taking PRPs.

Are PRPs safe for infants?

Colostral PRPs were designed by nature for newborns. Removal of the milk allergens and lactose leaves only the essence of the immunological information in the form of PRPs.

Why are PRPs different from other PRP products or colostrum products?

Within the spectrum of PRP activities, PRPs have a unique enhanced activity for several viruses, including Human Herpes Virus-6 (HHV-6) variants A and B, Epstein-Barr Virus (EBV) and Cytomegalovirus (CMV). This enhanced activity provides for an improved immune response against active HHV-6, EBV and CMV infections. This should lead to a decrease in viral activity and improved immune function since these viruses are known to be immunosuppressive. Colostrum itself does not have this unique activity.

What types of responses are possible with PRPs?

Overall, PRPs have shown very promising responses. In looking at a prototype group of patients with a history of chronic fatigue syndrome (CFS) or fibromyalgia (FM), improvement in symptoms has been seen in approximately 85% of those who have taken both TF560 and TF540 (now available as Immune Care™-64). Common symptoms such as fatigue, diminished activity level, muscle aches, joint aches, and impaired memory function have substantially improved when these patients took both TF560 and TF540. Some patients (approximately 25%) have noted a very dramatic reduction in symptoms, essentially resolution of all symptoms. Immune function appears to improve as well. Laboratory assessment of immune function utilizing the natural killer (NK) cell function assay has shown impressive improvements. 70% to 80% of patients' NK function assays improve from very low baseline levels to normal function values after taking PRPs.

What are the reasons some patients do not respond?

There may be a variety of reasons. The most widely studied herpes viruses have been Herpes simplex virus (HSV-1) and genital herpes (HSV-2). In the extensive literature regarding PRP administration in these patients, there was a definite reduction in overall symptoms and frequency of outbreaks. However, some pa-

tients did not respond. Thus, prior PRP studies have shown good responses for a variety of viruses, but responses vary. PRPs rarely result in a 100% response rate. It is intuitive that a similar pattern may be seen with newly developed concentrated PRP products (PRPS). A number of other factors may be involved with suboptimal or inadequate responses, including duration of illness, co-infections, hypercoaguable syndrome, and other chronic medical conditions (e.g., diabetes mellitus and cardiovascular disease).

Adverse side effects of taking PRPs?

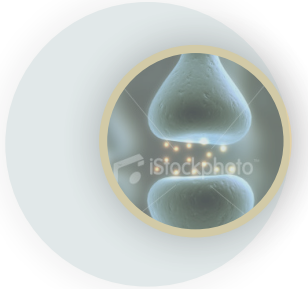
The majority of patients have no adverse effects at all. Some patients may notice a sense of bloating caused by taking more than the 2ml dose. This is caused by the moderate levels of lactose in PRPs (4% w/w of PRPS solution).

How should one take enhanced PRP products for Human Herpesvirus-6 (HHV-6) and Epstein-Barr Virus (EBV)?

It may be prudent to start at the lower dose and work up over a week or two. We would generally suggest starting at one dose (2ml, or 3 sprays) per day for 5–7 days, then increase to two doses per day for 5–7 days, and then increase to three per day. Slowly escalating the dose may diminish the bloating symptoms. If bloating symptoms are noted, do not increase the dose until the symptoms have resolved. The most effective dose for viral infections appears to be 2ml (3 sprays) six times per day for adults, albeit smaller doses may be effective in some individuals. For autoimmune disorders, three doses per day. For maintenance of a healthy immune system, two doses per day.

SUMMARY OF PRPS

- PRPs were discovered in the 1940s and have been extensively studied for the past fifty years.
- PRPs can transfer cell-mediated immunity (CMI) from an immune donor animal to a non-immune recipient.
- PRPs are manufactured by leukocytes (white blood cells), mainly T lymphocytes.
- The structure of PRPs has not been entirely established, but is a small peptide, probably with a small piece of RNA attached.
- PRPs stimulate cell-mediated immunity (CMI; for a specific antigen), probably via T lymphocytes.
- PRPs is antigen-specific, i.e., for each specific type of infection.
- PRPs can cross species lines and does not cause allergic reactions from one species to another.
- PRPs can be generated from the leukocytes of a donor animal. However, one of the most efficient ways to recover it is from colostrum.
- Once PRPs have been generated, they should be assayed and validated for their immunologic activity, which can be expressed as potency units.
- After PRPs are administered, they can induce internal PRP production by the recipient.
- The ability of an individual to produce internal PRPs varies, in that some do not synthesize internal PRPs very well.
- Most people can respond to externally administered PRPs with initial action within 24 hours.
- PRPs have been found to be extremely safe.
- Since PRPs can stimulate the immune system, they can give rise to flu-like symptoms when one first starts to take it.
- PRPs are most effective in regulating immunity to infections in which cell-mediated immunity (CMI, T cells) is important for controlling the infection.
- PRPs have been shown to increase natural killer (NK) cell activity.



APPENDIX A

BRIEF REVIEW OF THE IMMUNE SYSTEM

The immune response is a defense mechanism by which the body fights infection. It is divided into two functional systems, the ***innate immune system*** and the ***adaptive immune system***. The innate system is the first line of defense by which the host combats infectious agents and pathogenic microbes. This is a non-specific response, which proves effective against most infective agents. In case this primary response is not effective and the invading microbe is led to proliferate the adaptive immune system comes into action. The adaptive immune system produces a specific response in the form of antibodies to the infective agent that normally proves effective in neutralizing that agent. In the case of the innate system resistance (immunity) is not improved by repeated infection. The adaptive immune response involves ***memory*** and gives rise to resistance to repeated exposure to the same infective agent. Childhood diseases such as mumps, measles, and chickenpox produce life-long immunity following an infection.

Most infectious agents enter the body proper via the epithelial surfaces of either the upper respiratory, digestive or genito-urinary tract. Once infectious agents have penetrated the body a variety of physical and chemical defense mechanisms come into play to help protect these tissues from most infections. This involves a specialized set of cells called ***leukocytes*** (white blood cells) and their products that have evolved to help combat infection and disease. Leukocytes fall into two broad categories of cell types: ***phagocytes*** and ***lymphocytes***. Phagocytes form part

of the innate immune system and provide non-specific immunity. Included in this category are neutrophils, basophils, eosinophils, monocytes, and macrophages. Lymphocytes form the adaptive immune system and provide specific immunity. There are two types of lymphocytes ***B cells*** and ***T cells***. The B cells are differentiated in the bone marrow and found mainly in the lymph nodes and spleen. They are the cells that make ***antibodies (immunoglobulins)***. The T cells are differentiated in the thymus and fulfill two major functions. They regulate the activity of the B cells and directly attack infectious agents.

PASSIVE IMMUNITY

During embryonic development the unborn animal's immune system is not sufficiently developed to ward off potentially harmful microbes. Fortunately the fetus is protected from harmful environmental factors by its position in the womb; potentially harmful agents cannot pass the placental barrier. At birth the newborn without a complement of antibodies would find its environment very hostile, being quite susceptible to infection from invading organisms. To alleviate this potentially lethal situation a very interesting phenomenon, known as ***passive immunization***, has evolved. The maternal blood contains a full complement of antibodies to various antigens to which the mother has been exposed during her lifetime. In humans and apes the mother passively immunizes her young ***in utero*** by passage of antibodies through the placenta. In animals where the maternal antibodies are unable to pass the placental barrier (cattle, pigs, and sheep), the young are passively immunized immediately after birth by way of colostrum. In these species the maternal antibodies present in the colostrum are absorbed directly through the gut in the first few days after birth. When newborn cattle, pigs and sheep are deprived of colostrum, a significant increase in mortality rate is observed.[502,503] In a study conducted by the Invermay Agricultural Center it was shown that the post-treatment mortality of triplet lambs was significantly increased from 7.4% to 19.4%. The association of high neonatal survival rates and the successful transfer of colostrum has been reported.[504,505,506]

IgG is the form in which antibodies occur most abundantly. In all species of mammals IgG is passed from the mother to its young, although the actual mechanism

of transmission varies species to species. In humans and apes it has been shown that IgG and its complement of antibodies pass across the placental barrier from mother to fetus during the second two-thirds of gestation. This passage appears to be selective in that IgG is transferred but not the other immunoglobulins (IgA, IgM, IgE, IgD). Albumin is also transferred but to a lesser degree. Other plasma proteins are not transferred across the placental barrier. In cattle it appears that the same type of selection occurs in absorption of antibodies through the gut in that there is a preferential passage of IgG but not IgA, IgM, IgD or IgE.

PASSIVE LOCAL PROTECTION

In humans, passive transmission of maternal antibodies takes place prior to birth and occurs ***in utero***. After birth, the antibodies present in human milk function in local passive protection. Once again the predominant immunoglobulin in human breast milk is of the IgA class. In most other animals such as the horse, cow, pig and sheep there is no passive transmission of immunity prior to birth. In these animals passive transmission of maternal antibodies occurs in the first 20–48 hours after birth by way of colostrum. During this time they absorb intact antibodies via the newborn's digestive tract. After these first few days the direct absorption of intact antibodies ceases, and any antibodies present in the colostrum and milk then function in local passive protection of the gastrointestinal (GI) tract.

The importance of this passive local protection is evidenced in the newborn calf where diarrhea and other enteric infections (scours) can prove fatal.[507] It has been reported that the best source of nourishment for the infant mammal is mother's milk.[508] This has largely been attributed to not only the nutritional benefits of milk but also to the presence of milk immunoglobulins providing local passive protection to the GI tract. A very important aspect of this local immune protection is that it is not species specific and as such we as humans, and all other animals, can use bovine colostrum for its various health benefits.

The immune system is made up of two basic parts:

Innate immune system—nonspecific immunity, including barrier

defenses (skin, intestinal lining, brain-blood barrier, macrophages, neutrophils, dendritic cells etc.), airway cilia (remove antigens and small particles that are breathed in), mucus, chemicals such as lactoferrin, lactoperoxidase and lysozyme which are potent killers of pathogens, strong acids in the stomach, and so forth[509]

Adaptive immune system—system which consists of immune and scavenger cells (lymphocytes, macrophages, NK [natural killer] cells, mast cells, monocytes and other blood cells) that react to specific antigens

The adaptive immune system furthermore has two response modes:

Humoral Immunity—production of specific antibodies in response to an antigen, mediated by B cells

Cell-Mediated Immunity—production of cytotoxic lymphocytes, activated macrophages and NK cells, and cytokines in response to an antigen, mediated by T cells

Lymphocytes come in several different varieties. B lymphocytes (B cells) are produced in the bone marrow, and T lymphocytes (T cells) are produced in the thymus gland. T cells are further broken down into:

Cytotoxic or killer T cells (CD8)—the cells which actually kill invading pathogens

Helper T cells (CD4+)—cells which direct the immune response through the secretion of cytokines[510,511]

Suppressor T cells—inhibit the production of cytotoxic T cells when no longer needed to prevent excess tissue damage and turn down an adaptive immune response

Memory T cells—retain memory of an encountered antigen so that if encountered again the response time will be much shorter

Helper T cells secrete various cytokines to stimulate the production and dif-

ferentiation of cytotoxic T cells and B-cells, which produce antibodies. They also attract neutrophils (white blood cells) and stimulate macrophages to engulf and destroy pathogens.

Helper T cells also have subsets:[512,513]

TH1 cells—secrete the cytokines tumor necrosis factor-alpha (TNF-α) and interleukin 12 (IL-12) which control cell-mediated immunity; TH1 activation can inhibit TH2 cell activation

TH2 cells—secrete the cytokines IL-4 and IL-5 which control humoral immunity; TH2 cell activation can inhibit TH1 cell activation

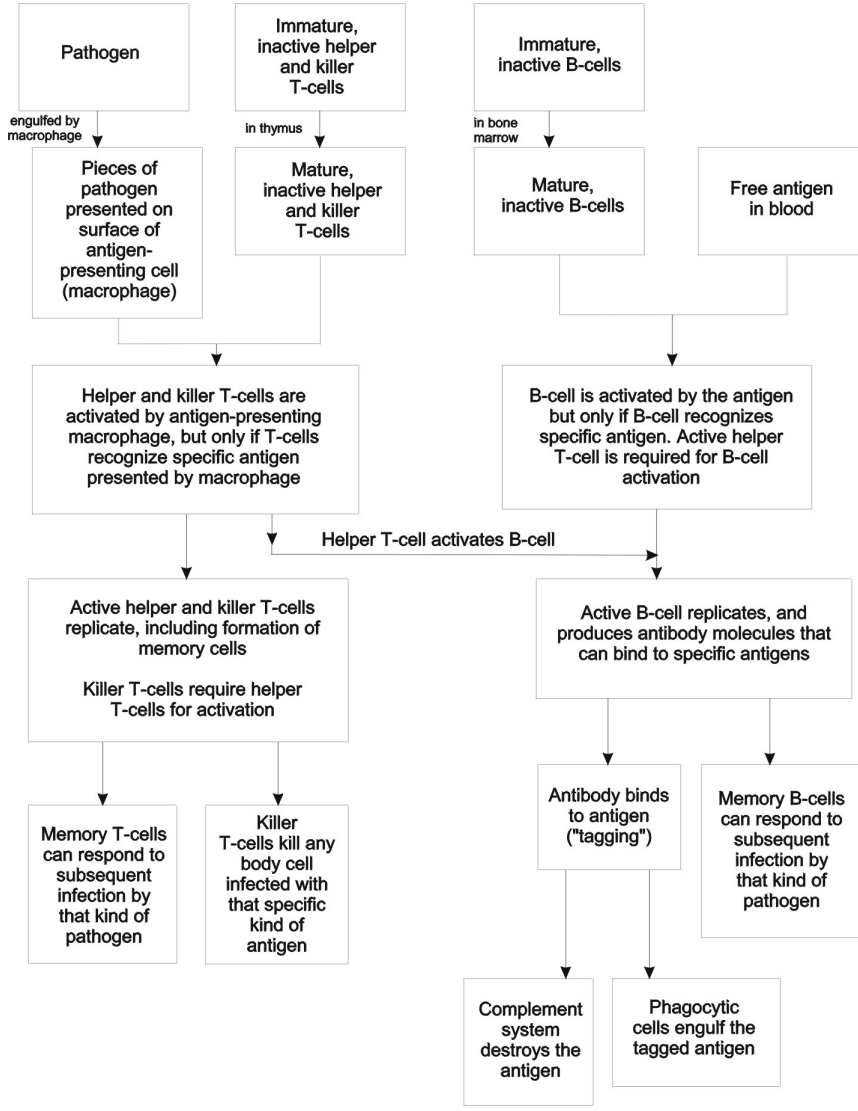
Regulatory TH3 (Tr) cells514—at least three different type of regulatory TH cells exist:

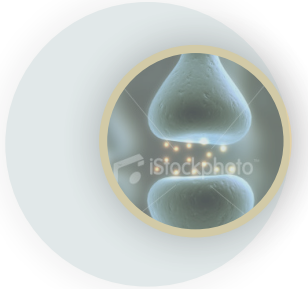
Type 1 (Tr1)—secrete large amounts of IL-10 and low-to-moderate amounts of transforming growth factor-beta (TGF-β), may help terminate TH1-related inflammatory responses

Type 3 (Tr3)—primarily secrete TGF-α regulates multiple facets of immune response

CD4+CD25+—inhibit immune responses through direct cell-to-cell contact

The following diagram may help clarify how the immune system works as a coordinated system to protect the organism:


Pathogen
Immature, inactive helper and killer T-cells
Immature, inactive B-cells
engulfed by macrophage
in thymus
in bone marrow
Pieces of pathogen presented on surface of antigen-presenting cell (macrophage)
Mature, inactive helper and killer T-cells
Mature, inactive B-cells
Free antigen in blood
Helper and killer T-cells are activated by antigen-presenting macrophage, but only if T-cells recognize specific antigen presented by macrophage
B-cell is activated by the antigen but only if B-cell recognizes specific antigen. Active helper T-cell is required for B-cell activation
Helper T-cell activates B-cell
Active helper and killer T-cells replicate, including formation of memory cells
Killer T-cells require helper T-cells for activation
Active B-cell replicates, and produces antibody molecules that can bind to specific antigens
Memory T-cells can respond to subsequent infection by that kind of pathogen
Killer T-cells kill any body cell infected with that specific kind of antigen
Antibody binds to antigen ("tagging")
Memory B-cells can respond to subsequent infection by that kind of pathogen
Complement system destroys the antigen
Phagocytic cells engulf the tagged antigen



APPENDIX B

TYPICAL SPECIFICATION OF A FIRST MILKING WHOLE COLOSTRUM POWDER

Description and Suggested Applications

Whole colostrum powder produced from raw colostrum collected only from milkings within 16 hours after birth. It should be processed both at low pressures and temperatures and spray or freeze dried using indirect steam to maintain maximum bio-activity. It should be free from antibiotics.

Suggested applications include: immune system enhancement, nutritional supplement, digestive health improvement, protein supplement and alternative treatment for general health.

Major Active Component Analysis

	Specification	Typical	Method
Protein % (Nx6.38) db	45.0 min	50.0	Kheldal
Total Immunoglobulins %	18.0 min	22.0	HPLC (dry basis)
Immunoglobulins (Type G1 & G2) %	15.0 min	18.0	HPLC (dry basis)
Immunoglobulins (Type A) %	2.0 min	2.60	HPLC (dry basis)
Immunoglobulins (Type M) %	0.75 min	1.40	HPLC (dry basis)
Immunoglobulins (Type D) %	0.15 min	0.20	HPLC (dry basis)
Immunoglobulins (Type E) %	0.10 min	0.15	HPLC (dry basis)
Lactoferrin %	0.5 min	0.75	HPLC (dry basis)

Transferrin (mg/g)	3.0 min	4.50	HPLC (dry basis)
Lactoperoxidase-thiocyanate %	0.3 min	0.45	HPLC (dry basis)
Proline-Rich Polypeptides (PRPSs) %	3.0 min	4.0	HPLC (dry basis)
Insulin Growth Factor (Type 1) µg/g	1.0 min	2.3	ELISA (dry basis)
Insulin Growth Factor (Type 2) ng/g	100 min	140	ELISA (dry basis)
Derived Platelet Growth Factor ng/g	3.5 min	4.2	HPLC (dry basis)
Epidermal Growth Factor µg/g	0.8 min	1.1	ELISA (dry basis)
Fibroblast Platelet Growth Factor ng/g	4.0 min	5.0	ELISA (dry basis)
Transforming Growth Factor Alpha ng/g	15.0 min	22.0	ELISA (dry basis)
Transforming Growth Factor Beta mg/g	0.15 min	0.21	ELISA (dry basis)
Nerve Growth Factor ng/g	8.0 min	11.0	ELISA (dry basis)
Leptin ng/g	35.0 min	50.0	ELISA (dry basis)

Vitamin Analysis*

Vitamin B6 µg/g	10.0 min	15.0	Mass spec. (wet basis)
Vitamin B12 µg/g	0.10 min	0.16	Mass spec. (wet basis)
Vitamin E µg/g	0.15 min	0.20	Mass spec. (wet basis)
Vitamin A µg/g	15.0 min	20.0	Mass spec. (wet basis)
Vitamin C µg/g	0.25 min	0.40	Mass spec. (wet basis)
Vitamin D µg/g	1.00 min	1.20	Mass spec. (wet basis)
Thiamin (Vitamin B1)µg/g	100.0 min	150	Mass spec. (wet basis)
Folic Acid µg/g	2.0 min	2.3	Mass spec. (wet basis)
Pantothenic Acid µg/g	2.0 min	2.3	Mass spec. (wet basis)
Riboflavin (Vitamin B2) µg/g	50.0 min	60.0	Mass spec. (wet basis)
Beta-carotene µg/g	18 min	22	Mass spec. (wet basis)
Glycoconjugates µg/g	2.0 min	2.4	Mass spec. (wet basis)
Glycogen µg/g	40.0 min	56.0	Mass spec. (wet basis)
Retinoic Acid µg/g	5.0 min	8.0	Mass spec. (wet basis)

Analytical and Microbiological Analysis*

	Specification	Typical	Method
Moisture %	5.0 max	4.50	CEM
Protein % (Nx6.38) db	45.0 min	50.0	Kheldal
Ash %	9.0 max	7.0	Mass Spec.

Fat %	24.0 max	22.0	Mojonnier
Lactose %	20.0 max.	16.5	by difference
Energy Content (cal./g)	10.0 max	6.0	
Sediment	B	A	Pad
pH	6.5 < 7.5	7.0	10% sol., 20C
Bulk density	0.25 < 0.35	0.30	grams / cc
Standard Plate Count (col/g)	50,000 max	5,000	Standard**
Yeast and Mold (col/g)	10 max	<10	Standard**
Coliform (col/g)	10 max.	<10	3M Petrifilm
E.Coli (col/g)	10 max.	<1	3M Petrifilm
Staphylococcus aureus	10 max.	<1	3M Petrifilm
Salmonella sp.	Neg. / 25g	Neg.	ELISA
Listeria sp.	Neg. / 25g	Neg.	ELISA

Essential Amino Acid Analysis* (weight/weight basis)(GC/MS)		Non Essential Amino Acid Analysis* (w/w) (GC/MS)	
Isoleucine	1.46%	Arginine	2.30%
Leucine	2.37%	Cystine	1.12%
Histidine	1.46%	Glutanic Acid	9.13%
Methionine	4.08%	Alanine	2.50%
Lysine	4.18%	Tyrosine	4.96%
Threonine	4.03%	Glycine	1.77%
Phenylalanine	2.42%	Proline	5.12%
Valine	2.16%	Aspartic Acid	5.57%
Tryptophan	1.17%	Serine	4.77%

Other Minor Components not Quantified

Beta 2- microglobulin, Enzymes, Haemopexin, Haptoglobin, Orotic Acid, Peroxidase, Xanthine Oxidase Enzyme, Gonadotropin-Releasing Hormone (GnRH), Prolactin, Insulin, Sulfur, Glycoproteins:—(Including Protease and Trypsin Inhibitors), Lactalbumin, MuAltimeric αLactalbumin, Cytokines, Lysozymes, Gamma Globulin, αlactoglobulin, Complement 3 & 4 (C3 & C4), Kappa Casein, Alpha 2-AP glycoprotein, Alpha 1-antitrypsin, Alpha 2-macroglobulin, Orosomucoids, Prealbumin, Albumin, Oligosaccharides, Non

Specific Inhibitors (NSI's), Secretory IgA (SigA), IgA Specific Helper

Mineral Analysis* and Physical Properties

Specification mg/100gm		Typical	Heavy Metals		Properties
Sodium	150 < 300	200	Lead	<1ppm	Solubility: Good
Calcium	150 < 400	250	Mercury	<1ppm	Flavor: Clean & Bland
Potassium	150 < 400	250	Arsenic	<1ppm	Odor: Clean
Magnesium	250 <500	400			Appearance: Free flowing
Chromium	30 < 60	40			& non-caking
Zinc	5 < 20	8			
Chloride	< 100	40			

Packaging, Shipping and Storage

Colostrum powders are hygroscopic and can absorb odors. Temperatures below 75 degrees F, relative humidities below 65% and an odor free environment will extend storage life. Stocks should be used in rotation and preferably within three years.

MATERIAL SAFETY AND DATA SHEET OF A COLOSTRUM POWDER

SECTION 1—COMPOSITION & INFORMATION ON INGREDIENTS

100% Whole Colostrum Powder

SECTION 2—HAZARDS IDENTIFICATIONS

• EMERGENCY OVERVIEW

Off-White. Non-flammable. Non-hazardous to eyes, skin and throat.

POTENTIAL HEALTH EFFECTS

ROUTES OF ENTRY: Eye contact, dermal, inhalation, ingestion

ACUTE EFFECTS OF OVEREXPOSURE:

Eyes—Nuisance dust

Skin—Non-hazardous

Inhalation—Non-hazardous

Ingestion—Non-hazardous

CHRONIC EFFECTS OF OVEREXPOSURE: None known
MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: None known.
CARCINOGENICITY: NTP: No IARC: No OSHA: No

SECTION 3—FIRST AID MEASURES

EMERGENCY AND FIRST AID PROCEDURES:
Eye Contact—If material comes in contact with the eyes, promptly wash the eyes with water. Get medical attention if any discomfort continues.
Skin Contact—No special precautions; flush with water.
Inhalation—If a person breathes in large amounts of this material, move the exposed person to fresh air at once. Other measures are usually unnecessary.
Ingestion—No special precautions.

SECTION 4—FIRE-FIGHTING MEASURES

Flash Point: N/A AUTO IGNITION TEMP: N/A
FLAMMABLE LIMITS IN AIR LOWER
UPPER % BY VOLUME N/A N/A
Extinguishing Media: Use appropriate media to extinguish source.
SPECIAL FIRE FIGHTING PROCEDURES: N/A
UNUSUAL FIRE AND EXPLOSION HAZARDS: None
HAZARD RATINGS: NFPA 704: Health—0 Fire—0 Reactivity—0

SECTION 5—ACCIDENTAL RELEASE MEASURES

No hazard

SECTION 6—HANDLING & STORAGE

HANDLING AND STORING: Store in a dry area.

SECTION 7—EXPOSURE CONTROL—PERSONAL PROTECTION

ENGINEERING CONTROLS: No requirements
RESPIRATORY EQUIPMENT: No requirements
EYE PROTECTION: No requirements
PROTECTIVE CLOTHING: No requirements
OTHER (SAFETY SHOWERS, EYE WASH STATIONS, ETC.): None

SECTION 8—PHYSICAL & CHEMICAL PROPERTIES

APPEARANCE: Off-White ODOR: N/A

BOILING POINT: N/A

SPECIFIC GRAVITY (water=1): N/A

VAPOR PRESSURE: Negligible

VAPOR DENSITY (air=1): Negligible

SOLUBLE IN WATER: Not soluble EVAPORATION RATE (ether=1): negligible

SECTION 9—STABILITY & REACTIVITY

STABILITY: STABLE X

UNSTABLE

INCOMPATIBILITY: N/A

HAZARDOUS DECOMPOSITION PRODUCTS: N/A

HAZARDOUS POLYMERIZATION: Will not occur

CONDITIONS TO AVOID: N/A

MATERIALS TO AVOID: N/A

SECTION 10—TOXICOLOGY INFORMATION

Bovine Colostrum Powder has no established ingestion limits.

Toxicology reports on Colostrum by the United States regulatory body of National Nutritional Foods Association (NNFA).

SAFETY OF BOVINE COLOSTRUM POWDER DERIVED FROM COLOSTRUM AND ITS TOXICOLOGY

There appear to be no reports of adverse effects due to the use of colostrum or Bovine Colostrum Powder as a dietary supplement. The presence of IGF in colostrum, and the reported increase in serum levels of IGF following colostrum use, if confirmed, do, however, raise some concern about its safety. However the levels of IgF-1 and other growth factors in Bovine Colostrum Powder are undetectable. Please visit http://www.nnfa.org for complete article and references.

Bovine Colostrum Powder is extracted from colostrum. Since colostrum is derived from bovine lacteal sources it Generally Regarded as Safe (GRAS) by the United States Department of Agriculture (USDA).

Bovine Colostrum Powder is approved as a dietary supplement, but not as a drug, according to Dr. Fudenburg in Progress in Drug Research 42:378 (1994). Foods and dietary supplements are not approved per se by the FDA and food supplements derived from milk would certainly fall under the category of Generally Recognized As Safe [GRAS], and because colostrum comes from a bovine milk source it is Generally Recognized As Safe [GRAS].

SECTION 11—ECOLOGICAL INFORMATION

Note: Advanced Protein Systems LLC. has not conducted specific ecological tests on this product.

SECTION 12—DISPOSAL CONSIDERATION

Use normal waste disposal procedures that are in compliance with federal, state, and local regulations.

SECTION 13—REGULATORY INFORMATION

DOT PROPER SHIPPING NAME: Not regulated by DOT
DOT HAZARD CLASS: N/A
DOT IDENTIFICATION NUMBER: N/A DOT EMER. RESPONSE GUIDE NO.: N/A

SECTION 14—OTHER INFORMATION

This product does not contain toxic chemicals subject to the reporting requirements of SARA Section 313 of the Emergency Planning and Community Right-To-Know Act of 1986 and of 40 CFR 372.

SARA SECTON 311-312 HAZARD CATEGORIES (40 CFR 370.2):
FIRE: No
SUDDEN RELEASE OF PRESSURE: No
REACTIVE: No
ACUTE: No

TYPICAL PRODUCT SPECIFICATIONS OF A *LIQUID PRPS ISOLATE*

1.0 Characteristics

Item	Item Description		Specification
1.1	Dosage form		Spray
1.2	Route of Administration		Oral
	Appearance		Greenish liquid
1.3	Serving size		.7 ml per spray
1.4	Shelf life		Two years
1.5	Storage conditions		25°C ± 2°C
1.6	Pack size		4.25 oz. (125.7 ml)
1.7	Container:		
	1.7.1	Product container	Bottle 4.25 oz., HDPE, white
	1.7.2	Closure system	.7 ml spray dispenser
	1.7.3	Product carton	9.75 x 8 x 6.25
	1.7.4	Tamper evident features	None
1.8	Insert(s)		None
1.9	Daily dosage		
	1.9.1	Minimum	1 spray
	1.9.2	Maximum	4 sprays

2.0 Active Ingredients per serving

Item	Ingredient	Label Claim		Input w/Over		Over %	Ref/Std
2.1	Bovine Colostrum @ .33 % protein	.434	ml	.434	ml	-	

3.0 Non-Active Ingredients

Item	Ingredient	Input Amount		Ref/Std
3.1	Sodium Benzoate	.0007	MI	
3.2	Potassium Sorbate	.0007	MI	
3.3	Natural Vanilla Flavoring	.0035	MI	
3.4	Make up water	.261	MI	

4.0 Purity Assays

Item:	Test	Release limits:	Method:
4.1	Heavy Metal		AA/ICP
	4.1.1 Arsenic	< 0.14 µg/kg b.w./day	ICPMMS
	4.1.2 Cadmium	< 0.09 µg/kg b.w./day	ICPMMS
	4.1.3 Lead	< 0.29 µg/kg b.w./day	ICPMMS
	4.1.4 Mercury	< 0.29 µg/kg b.w./day	ICPMMS
4.2	Pesticides	USP Limits	USP
4.4	Solvent Residues	USP Limits	USP
4.5	Identification	NLT 80% or top five matches	FTIR/Visual

5.0 Chemical Assays

Item:	Ingredient:	Release Limits:	Method:
5.1	Protein	NLT 80% of Label (0.3 % protein)	AOAC 991.20.1

6.0 Microbiological Assays

Item:	Test	Release limits:	Method:
6.1	Total plate count	NMT 10 cfu/g	BAM 8th ED.
6.2	E. Coli	Negative	BAM 8th ED.
6.3	Salmonella	Negative	BAM 8th ED.
6.4	Staphylococcus Aureus	Negative	BAM 8th ED.
6.5	Yeast and mold	NMT 1 cfu/g	BAM 8th ED.

MATERIAL SAFETY AND DATA SHEET OF A PRPS ISOLATE

SECTION 1—COMPOSITION & INFORMATION ON INGREDIENTS

Bovine Colostral Whey Permeate liquid dairy product:

Active Components:

Proline Rich Polypeptides (PRPS) (0.3% PRPS solids)

Inactive Components:

Vitamins A, B1, B2, B5, B6, B12, B13, C, E, Folic Acid, Beta-carotene, and Retinoic Acid, Sulphur. (<0.5% vitamin solids)

Lactose sugar (3% sugar solids)

This product contains 96% filtered water.

SECTION 2—HAZARDS IDENTIFICATIONS

• EMERGENCY OVERVIEW

Transparent green liquid. Non-flammable. Non-hazardous to eyes, skin and throat.

POTENTIAL HEALTH EFFECTS

ROUTES OF ENTRY: Eye contact, dermal, inhalation, ingestion

ACUTE EFFECTS OF OVEREXPOSURE:

Eyes—Non-hazardous

Skin—Non-hazardous

Inhalation—Non-hazardous

Ingestion—Non-hazardous

CHRONIC EFFECTS OF OVEREXPOSURE: None known

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: None known.

CARCINOGENICITY: NTP: No IARC: No OSHA: No

SECTION 3—FIRST AID MEASURES

EMERGENCY AND FIRST AID PROCEDURES:

Eye Contact—If material comes in contact with the eyes, promptly wash the eyes with water. Get medical attention if any discomfort continues.

Skin Contact—No special precautions; flush with water.

Inhalation—If a person breathes the spray in large amounts of this material, move the exposed person to fresh air at once. Other measures are usually unnecessary.
Ingestion—No special precautions.

SECTION 4—FIRE-FIGHTING MEASURES

Flash Point: N/A AUTO IGNITION TEMP: N/A
FLAMMABLE LIMITS IN AIR LOWER
UPPER
% BY VOLUME N/A N/A
Extinguishing Media: Use appropriate media to extinguish source.
SPECIAL FIRE FIGHTING PROCEDURES: N/A
UNUSUAL FIRE AND EXPLOSION HAZARDS: None
HAZARD RATINGS: NFPA 704: Health—0 Fire—0 Reactivity—0

SECTION 5—ACCIDENTAL RELEASE MEASURES

No hazard

SECTION 6—HANDLING & STORAGE

HANDLING AND STORING: Store in a cool dry area or at standard room temperature and pressure.

SECTION 7—EXPOSURE CONTROL—PERSONAL PROTECTION

ENGINEERING CONTROLS: No requirements
RESPIRATORY EQUIPMENT: No requirements
EYE PROTECTION: No requirements
PROTECTIVE CLOTHING: No requirements
OTHER (SAFETY SHOWERS, EYE WASH STATIONS, ETC.): None

SECTION 8—PHYSICAL & CHEMICAL PROPERTIES

APPEARANCE: Light green transparent liquid: N/A
BOILING POINT: 212F (100degC)
SPECIFIC GRAVITY (water=1): 1
VAPOR PRESSURE: 2.86 kPa at 25degC (standard room temperature)
VAPOR DENSITY (air=1): 1

SOLUBLE IN WATER: It is 96% water.

SECTION 9—STABILITY & REACTIVITY

STABILITY: STABLE X

UNSTABLE

INCOMPATIBILITY: N/A

HAZARDOUS DECOMPOSITION PRODUCTS: N/A

HAZARDOUS POLYMERIZATION: Will not occur

CONDITIONS TO AVOID: N/A

MATERIALS TO AVOID: N.A

SECTION 10—TOXICOLOGY INFORMATION

Colostral Whey Permeate has not established injestion limits,

Toxicology reports on Colostrum by the United States regulatory body of National Nutritional Foods Association (NNFA). There appear to be no reports of adverse effects due to the use of colostrum or colostral whey permeate as a dietary supplement. The presence of IGF in colostrum, and the reported increase in serum levels of IGF following colostrum use, if confirmed, do, however, raise some concern about its safety. However the levels of IgF-1 and other growth factors in Colostral Whey Permeate are undetectable. Please visit http://www.nnfa.org for complete article and references.

Colostral whey permeate is extracted from colostrum. Since colostrum is derived from bovine lacteal sources it Generally Regarded as Safe (GRAS) by the United States Department of Agriculture (USDA).

Colostral Whey Permeate is approved as a dietary supplement, but not as a drug, according to Dr. Fudenburg Prog in Drug Res. 1994, 42, p378. Foods and dietary supplements are not approved per se by the FDA and food supplements derived from milk would certainly fall under the category of Generally Recognized As Safe [GRAS].

SECTION 11—ECOLOGICAL INFORMATION

Note: Advanced Protein Systems LLC. has not conducted specific ecological tests on this product. Biological Oxygen Demand (BOD) is 30mg/L, Chemical Oxygen Demand (COD) is 100mg/L.

SECTION 12—DISPOSAL CONSIDERATION

Use normal waste disposal procedures that are in compliance with federal, state, and local regulations.

SECTION 13—REGULATORY INFORMATION

DOT PROPER SHIPPING NAME: Not regulated by DOT

DOT HAZARD CLASS: N/A

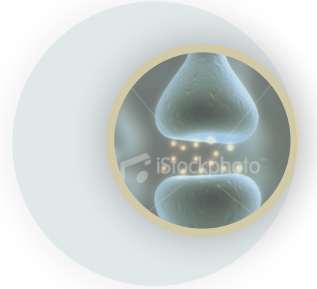
DOT IDENTIFICATION NUMBER: N/A DOT EMER. RESPONSE GUIDE NO.: N/A

SECTION 14—OTHER INFORMATION

This product does not contain toxic chemicals subject to the reporting requirements of SARA Section 313 of the Emergency Planning and Community right-To-Know Act of 1986 and of 40 CFR 372.

SARA SECTON 311-312 HAZARD CATEGORIES (40 CFR 370.2):

FIRE: No SUDDEN RELEASE OF PRESSURE: No REACTIVE: No ACUTE: No CHRONIC: No



APPENDIX C

INSTITUTE FOR COLOSTRUM RESEARCH

The Institute for Colostrum Research is an organization dedicated to being a central information resource for consumers, health practitioners, and researchers on the subject of colostrum and its components. Located in New Zealand, where the use of colostrum as a nutritional supplement is well established, the center's Web site is a good source of research articles and general information about colostrum and its uses.

Michail Borissenko, Chief Scientist at the Institute, has graciously allowed us to reprint several articles and a FAQ from their Web site, www.colostrumresearch.org.

ICR QUALITY SCALE

MICHAIL BORISSENKO
Chief Scientist
Institute of Colostrum Research

Background

Colostrum is not only a highly nutritious functional food but also a substance that contains many life supporting and health promoting substances. The significance of colostrum is best illustrated by the fact that most animals require colostrum just after birth to survive. Some of these life supporting and growth

promoting substances are as follows: antibodies, immune factors, growth factors, attachment factors, cytokines, oligosaccharides, essential fatty acids, and phospholipids. The remarkable thing about colostrum is that all these substances act synergistically in such a way as to enhance the overall affect of each individual component.

Colostrum has many functions and properties which make it most probably the single most important food in the world. Among these properties are the abilities to fight disease and to promote growth and well-being. Colostrum has also been shown to speed up the recovery process following injury and stress. Other attributes associated with colostrum include anti-aging properties, balanced blood sugar levels, increased performance, increased mental alertness and weight loss—specifically, accelerating the burning of fat.

Overall health begins in the gut, and this is where colostrum's actions begin. The significance of colostrum is self-promoting in that good health has no substitute. Whether young or old, fit or weak, colostrum can be of benefit. Backed by literally thousands of research studies and clinical trials, colostrum has been shown to be an effective means by which overall health can be obtained.

The sales of colostrum for the basic maintenance of good health are rising dramatically. Add to this the increased use of colostrum in the medical, nutrition and nutraceutical markets. This growth is fantastic as colostrum is truly nature's wonder food. It is not only a highly nutritious food but also contains numerous factors which not only help fight disease, but also help to promote growth and the healing process. In short, colostrum helps to promote overall good health and well-being. It does this by removing existing deficiencies, promoting the power of resistance, and supporting the healing process.

With the increase in consumption of colostrum, a dramatic rise in the number of manufacturers, suppliers, and distributors has been observed. Add to this the dramatic rise in various types of formulated colostrum products available to the consumer. Unfortunately, associated with this growth, it has been observed that the quality of some colostrum products are better then others, and more

concerning is that many claims by some distributors of colostrum products are confusing, incorrect or clearly misleading.

The Institute of Colostrum Research (ICR) has undertaken to establish criteria by which colostrum products can be evaluated. ICR has undertaken this task to educate the consumer as to how to judge colostrum products from different distributors. In this way the consumer can make a more educated choice as to what colostrum product is best.

What is the ICR Quality Scale? Simply put, it is a method by which one can quantify or measure the quality of a colostrum product. Different manufacturers use various processes to manufacture their colostrum products. They also source their colostrum from different suppliers. In addition, manufacturers vary as to what additives and ingredients they add to their colostrum products. The ICR Quality Scale is designed to measure or quantify the quality of colostrum products.

Key Quality Indicators of colostrum are as follows:

1) Pasteurization
2) Low Temperature Processing
3) Immunoglobulin Values—levels of IgG, IgA, and IgM
4) Growth Factor Values—IGF, TGF, TNF, EGF
5) Immune Factors—lactoferrin, cytokines, lysozyme, lactoperoxidase
6) Environmental factors influencing quality
7) Quality manufacturing
8) Additives
9) Solubility (dispersibility)
10) Science

Pasteurization

This is a crucial step in any commercial dairy process. Do not purchase any colostrum product that has not been pasteurized. There are alternative methods

that employ other means of sterilization, but these must meet the same International Standards as pasteurization.

Low Temperature Processing

It is imperative that colostrum be processed in such a way as to avoid prolonged exposure to heat. Pasteurization is necessary and is performed so as to ensure microbiological quality. Typically this is performed at 72°C for a period of 15 seconds. It has been shown that pasteurization has no significant negative effect on the bioactive molecules present in colostrum. The drying process used by some colostrum manufacturers may have a detrimental effect on colostrum quality. Specifically, in the case of spray-drying—which is the most common method of drying colostrum—some manufacturers of colostrum powder may incorporate high heat for prolonged periods. This can be evidenced in the final product in the form of discolored product, poor solubility, very low or no growth factors present, low levels of immunoglobulins and other proteins.

Immunoglobulins

The great majority of colostrum retailers stipulate only Immunoglobulin G (IgG) values. Colostrum is more then just IgG—in fact, IgG is only one of the immunoglobulins. The immunoglobulin fraction present in colostrum consists of IgG, IgA, IgM, IgD, and IgE. Both IgD and IgE are present in very low quantities whereas IgG, IgA, and IgM are found in considerable amounts. Thus commercial sources will optimally give also IgA and IgM, in addition to IgG, values.

Affinity vs. Immunoassay

Currently, most manufactures of colostrum determine IgG concentration by using a technique called Protein G HPLC. Protein G can only be used for obtaining IgG values and cannot be used for determining IgA and IgM. Further, Protein G was not designed for determining IgG values but rather for the processing of IgG.

The use of Protein G to determine IgG values was a nice little trick developed by

the New Zealand Dairy Research Institute. The basis for using Protein G is that it possesses an affinity to a portion of the IgG molecule (Fc portion). As such this technique can be referred to as an affinity assay.

The commonest and most recognized methods employed to measure specific protein levels are commonly referred to as immunoassays. These types of assays employ specific antibodies that are directed towards the protein (antigen) under investigation. In fact, these antibodies are not only specific but are also monospecific in that they will only react with that specific protein. With the exception of IgG, all the other proteins are quantified using immunoassay.

There are various types of immunoassays, such as radial immunodiffusion (RID), enzyme-linked immunoassay (ELISA), nephelometry, turbidometry, and (RIEP). In some cases these techniques are highly automated (nephelometry), whereas others are labor intensive (ELISA). In some cases immunoassays are available in commercially available kit form (RID and ELISA).

Standardization

Approximately 20 years ago the World Health Organization (WHO) in conjunction with the American Association of Clinical Pathologists (AACP) conducted a study to establish a world standard for human plasma proteins. Unfortunately, at the time of this writing, no such equivalent exists for bovine colostrum proteins. This means there is a lack of standardization involving the quantization of bovine proteins. Though this may seem to be a minor issue, the reality is that it is a major issue indeed. This is especially true when comparing different colostrum products from different manufacturers who use different methods to measure the proteins present.

A major problem associated with assigning specific protein values to colostrum products at present is that there appears to be a very wide variation in what is actually present. Most suppliers of colostrum provide IgG values for their products. At present this is how most colostrum is judged—by its IgG content. A preliminary investigation was conducted comparing Protein G and RID quantization of IgG.

In this investigation involving four commercially available RID kits, it was revealed that a variation of up to 40% in quantified IgG value was observed between the kits. This variability is simply not acceptable. Until there is a universally accepted standard for IgG and the other bovine colostrum proteins, the best advise to the consumer is simple— "Let the buyer beware."

Very recently we conducted a comparison study involving four commercially available colostrum products. These products were sent to an independent registered and accredited laboratory in order to have the (IgG) determined. The method of analysis was Protein G HPLC. The quantified values determined by the independent laboratory were then compared to the respective label values of the products. The results ranged from 46.7% lower IgG than stated to 50% more IgG than stated on the label—an overall variability of close to 100%. Once again, simply not good enough!

Growth Factors and Immune Factors

Commercially available immunoassay kits are presently available for the quantization of lactoferrin, lactoperoxidase, lysozyme, interleukins, interferons, insulin-like growth factor, tumor necrosis factor, transforming growth factors and epidermal growth factor. In addition, immunological reagents in the form of primary antibodies reactive to these molecules are also commercially available. Why aren't these growth factors and immune factors routinely assayed in all colostrum products?

Prolonged exposure to heat or over processing can have a detrimental effect on any or possibly all these bioactive molecules. As such it is imperative that to ensure high quality and bioactivity the colostrum must be produced in such a way as to avoid elevated temperatures. Low growth factor levels will indicate that most probably the colostrum was subjected to high heat processing.

Environmental Factors

The environment from which the colostrum is sourced is key to the supply of

good quality colostrum. A recent investigation conducted at Otago University in New Zealand revealed that a natural, non-hyperimmunized, commercially available product had significantly higher specific antibody titers to 19 pathogens compared to a commercially available equivalent which was derived from cows actively hyperimmunized (vaccinated) against these same 19 pathogens.

These results are significant in that it appears that natural immunization in the form of chronic low dose exposure via the oral route is far superior to active hyperimmunization. The non-immunized colostrum product in the Otago study was derived from the colostrum or early milk of healthy, untreated, pasture-fed cows.

Additives

Various manufacturers add any one of a number of additives to their colostrum products. The important thing is that the additives not hinder the effectiveness and bioavailability of the colostrum. It is also important that any additive not have a negative or detrimental effect on the colostrum. A case in point is one manufacture who utilizes papain as an additive in one of their colostrum products. Papain is an enzyme derived from the papaya fruit and is typically used as a digestive aid. Unfortunately, this manufacturer obviously doesn't realize that papain is a proteolytic enzyme that digests proteins. In fact, papain is typically used to cleave the IgG molecule in certain research applications. It most certainly also cleaves (partially digests) the other immunoglobulins as well. Its effect on growth factors, immune factors and other bioactive constituents in colostrum? Who knows?

Quality Manufactured Product

Is the colostrum manufactured to the highest standards? To make sure, only government certified colostrum producers and processors should be used. These organizations would have Product Safety Programs in place so as to ensure that all the colostrum they produce is of the highest standard.

Solubility

Solubility is an important issue to consider. This is especially true since poor solubility can reflect poor bioavailability of product. Causes of poor solubility are usually linked with flaws in manufacturing, such as high heat exposure, overprocessing and drying conditions. Is the colostrum powder soluble in water? It should be if it was processed correctly. If it is not, then it most likely is second rate.

Science

Many claims by some distributors of colostrum products are confusing, incorrect or misleading. Does the manufacturer or distributor of the colostrum back their product with proper science? Is the scientific and technical information associated with the product correct? A credible supplier of colostrum products will back up any such information with referenced material.

Further, no responsible supplier of nutraceutical products, such as colostrum, would make any direct health claims. This is especially true as labeling and product information restrictions are quite clear in that only registered drugs (pharmaceuticals) can make any specific health claims. It must be noted that there are a number of lunatic fringe type of companies that are operational in the field, unfortunately. Their marketing is truly aggressive, and their credibility is questionable. Hopefully their existence will be short-lived.

BOVINE LACTOFERRIN

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Lactoferrin is the best example of a powerful bioactive derivative of colostrum that is close to reaching a bio-pharmaceutical status. Several manufacturers around the world are isolating lactoferrin on a commercial scale. It is showing great promise and has recently gained a great deal of international attention based on its broad range of beneficial physiological effects. Lactoferrin is a unique protein that influences cell proliferation and differentiation. It functions as an immune modulator, antimicrobial, antiviral, anticancer, anti-inflammatory, iron carrier, antioxidant and promoter of balanced intestinal flora.

Lactoferrin was first isolated in milk, but it is also found in other secretions such as tears and saliva. Its main biological function relates to its very high affinity for iron. Because of this, lactoferrin is an excellent inhibitor of a wide range of microorganisms that require iron for growth and proliferation. Lactoferrin activates the non-specific immune response by stimulating phagocytosis and complement. Recent scientific evidence has linked lactoferrin with significant potential beneficial effects in the treatment of cancers, specifically in the reduction of tumors. Though the actual mechanism of action is yet to be elucidated, lactoferrin has been shown ***in vitro*** to suppress colon cancer tumors and also to inhibit lung cancer metastasis. Further, it has also been shown to successfully inhibit hepatitis C virus in patients suffering from chronic infection.

Lactoferrin plays a significant role in cellular defense. This most likely is by modulating macrophage activity and stimulating the proliferation of lymphocytes. A very important function of lactoferrin is modulating the immune response, and colostrum has been shown to be very effective in preventing the immune response from getting out of control. In animal studies it has been shown that orally administered lactoferrin results in an increase in total immunoglobulin levels present in intestinal fluid, thereby stimulating the mucosal immune system.

Lactoferrin has been shown to be effective against a wide variety of microbes and function as both a bacteriostatic (not allowing pathogens to grow) and bactericidal agent (destroying pathogens). The bacteriostatic function is attributed to its ability to remove free iron and thus limit the growth or colonization of pathogens requiring iron in order to proliferate—iron deprivation. The bactericidal function is attributed to lactoferrin's ability to act directly with pathogens and neutralize them. In this manner lactoferrin has been shown to be effective against a wide variety of pathogens including the following pathogens: ***Salmonella, Staphylococcus, Listeria, Campylobacter, Clostridia***, and ***E. coli*** O157:H7. Further, it has been demonstrated that lactoferrin can reduce the severity and duration of enteric infection thus limiting the spread of disease. It is also of interest that Lactoferrin has been shown to act synergistically with antibiotics and antifungal agents, thus increasing their effectiveness.

Lactoferrin's action as an antiviral agent has recently come to light. The mode of action appears to be that lactoferrin inhibits the binding of virus to the cell wall. Significant beneficial results were observed against HIV, cytomegalovirus, herpes type 1&2, hepatitis C, influenza, and rotavirus.

Lactoferrin has been shown to help promote the growth of probiotic or good bacteria, such as Bifidobacterium, in the gut. It does this by inhibiting the growth of various pathogenic microbes, thereby ensuring a balance of intestinal flora.

Lactoferrin has a very high affinity for iron. Because of this, lactoferrin is an optimal transporter of iron. In this way, lactoferrin increases the bioavailability of iron. Lactoferrin is a natural antioxidant due its ability to bind iron. As an iron scavenger, lactoferrin prevents the formation of free radicals caused by the oxidation process. Lactoferrin functions to reduce inflammation by regulating potent stimulators of cytokines. Cytokines are substances that are produced by the immune system in response to infection and inflammation. Lactoferrin regulates the immune response, thus limiting inflammation.

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GROWTH FACTORS

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Colostrum is a very complex mixture containing many substances that have yet to be fully appreciated. Among these substances are a group of low molecular weight peptides collectively referred to as growth factors. Growth factors are hormone-like peptides that either act alone or in conjunction with other substances to affect the growth (proliferation) and maturation of various cell types. For example, some growth factors help epidermal cells (skin and digestive tract) grow faster, while other growth factors stimulate muscle and bone cell proliferation and development. Of significant interest is the fact that bovine growth factors found in colostrum are almost identical to that of human in both structure and function. In addition to growth factors, there are also cytokines present in colostrum. Two of these, interferon and interleukin, also demonstrate growth promoting actions.

Growth factors and cytokines present in colostrum and their respective actions include:

Epidermal Growth Factor (EGF)—Stimulates tissue repair and wound healing and maturation of the digestive tract in infants
Insulin-like Growth Factors 1 & 2 (IGF-1 & IGF-2)—Stimulates muscle and bone cell proliferation and development, associated with the anti-aging process.
Fibroblast Growth Factor (FGF)—Stimulates muscle and bone cell proliferation and development
Platelet-Derived Growth Factor (PDGF)—Stimulates the proliferation and development of a wide range of cell types
Transforming Growth Factor (TGF)—Stimulates tissue repair and wound healing
Interleukins—Stimulates the immune response by promoting proliferation and maturation of activated T cells

Interferons—Antiviral, stimulate the immune response by modulating the activity of natural killer cells

Insulin-like growth factor 1 is found in relatively high concentrations in bovine colostrum and is of specific interest in regard to athletic performance and the anti-aging process. Specifically, this growth factor mediates the growth or metabolic effects of growth hormone. On a molecular level, IGF-1 functions to stimulate muscle and bone cell proliferation and development, i.e., helps to build muscle and strong bones. In a recent study it was shown that oral supplementation with bovine colostrum enhances the recovery process following physical exercise or exertion. Thus it allows harder training with improved recovery. Two further studies have shown that bovine colostrum has a positive effect on maximal power output—increases vertical jump performance and improves rowing performance in elite female rowers. It has been demonstrated in laboratory studies that IGF-1 can promote an increase of up to 15% in muscle mass and a 14% increase in strength. Further, it has been shown that IGF-1, through its action on growth hormone, can retard the aging process, including decreasing cardiovascular associated mortality, reducing osteoporosis and improving brain function.

Transforming growth factors and epidermal growth factors are also found in relatively high amounts in bovine colostrum. Both these growth factors stimulate tissue repair and wound healing. Physical exercise and training cause muscle and tissue damage. The degree of damage and time required for repair depends on various factors, such as physical condition, level of stress, dietary and medicinal considerations. Bovine colostrum has been shown to help in this recovery process.

Inflammation is associated with physical exertion and strenuous exercise. Though typically inflammation is centered in the joints, it also observed in the digestive tract and in muscle tissue. There are various anti-inflammatory agents available to treat inflammation. Unfortunately, there are also potential side effects and adverse reactions associated with these compounds. In fact, the adverse side effects associated with certain anti-inflammatory agents limit their use. The most commonly used compounds used to treat inflammation are non-steroidal anti-

inflammatory drugs (NSAIDs), such as aspirin or salicylates. Commonly observed side effects associated with these compounds include gastric upset and gastric bleeding. It has been observed that the use of bovine colostrum has been proved effective in the treatment of gastrointestinal disorders caused by aspirin and other non-steroidal anti-inflammatory medications.

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IGF-1 AND CANCER—NOT! DAIRY PRODUCTS AND CANCER: THE REAL FACTS

By Alfred E. Fox, Ph.D.

There has been considerable adverse publicity and confusion recently regarding the relationship between the intake of dairy products, particularly milk, and the development of certain types of human cancer. One of the most outspoken antagonists supporting programs that attack the intake of dairy products is Robert Cohen, who identifies himself as the Executive Director of the Dairy Education Board. In reality, Mr. Cohen is an investigative reporter who has found a cause to champion and uses the Dairy Education Board, an "organization" he founded, as a soapbox. Mr. Cohen has published a book on the subject, ***MILK—The Deadly Poison***, and authors a Web site (www.notmilk.com) as a means to disseminate his views and those of his supporters.

When one looks at the Web site of Mr. Cohen, it is evident that although he professes to state only the facts, he has grossly distorted them to suit his own needs. For example, in a supposed factual newsletter written in June 1998, but still used on the Web site, Mr. Cohen reports that Virgil Hulse, MD, wrote a book entitled ***Mad Cows and Milk Gate*** in which he reported that most of the dairy cows in America have bovine leukemia, bovine immunodeficiency virus or bovine

tuberculosis. Mr. Cohen then states "We drink body fluids from diseased animals in the name of good health." Anyone familiar with the dairy industry in America, or who will take the time to properly investigate it, knows that all dairy cows are vaccinated against these diseases and that such vaccinations are mandatory if the dairy farmer intends to sell milk for human consumption. Further, virtually all milk sold in commercial outlets for human consumption is pasteurized at temperatures that would destroy these microorganisms even if they were present.

Mr. Cohen's attack on milk has focused primarily on insulin-like growth factor-1 (IGF-1) wherein he claims that this hormone makes human cancers grow. Throughout the Web site, he cites scientific articles by reputable authors from prestigious institutions that he claims state that IGF-1 is a key factor that promotes the growth of prostate, breast and colon cancers. The Web site contains an article written by Hans R. Larsen, a chemical engineer, which makes similar misrepresentations of scientific findings. Mr. Larson cites numerous articles and then makes statements about them, such as the following.

"On January 23, 1998, researchers at the Harvard Medical School released a major study providing conclusive evidence that IGF-1 is a potent risk factor for prostate cancer."

"In 1995, researchers at the National Institutes of Health reported that IGF-1 plays a central role in the progression of many childhood cancers and in the growth of tumors in breast cancer, small cell lung cancer, melanoma, and cancers of the pancreas and prostate."

"In September 1997, an international team of researchers reported the first epidemiological evidence that high IGF-1 concentrations are closely linked to an increased risk of prostate cancer. Other researchers provided evidence of IGF-1's link to breast and colon cancers."

These statements are inaccurate misrepresentations of the actual conclusions drawn by the scientific investigators in their publications. The investigators' findings have been distorted to try and lead the reader to the erroneous conclusion

that the intake of IGF-1 will lead to enhanced tumor development in human cancers. The truth is that no one has ever demonstrated a cause-and-effect relationship between IGF-1 and cancer. In fact, when the quoted articles are reviewed, one finds that none of the investigators ever even suggested that IGF-1 was a causative agent in tumor development associated with human cancers but instead found that people with certain types of tumors had high levels of IGF-1 in their circulation as a manifestation of their disease. The elevated levels of IGF-1 seem to occur very early in tumor development and several authors cited by Mr. Larson have actually suggested that measurement of IGF-1 in the blood of people may be an early warning indicator that a tumor could be developing in the body. They believe that making such measurements of IGF-1 could mean possible earlier diagnosis and treatment. This situation is analogous to the elevated white blood cell count seen in association with appendicitis. The elevated white blood cell count is a manifestation of the condition and an indicator of infection. No reasonable person would say that it caused the appendicitis.

What are the real facts about IGF-1?

Insulin-like growth factor-1 and its closely related counterpart insulin-like growth factor-2 are potent hormones that are found in association with almost all cells in the body. IGF-1 is the best described and most potent of this pair. These molecules are produced by all mammals and in every case have a very similar chemical structure regardless of the species. IGF-1 is essential for normal cell growth and for the development of the fetus in the uterus.[4] Both IGF-1 and growth hormone are required for normal postnatal development,[7] and that is why they are both present in colostrum. The IGFs are structurally very similar to insulin and in fact, in certain diseases the specific receptors for insulin on cells in the body are sometimes incapable of distinguishing between IGF-1 and insulin.

Scientific knowledge about the IGFs, what they do and how they act on cells in the body, has evolved very rapidly during the past few years. It is now known that there are specific receptors on almost all cells in the body capable of interacting with IGF-1 and triggering a series of chemical events within the cell.[8] There are also six different proteins present inside the cell and on cell surfaces that control

the actions of IGF-1 on the cell after it binds to a receptor. These are called insulin-like growth factor binding proteins (IGFBPs). In addition, there are at least 87 other related proteins either capable of binding to IGF-1, altering its actions, or influencing the effects of the IGFBPs. These are called insulin-like growth factor binding protein-related proteins (IGFBP-rPs). The entire collection of these proteins is referred to as the insulin-like growth factor binding protein (IGFBP) super family.[9] The key event that triggers the effects of any of these proteins appears to be the interaction of IGF-1 with its specific cell-surface receptor, an event that some of these proteins regulate.

The multitude of available IGF-1 binding proteins and related proteins available in the cell is indicative of the many potential effects that the binding of IGF-1 to its specific cell-surface receptor can have on cells. To keep these many effects under control, some of the binding proteins act as checks and balances, allowing the secondary chemical switches in a cell to be turned on and then turning them off when it is appropriate. Therefore IGF-1 is like the captain of a ship. When it binds to its specific receptor, the ship can move forward, but there are all kinds of systems in place to keep it moving at the right speed and in the right direction. The main triggered events include activation of the process by which the cell grows and reproduces itself and maintenance of the metabolic pathways by which the cell converts glucose into glycogen and uses amino acids to create proteins. The actual pathway by which the cell uses glucose and converts it to glycogen is first switched on by the binding of insulin to its specific cell surface receptors. Glycogen is stored in the liver and muscles and is the main source of readily available energy when the muscles are exercised. The IGFBP super family also has a direct role in how the cell uses amino acids to build proteins. As we age, the ability of our body to create an adequate supply of IGF-1 is diminished. Thus, by eating a well-balanced diet and maintaining a constant supply of IGF-1 in our body, we can keep the ship moving at the right speed and in the right direction. And when we exercise, this becomes even more critical since there is an increased demand for glycogen to provide energy to our muscles, and the preference is to build more muscle protein. Even more importantly, as we age, the cells in our body do not reproduce themselves as well, and since IGF-1 is a primary factor in the ability of cells to grow and reproduce, it is highly desirable to have an appropriate level of

IGF-1 in the circulation through dietary supplementation to limit the ever increasing rate of cell senescence.

Why is there excess IGF-1 in the circulation in certain types of cancer?

You will recall that Mr. Hans Larsen, writing on behalf of Mr. Robert Cohen, drew the following conclusion in his article on Mr. Cohen's Web site:

"In 1995, researchers at the National Institutes of Health reported that IGF-1 plays a central role in the progression of many childhood cancers and in the growth of tumors in breast cancer, small cell lung cancer, melanoma, and cancers of the pancreas and prostate."

In actual fact, in the 1995 article cited,[1] these researchers reported that the cell surface receptors for IGF-1 mediate most of the effects of IGF-1, and despite its structural similarity to the insulin receptor, the IGF-1 receptor is mainly involved in the support of growth and sends different types of signals than the insulin receptor. They concluded that the gene encoded for the IGF-1 receptor is expressed by most cells in an organism, which is consistent with the role of IGFs as survival factors, and that the receptor gene is modulated by many physiological and pathological factors, including developmental stage, nutritional status, hormones, growth disorders and malignancy. In 1996,[2] the same researchers reported that the IGF-1 receptors are integral cell membrane proteins that demonstrate important effects on the regulation of cellular processes. The same investigators and others[3] also found that the IGF binding proteins (IGFBPs) were made by cells and could be secreted such that they could accumulate on external cell surfaces. As such, the IGFBPs were found to be involved in regulating cell processes by modulating the interaction of the IGFs with their cell surface receptors. Later it was recognized that certain of the IGFBPs were growth inhibitory molecules and as such, were primary regulators of the effects of IGF-1 interaction with its cell surface receptor on cell growth.[5,6]

Multiple studies have shown that there is an elevated level of IGF-1 in the cir-

culation of patients with certain types of malignancies including, prostate cancer,[11,12,13,14,15] breast cancer,[17,18,19,20,21,22,23,24,25] colorectal cancer,[26] acute lymphoblastic leukemia,[27,28] and non-small cell lung cancer.[29] Many of these studies also reported other associated factors. A group from the Harvard School of Public Health investigated the relationship of intake of dairy products to the risk of prostate cancer and found such patients also had reduced circulating levels of vitamin D, a factor believed to be protective for prostate cancer.[13] In several cases, increased circulating levels of IGF-1 were paralleled by extremely low levels of a particular IGFBP (IGFBP-3) known to be a very potent inhibitor of the cell growth-promoting effects of IGF-1 and IGF-1 receptor interaction.[24,25,26] More recent studies have shown that levels of some of the IGFBP-related proteins that control the inhibitory effects of IGFBP-3 are also altered in certain malignant diseases.[15,22] One study has shown that another IGF-binding protein (IGFBP-6) that is involved in programmed cell death is increased in non-small cell lung cancer.[29] In some studies, associations have been drawn between the levels of certain hormones, increased circulating IGF-1 and cancer risk. In prostate cancer there have been proposed relationships to high levels of testosterone[10] and in breast cancer with the progestins, which seem to interfere with the interaction of IGF-1 and its cell surface receptors.[18,22]

It is difficult to understand how a comprehensive review of the scientific literature would lead one to the conclusion that IGF-1 is responsible for enhanced tumor development in certain types of human cancer. This is particularly true when it is seen that the same increased circulating levels of IGF-1 and modifications of certain controlling protein substances have been found in various nonmalignant diseases. For example, similar alterations in IGF-1 and IGFBP-3 are found in patients with benign prostatic hyperplasia.[16] In both Type 1 and insulin-resistant Type 2 diabetes, patients demonstrate increased circulating levels if IGF-1[30,31,32] and in Type 2 diabetes patients an inverse correlation between levels of insulin and a particular IGFBP (IGFBP-1) has been shown.[30] In another study from the Harvard School of Public Health, it has been shown that men with higher levels of testosterone are more likely to have vertex baldness and in those that additionally have higher than normal blood levels of IGF-1 the odds of vertex baldness is doubled.[33] Published studies have also shown that in growth-retarded individuals

the gene encoding for the IGF-1 receptor is defective, and as a result, these individuals have substantially elevated levels of circulating IGF-1.[34]

There is no question that there is an increased circulating level of IGF-1 in patients with prostate, breast, colorectal, lung cancer and some leukemias. The effects of IGF-1 on the cells, which include cell growth, survival and transformation, are mediated through its interaction with IGF-1 receptors on cell surfaces. The interaction of IGF-1 with its receptors is further controlled by the IGFBPs, some of which can independently act on cell processes. The controlling aspects of the IGFBPs are further modulated by many additional regulating substances in both normal and disease processes.[36,37] Studies from the National Institutes of Health have shown that in malignant disease there are more than enough IGF-1 receptors on cell surfaces, but the ability of these receptors to interact with IGF-1 is significantly reduced. They were also able to demonstrate that the most frequently mutated gene in human cancer, p53, lowers the ability of the IGF-1 receptors to bind IGF-1 and function.[35] Studies from Germany reported in September 2000 have added to the understanding of this process.[38] These investigators found that a protein encoded by the human papilloma virus binds to IGFBP-3, which restricts cell growth following the interaction of IGF-1 with the IGF-1 receptor, and enzymatically degrades it. This protein is a product of the p53 gene, and it has long been known that it can immortalize primary human cells and overcome cellular senescence. Therefore the underlying cause for elevated levels of IGF-1 seen in cancer is related to a cascade of events that begin with an alteration of basic genetic information and culminate in an impaired functioning of the IGF-1 receptors on the surface of the cells. In this case, other IGFBP and related proteins that can act independent of IGF-1 interaction with its receptors have apparently redirected cell growth without the involvement of IGF-1. Since IGF-1 does not have operating, functional receptors to interact with, it naturally backs up in the circulation as a manifestation of the disease process.

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GLUTATHIONE: A POWERFUL ANTIOXIDANT FOUND IN COLOSTRUM

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Colostrum is the most significant food in the world. It was designed by nature to protect the newborn. The significance of colostrum and the role it plays is best illustrated in the typical farm animal. Take the horse, cow, sheep, goat, cat, dog—unless these and most other animals receive colostrum in the first day or two of life they have a very significant chance not surviving. This phenomenon is due to a wonderful mechanism by which the mother can pass on her complement of antibodies to her newborn, known as passive transmission of immunity.

Because of this and the role that colostrum plays in the newborn, some other very important actions or properties associated with the biological function of colostrum have been overlooked. One of these properties is the fact that colostrum, in addition to all its other benefits, is a source of a wide range of antioxidants. One such antioxidant, glutathione, has been described as the ultimate antioxidant. It is very well documented that glutathione and its precursors are present in colostrum in relatively high levels. In this capacity, glutathione and glutathione precursors play an important part in colostrum's role in overall health.

Glutathione also referred to as GSH, is a naturally occurring peptide or small protein which has a primary function as an **antioxidant**. Linus Pauling was a leading advocate of antioxidants and their respective role in prevention of disease and the promotion of overall good health. Antioxidants, for the most part, are naturally occurring compounds that possess the ability to neutralize unstable **free radicals**. Unchecked, these free radicals have been linked, at least in part, as the causative agents of a number of disease conditions including cancer, heart disease, stroke, and improper nervous and immune system function. A growing number of scientific and medical research studies have shown that antioxidants can deactivate free radicals and thus limit the spread of certain disease states. Basically, an-

tioxidants act as free radical scavengers that remove them from the body before they can cause their harmful effects. Many foods such as fruits, vegetables, grains and oils contain vitamins and minerals that have antioxidant properties. Vitamins A, C and E, carotenoids and flavonoids are probably the best known antioxidants. The growing body of scientific and medical research substantiates the role that glutathione and other antioxidants play in sustaining health and combating disease. This mountain of evidence suggests that by simply increasing one's levels of glutathione, a corresponding increase of overall good health can be envisioned.

The development of cancer and disease is usually a long, slow process. One exception is childhood cancers, which are usually attributed to inherited defective genes. Cancer cells in adults contain a large number of mutations acquired over a lifetime's exposure to environmental carcinogens, toxins and free radicals. These substances damage the body's DNA—the blueprint of life. Antioxidants have been shown to protect DNA from excessive damage and help in its synthesis and repair. In fact, the glutathione levels have been described as a predictive factor in determining our life expectancy.

Glutathione regulates the actions of other, less effective antioxidants, such as vitamins C and E. It has been reported that low levels of glutathione are associated with liver and immune system malfunction, heart disease, premature aging and death. Further, it has been reported that glutathione functions in not only detoxification of toxins but also neutralizing carcinogens.

Glutathione has also been described as having potent antiviral and antibacterial properties. Glutathione has also been shown to have a wide variety of functions that help boost the immune system. Lymphocytes (T cells and B cells), so vital in the immune response, have been shown to be dependent on glutathione for proper function. As we age, our levels of glutathione drop. These lower levels of glutathione have been implicated in diseases associated with aging. Finally, glutathione has been shown to enhance athletic performance by increasing muscle strength and weight gain.

As an antioxidant, glutathione helps protect the overall integrity of every cell and

tissue against damage caused by free radicals and disease. Acting as a scavenger of free radicals, glutathione helps to protect us from pollutants and other disease-causing agents. Glutathione is a trimer composed of three amino acids—glycine, glutamic acid and cysteine. Though free glutathione is surely of benefit, the main benefit comes from the internalization of its precursors and subsequent assembly and action within the cell. In fact, a recent investigation involving piglets showed that intercellular glutathione production was almost exclusively from dietary consumption of glutathione precursors.

There are a number of products available that contain glutathione and its precursors. For the most part they are derived from colostrum, milk, and/or whey. They are typically referred to as whey protein isolates. A number of these products are being marketed as significantly higher in glutathione and its precursors. The fact is that compared to low temperature processed colostrum, these products do not have significantly higher levels of either glutathione, glutathione precursors or other bioactives that are present in properly processed colostrum. In fact, it has been recently reported that the antioxidant activity of bovine colostrum is significantly greater than a number of such products, including whey protein hydrolysates. Figure 1 illustrates the lack of any significant difference between a whey protein glutathione-enriched product and a quality produced colostrum. Note the glutathione precursors, glycine, glutamic acid, and cystine, and the relative values found in the respective products.

Amino Acid	Whey Derived Product	Colostrum 20% Ig's
Glycine	20mg/g protein	18.1 mg/g protein
Glutamic Acid	201	126.3
Cystine	24	16.8
Proteins		
Lactalbumin	9.7%	2%
Lactoglobulin	59.1%	19%
Lactoferrin	0.14%	0.15%
Total Immunoglobulins	24.6%	25%
IGF-1		1000ng/g
IGF-2		250ng/g
TGF–β1		150ng/g
TGF-β2		950ng/g
EGF		250µg/100g
Vitamins		
A		100 IU/100g
B1	1.5—2.0 mg/60g	
B2	1.7—2.2 mg/60g	1.12 mg/100g
B6		0.03 mg/100mg
B12		13.6 µg/100g
C		2.5 mg/100g
D		< .2µg/100g
E		130µg/100g

Figure 1. Reported composition of a commercially available whey protein isolate which is reportedly enriched with glutathione and its precursors and a quality processed colostrum product.

It is of interest that the whey protein isolate, which is reportedly enriched with glutathione and its precursors, does not contain a significantly greater amount of glutathione precursors than the quality colostrum product. This is also true of other constituents that make up the composition of the respective products. It is also of interest that cysteine has been reported to be a rate-limiting amino acid for the biosynthesis of glutathione. The fact that lactoglobulin and lactalbumin are a rich source of this essential amino acid and that both are found in relatively high amounts in colostrum should also be noted.

Of utmost importance is the simple fact that if there is a substance that can improve quality of life, then this information should be available to and shared by everyone. The scientific and medical evidence generated from producers of whey protein isolate products is significant. However, most, if not all, their claims based on their findings can and for the most part have been attributed to colostrum.

Further, the process of manufacturing whey protein isolate products for the most part includes ultrafiltration or microfiltration of raw material in order to concentrate the various constituents responsible for bioactivity. Typically this requires that this material is subjected to filtration through a 10,000 molecular weight (Daltons) membrane. Thus many small molecular weight molecules are removed from solution. These include many factors that are involved with the healing and recovery process, including growth factors and cytokines which have a wide variety of biological functions. This is indicated by the fact that the manufacturers of whey protein isolates who claim enriched glutathione levels typically do not include growth factor and cytokine levels as part of their respective compositional information.

Colostrum is a magical substance composed of many, many substances that work together in a synergistic manner in such a way that the overall effect of colostrum is greater than the individual components. In regard to whey protein isolate products, they have attributed the action to one constituent—glutathione. This is only part of the answer as many other bioactive molecules are involved—antibodies, immune factors, growth factors, cytokines, etc. In reality, it is an ever changing

story with only part of the answer on how colostrum and its derivatives, such as whey protein isolates, actually function and work. The wonderful thing is that they actually do work and that this is backed by scientific and medical evidence.

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COMPLEX LIPIDS

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Introduction

Phospholipids are complex lipids and the predominant structural element of all physiological membranes. Amphipathic lipid compounds are essential components of all biological membranes. Phospholipids are present in every cell of animals and plants. In animals, they are found abundant in the tissues of the brain, heart, liver, muscle, kidneys, and bone marrow. Though phospholipids function primarily as structural elements they are also essential in three very critical areas—the growth, maturation and proper functioning of the cells in the body.

Phospholipids are either derived from glycerol or sphingosine and are designated either glycerophospholipids or sphingolipids respectively. The predominant form of phospholipids are the glycerophospholids of which phosphatidylcholine (lecithin), phosphatidylserine, phosphatidylethanolamine, and phosphatidylinositol are the predominant species.

Sphingolipids are specific to animal sources and are not found in plants (such as soy). There are two types of sphingolipids: sphingophospholipids and sphingoglycolipids. As the nomenclature implies, the sphingophospholipids are phospholipids with a sphingosine backbone. Sphingoglycolipids also have a sphingosine backbone but instead of containing a phosphate group have a sugar group. Prime examples of sphingophospholipids and sphingoglycolipids are sphingomyelin and gangliosides respectively.

Phospholipids are an excellent source of choline, which has been shown to increase brain function. Phospholipids, in particular phosphatidylserine, have been associated with improved memory. Phospholipid supplementation has been shown to be beneficial in the treatment of Alzheimer's and similar diseases. Phospholipids have also been shown to reduce mood swings and elevate depression. Phospholipids, in particular phosphatidylcholine, have been shown to have a protective effect on the liver, protecting it against damage caused from toxins, including alcohol, drugs and viruses.

Sphingomyelin

The sphingolipid sphingomyelin represents 25–33% of the total phospholipids present in milk. Sphingolipids function in variety of physiological roles, from initiating cellular defense, tumor suppression and cholesterol mobilization, to making liposome membranes rigid.

Milk-derived sphingomyelin has been shown in ***in vitro*** studies using a human cell line to boost cellular production of interferon-beta, which plays an important role in cellular defense against viral infection. The breakdown products of sphingomyelin are sphingosine and ceramide. Sphingosine has been shown to inhibit protein

kinase, C an important component in the internalization of growth factors into the cell. Thus it has been theorized that sphingomyelin contains components that act as second messengers which are important in cell growth and regulation. The digestive products of sphingomyelin have also been shown to be highly antimicrobial and be effective ***in vitro*** against such pathogens as ***Salmonella, Campylobacter, Vibrio, Listeria***, and pathogenic ***E. coli***.

Along with other phospholipids in milk, sphingomyelin can protect gastric mucosa against injury caused by acid, pepsin or exogenous irritants. Sphingomyelin, along with phosphatidylcholine, is an important source of choline which is important for brain function. Sphingomyelin accounts for approximately 10% of the lipids present in the brain—primarily associated, as their name implies, with the myelin sheathes of nerves.

Considerable research has been undertaken on the functions of phospholipids and, more recently, sphingolipids in health and disease. Recently it has been shown that both sphingolipids and their breakdown products—ceramide and sphingosine—are highly bioactive compounds that have a profound effect on various biological functions in the body. Regulation of cell growth, differentiation, signaling, and programmed cell death (apoptosis) have all been attributed to sphingolipids. Further, sphingolipids have also been implicated in playing a vital role in neuronal development. In animal studies it has been revealed that dietary sphingolipids inhibit colon carcinogenesis.

Studies on mice who were administered with 1,2 dimethlylhydrazine—a powerful tumor inducing agent—revealed that an up to 70% reduction of tumors was observed after being fed milk derived sphingomyelin. With longer feeding, an even greater reduction of tumors was observed. Mice fed as little as 25mg of sphingomylein/100g of diet had a 57% reduction in incidence of colon tumors. Further studies on mice fed milk-derived sphingomyelin, as compared to a control group fed a standard diet, showed a reduction in aberrant colon tumors and most importantly revealed a shift from malignant tumors to ones that were benign. Thus it has been postulated that sphingomyelin-containing foods may have anticancer activity. Though no clinical trials have been conducted on humans to date,

the results of ***in vitro*** studies using human cancer cells lines show great promise. Sphingomyelin also has been shown to increase the effectiveness of chemotherapy agents in killing cancer cells.

Gangliosides

The sphingoglycolipids, such as gangliosides, are present in substantial amounts in nerve cell membranes. In addition, gangliosides are found in the membranes of white and red blood cells. It is of interest that ganglioside content is diminished in the brains of Alzheimer's patients. Of further interest is the significant and vital role gangliosides play in the brain development of the young.

Gangliosides, like sphingomyelin, exhibit a high level of antimicrobial activity in that they are both bactericidal and bacteriostatic to organisms that are frequently associated with causing diarrhea in young mammals. In addition, gangliosides have been shown to protect the intestine against disease.

Phosphatidylserine

Phosphatidylserine (PS) makes up approximately 8% of the total phospholipid in bovine milk. There is substantial evidence that indicates that PS improves memory and improves brain function. PS is most concentrated in the brain where it functions to support many crucial nerve cell functions. It is the primary component of the cell membranes of neurons. In brain disorders such as Alzheimer's, Parkinson's, and multiple sclerosis, there is an association with neuron degeneration and dysfunction. PS has been shown to stimulate the production of a brain messenger chemical (dopamine) that helps regulate memory. PS has also been shown to stimulate protein kinase C production and help modify mood changes arising from stress. In addition, a growing amount of evidence is associated with the beneficial aspects of PS in mood elevation and reducing the symptoms of depression. PS has been shown to have positive effects in treating early Alzheimer's and the onset of premature memory loss due to dementia.

Phosphatidylethanolamine

Phosphatidylethanolamine (PE), also known as cephalin, makes up approximately 30% of the total phospholipid content of bovine milk. PE comprises the backbone of cell membranes and contributes to the fluidity and structural environment of cells. In regard to the brain and nervous tissue, PE plays an important role in myelin structure and nerve endings in the brain. Phospholipids, particularly PE, have been shown to be beneficial in lowering serum cholesterol levels and thus reducing the risk of heart disease.

Phosphatidylcholine

Phosphatidylcholine (PC), also known as Lecithin, makes up approximately 30% of the phospholipid present in bovine milk. Along with sphingomyelin, PC is a major source of choline. Choline is a major neurotransmitter, acetylcholine. Dietary PC has been shown to improve neurological malfunctions such as tremors, ataxis and mood swings. Choline is required to sustain tissue growth, and thus a ready supply of this phospholipid is required for maintenance of good health.

PC is a major building block for all cell membranes, and it supports cellular, tissue and organ function. This is particularly true of the liver with its vast network of cell membranes. Thus the liver is particularly dependent on PC for proper function. In fact, it has been shown in clinical trials that dietary PC has beneficial aspects in helping individuals recover from toxic liver damage. PC has also been shown to protect the liver from damage due to viral infection, medication, alcohol, and nutritional deficiency. It has also been shown to be beneficial in speeding the recovery process resulting from liver damage.

Phosphatidylinositol

Phosphatidylinositol (PI), also known as inositol, comprises approximately 5% of the total phospholipid present in milk. Inositol is necessary for the proper functioning of the brain, nerves and muscle. Inositol is a "lipotropic" substance helping

to prevent build-up of fatty deposits in the liver. Inositol is also an essential nutrient for proper growth in newborn children.

Phospholipids Are Natural Emulsifying Agents

Phospholipids, in particular sphingomyelin, are natural emulsifying agents and are used in a wide variety of applications. The ability of sphingomyelin to form very stable micelles and liposomes makes it an ideal candidate in developing delivery systems. These delivery systems can be utilized to increase dispersibility and target specific target dissolution. With the advent of new technologies in isolation and purification of phospholipids, specific phospholipids can now be targeted for end use.

Milk-derived Phospholipids vs Soy Lecithin

The significant difference between plant-based soy lecithin and milk-derived phospholipid is the actual composition of the phospholipids in question. As was mentioned previously, only animal based phospholipid preparations contain sphingomyelin. In addition, milk-derived complex lipids are more similar to human lipids than vegetable sources. Further, the emulsion properties of sphingomyelin are far more superior to that of soy lecithin. The actual phospholipid compositional differences are seen below:

Phospholipid Class	**Soybean***	**Milk***
Phosphatidylcholine	30%	30%
Phosphatidylethanolamine	20%	30%
Phosphatidylserine	3%	10%
Phosphatidylinositol	20%	5%
Sphingomyelin	Not present	25%

*Expressed as total phospholipid present

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to replace the services or recommendations of a physician or qualified health care practitioner. Those with health problems or pregnancy are specifically advised that they should consult their physician before taking colostrum or any nutritional supplement.

LACTOSE INTOLERANCE, DAIRY PRODUCTS, AND COLOSTRUM

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Introduction

The main carbohydrate present in milk is **lactose**. This milk sugar is a disaccharide (two sugars) composed of glucose and galactose subunits. Normally lactose is digested in the small intestine by the enzyme **lactase** into its subunits, and the **glucose** and **galactose** are then absorbed through the intestinal wall into the bloodstream. The enzyme lactase is normally found in high levels in babies, infants, and children, and as such the young generally can consume high levels of foods containing lactose. In the majority of population, excluding Caucasians, as the infant grows, the relative levels of lactase present in the intestine gradually decline to the point where certain adults are not able to digest the lactose properly. This inability to digest lactose has been termed **lactose intolerance** or **lactose maldigestion**. Symptoms of lactose intolerance include bloating, abdominal pain, diarrhea, and flatulence. It is important to note that these symptoms are typically only observed in individuals who are lactose maldigesters and who consume large quantities of lactose containing dairy products. **Research has shown that even lactose maldigesters can easily tolerate 1-2 cups of milk per day, cheese (which contains little if any lactose), yogurt and even colostrum.**

What Is Lactose Intolerance?

The main carbohydrate present in milk is lactose. In fact, this disaccharide sugar is one of the main components of mammalian milk. It is made up of monosaccharide sugar subunits glucose and galactose linked by a 1,1,4 β-glycosidic bond. In the human small intestine lactose is normally broken down or digested by the enzyme lactase (known also as β-galactosidase) into its monosaccharide sugar subunits and then absorbed through the intestine into the bloodstream.

In humans, intestinal lactase activity changes with age, reaching its peak at birth in the young and remaining high during infancy and early childhood. In a great percentage of the world's population there is then a gradual decline in intestinal lactase activity with age. However, in a small minority of people, mainly individuals of European heritage, high levels of lactase activity remain well into adulthood. These individuals can readily and easily digest large quantities of lactose and are often referred to as being **lactose persistent**.

However, as previously mentioned, the majority of adults in the world have reduced levels of lactase in the small intestine. In these individuals, if they consume more lactose then there is lactase present to digest it, symptoms may appear. The undigested lactose is fermented by the enteric bacteria present in the large intestine to produce lactic acid, short chain fatty acids, carbon dioxide, hydrogen and methane gas. It is this fermentation of the undigested lactose which causes the gastrointestinal symptoms of lactose intolerance.

Lactose Intolerance Defined

Lactose intolerance, also referred to as **hypolactasia,** can be defined as an inability to tolerate a standard or test dose of lactose without developing diagnostic biochemical changes with or without clinical signs and symptoms of bloating, flatulence, abdominal pain and diarrhea. The standard dose of lactose used to determine lactose intolerance is 50 grams.

Incidence of Lactose Intolerance

The incidence of lactose intolerance varies greatly between races and populations worldwide. However, a majority of adults world wide have a reduction in lactase activity. This appears to be especially true in post-weaning Asian and African populations, Eskimos, Native American Indians and African-Americans. The exceptions in African peoples are the cattle raising populations of Niger and Nigeria. It is quite a different story in European, North American, and Australian populations where the incidence of lactose intolerance is typically observed in less than 30% of adults. The general belief is that lactase persistence is genetically linked and not environmentally triggered.

Lactose in Milk and Dairy Products

The relative levels of lactose in the milk of common species is as follows:

Species	Lactose (grams/liter)
Human	7.0
Cow	4.7
Sheep	4.8
Goat	4.1
Horse	6.2

The lactose present in fermented dairy products is broken down by lactic acid bacteria used in the culture. This accounts for an approximate reduction of 30% present as compared to milk. In other dairy products such as butter, cream, cottage cheese, etc., the lactose is reduced in similar quantity. The great majority of cheese types contain little if any lactose as it is completely broken down to glucose and galactose in the cheese ripening process. The actual level of lactose in some dairy products can be seen as follows:

Dairy Product	Lactose (grams/100grams)
Natural Yogurt	3.4
Flavored Yogurt	2.9—4.2
Full Cream	3.1
Half Pasteurized Cream	3.3
UHT Milk	3.7
Coffee Cream	3.8
Butter	0.6
Cottage Cheese	2.2
Cheese (Both Soft & Hard)	0.011—0.085
Whole Milk Powder	40 -45
Colostrum Whole	15
Colostrum Skim	5.9

Minimal Dose of Lactose to Cause Symptoms

The standard dose of 50 grams of lactose, used in the lactose test, will induce symptoms associated with intolerance in most individuals who are lactose maldigesters. The actual minimal dose of lactose required to induce symptoms in lactose intolerant individuals has yet to be determined. However, a double-blind, randomized trial involving 13 healthy individuals determined to be lactose intolerant revealed that no significant symptoms arose when they were administered 0, 2, 6 ,12 and even 20 grams of lactose in 240 ml aqueous solutions.

How Much Colostrum Can Be Tolerated?

Further studies have confirmed these results and established the fact that almost everyone, including individuals who are lactose intolerant, can easily tolerate up to 12 grams of colostrum per day without any negative side effects or symptoms. An important point to make is that this corresponds to 2 cups of milk or 200 grams of skim colostrum powder (400 500mg capsules) per day. It must be obvious that 400 capsules of colostrum a day is an insurmountable amount to

ingest, but it does illustrate that even individuals who are lactose intolerant can most likely tolerate the recommended daily 2-4 capsules.

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advised that they should consult their physician before taking colostrum or any nutritional supplement.

COLOSTRUM PLUS PROBIOTICS, PREBIOTICS, AND COMPLEX LIPIDS THE IDEAL COMBINATION

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Introduction

The combination of three very unique substances may just prove to be the making of the world's most unique and most powerful food formulation in the treatment of disease and promotion of good health.

The significance of colostrum in the area of overall health lies in two very important features. First, it is a highly nutritious food. Second. it contains many bioactive substances that have been shown to prevent disease and promote overall good health. Bovine Colostrum supplementation has been shown in clinical trials to help prevent disease in a number of species, including humans.

The idea of ingesting beneficial bacteria to maintain a healthy gastrointestinal microbial balance is nothing new. In fact, it was first proposed some 100 years ago. **Probiotics** are the beneficial bacterial inhabitants of our digestive tract. The term "probiotics" was coined to describe the deliberate ingestion of health promoting microorganisms. In addition, probiotic refers to those microorganisms which may prevent or reduce the effect of an infection caused by a pathogenic (disease-causing) microorganism. These pathogenic effects can range from mild discomfort to severe conditions such as irritable bowel syndrome and even cancer. Probiotics have been shown to neutralize these effects.

A **Prebiotic** is a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, thus improving the host's health. They selectively and preferentially stimulate the growth of probiotics. In addition, prebiotics inhibit the binding of pathogenic microbes to the gut wall, thus minimizing their threat.

Phospholipids are complex lipids (fats) and are the predominant structural element of all physiological membranes. Though phospholipids function primarily as structural elements, they are also essential in three very critical areas: the growth, maturation and proper functioning of the cells in the body. Phospholipids are an excellent source of choline, which has been shown to increase brain function. Phospholipids, in particular phosphatidylserine, have been associated with improved memory. Phospholipid supplementation has been shown to be beneficial in the treatment of Alzheimer's and similar diseases. Phospholipids have also been shown to reduce mood swings and elevate depression. Phospholipids, in particular sphingomyelin, are natural emulsifying agents and thus are used in a wide variety of applications. The ability of sphingomyelin to form very stable micelles and liposomes makes it an ideal candidate in developing drug delivery systems. These delivery systems can be utilized to increase dispersibility and target specific target dissolution.

Colostrum

The bioactive molecules in colostrum include such things as immunoglobulins, immune factors, growth factors, and antioxidants. **Immunoglobulins,** also known as **antibodies,** and other **immune factors** act to ward off disease. **Antibodies** are large protein molecules produced by the animal's immune system to combat and neutralize foreign, potentially disease-causing agents (antigens). The interesting feature of antibodies is that they are specific in that there is a separate and specific antibody produced for every type of antigen.

Colostrum is produced by the mammary gland of all mammals. It is also known as pre-milk as it is the first milk produced by the mother following the birth of her young. The significance of colostrum lies in the fact that it is the first food the

young animal receives after it is born. As such, colostrum is a highly nutritious food. Of paramount importance is the fact that colostrum is involved in a phenomenon known as passive transmission of immunity. This is a life-supporting function and is best exemplified in farm animals such as the horse, cow, dog, sheep, goat, etc. Unless these animals receive colostrum in the first day or two of life they most likely will die. Unlike humans, who are passively immunized in the womb via the placenta, these animals are born without any defense mechanism—immune system—by which they can fight off infection. Colostrum contains antibodies produced by the mother against disease-causing agents she has been exposed to during her lifetime.

At the time of birth, the gut of these animals is not yet sealed, and whole antibody molecule can be absorbed through the gut wall directly into the blood system. By ingesting colostrum, the newborn is able to obtain antibodies from the mother to help them survive until their own immune system is sufficiently developed to fight off disease. After a day or two of life, the gut seals, and the antibodies present in the colostrum and milk function in local immune protection of the gut. This local immune protection is not species specific, and as such we as humans, and all other animals, can use bovine colostrum for its various health benefits.

Antibodies belong to a group of bioactive molecules referred to collectively as immunoglobulins. Antibodies function to hunt down, fight, and destroy disease-causing agents or pathogens. Colostrum supplementation has been shown to be an effective means by which infections of the gastrointestinal tract and other areas can be prevented. It has been shown in clinical trials that colostrum supplementation can be effective in preventing and treating diarrhea (scours) and other infections. In a recent study conducted in collaboration with the Department of Microbiology, Otago University, New Zealand, it was revealed that colostrum derived from non-immunized, pasture-fed cows had significant specific antibody potency (titer) against a very wide variety of potentially pathogenic (disease-causing) microbes. Bovine colostrum has been shown in clinical trials to have a safe, protective effect in a variety of species, including humans, dogs, cats, horses, and pigs.
In addition to antibodies, colostrum also contains many other substances which help promote good health in the form of growth, maturation and development.

These include growth factors and immune factors. Growth factors include Epidermal Growth Factor (EGF), Transforming Growth Factor (TGF), Insulin-Like Growth Factor (IGF), and Fibroblast Growth Factor (FGF). These factors function primarily in the growth, development, and maturation of cells, organs, nerves, muscle, and tissues. Growth factors are also involved with the healing and recovery process. Immune factors include Lactoferrin, Cytokines, Lysozyme, Lactoperoxidase and Transfer Factor. These factors have a very wide assortment of actions including augmenting the action of antibodies and modulating the actions of the immune system.

The direct benefits of colostrum are numerous, and they include overall good health, prevention of disease, improved performance, reduced healing period, increased recovery, and improved immune protection. These benefits are obvious and can be explained through biochemical pathways and various specific actions of specific components present in colostrum. However, the indirect effects of colostrum are not so clear cut. What is clear is that all the wonderful things in colostrum work together in such a way as to increase the effectiveness of each component.

Probiotics

The main function of the digestive system is to prepare food so it may be available to the body for use in energy, growth, and structural maintenance. The digestive tract accomplishes this by the act of digestion where large, complex molecules of food are broken down into much smaller molecules. This begins with physical digestion where the act of chewing helps to break down food into smaller subunits and continues with chemical digestion with enzymes present in the saliva. As the food enters the stomach, it is further partially digested by acids and enzymes. Final digestion occurs in the intestine by literally billions of microorganisms where it is metabolised and absorbed through the gut wall into the body. These microorganisms are bacteria, and they exist in a very complex and delicate ecosystem consisting of more than 400 species. Many of these billions of microorganisms work synergistically in such a way as to help one another. Though most of these microorganisms are beneficial (friendly or probiotic bacteria) to the host, some may be pathogenic if they are allowed to proliferate. A critical bal-

ance needs to exist between the various bacteria in order to maintain a healthy intestine. Health starts with the intestine, and so does disease. This critical balance can be affected due to changes in diet, health status, age, immune status, stress, and even medication. If the result of this imbalance causes a reduction in friendly bacteria, it may lead to intestinal distress which can range from mild discomfort to severe conditions such as irritable bowel syndrome and even cancer.

The idea of ingesting beneficial bacteria to maintain a healthy gastrointestinal microbial balance is nothing new. In fact, it was first proposed by Dr. Elie Metchnikoff some one hundred years ago. Though fermented dairy products have been consumed for centuries, the significance of Dr. Metchnikoff's findings are exemplified by the fact that he was awarded the Nobel Prize in 1908 for his work.

Probiotics are the beneficial bacterial inhabitants of our digestive tract. The term ***probiotics*** was coined to describe the deliberate ingestion of health promoting microorganisms. In addition, probiotic refers to those microorganisms which may prevent or reduce the effect of an infection caused by a pathogenic organism. The predominant microorganisms associated with these effects are from the genera ***Lactobacillus*** and ***Bifidobacterium.***

Lactobacilli are also distributed throughout the gastrointestinal (GI) and genitourinary (GU) tracts of humans and all other mammals. They play a very important role in the fine balance of the gut micro-ecosystem. The actual distribution of these microorganisms throughout the gut is based on a number of factors: pH, available oxygen, substrates present, presence of secretions, and bacterial interactions. These are regarded as health promoters.

Bifidobacteria are microorganisms of significant importance in the complex balance of the intestinal micro-ecosystem of all mammals. They are found throughout the whole GI and GU tracts. Bifidobacterium is the first to populate the digestive tract of infants and in early life is the dominant microorganism present. With increasing age, this bacteria's presence decreases. Eventually it becomes the third most abundant, accounting for approximately 25% of the total gut flora. The other two genera of bacterium represented are ***Bacteroides*** and

Eubacterium. With the onset of old age a significant reduction of bifidobacterium is observed.

It has been recommended that adults should routinely supplement their diet with three of these bacteria, ***Lactobacillus acidophilus***, ***Bifidobacterium bifidum***, and ***Lactobacillus bulgaricus***. In the case of infants it has been recommended that they be supplemented with ***Bifidobacterium infantis***.

Intestinal Health

Enteric (gut) infection is a major cause of infant disease and death worldwide, especially in developing countries. Significant research has shown that probiotics are beneficial in the treatment of many types of diarrhea, including diarrhea associated with antibiotic treatment, traveler's diarrhea, and childhood rotavirus-associated diarrhea. Probiotics have also been shown to preserve intestinal integrity and mediate the effects of inflammatory bowel diseases, including irritable bowel syndrome, colitis, and alcoholic liver disease. In addition, lactic acid can improve intestinal mobility and relieve constipation, particularly in seniors.

Immune System

Research suggests that probiotics can enhance both the specific and non-specific immune response. This mode of action is most likely the result of activating macrophages, increasing local levels of cytokines, increasing natural killer cell activity, and/or having an effect on the immunoglobulins.

Lactose Intolerance

Lactic acid bacteria, such as ***S. thermophilus***, ***L. bulgarucus*** and other lactobacilli can alleviate symptoms of lactose intolerance. These organisms provide bacterial lactase to the stomach and intestine and thereby digest the lactose.

Allergy

Probiotics have a beneficial effect on mucosal barrier function, thus reducing allergic reaction. They also beneficially affect immune system development. Probiotics, such as Lactobacillus, may help in reducing some of the symptoms of food allergies. In addition, probiotics have a very significant influence on the treatment and management of other allergic conditions, such as atopic eczema, asthma, and hay fever.

Cancer

Research has shown that probiotic consumption may reduce colon cancer risk by reducing the incidence and number of tumors.

Nutrition

Probiotics may improve the digestibility of some dietary nutrients such as protein and fat. Probiotics have also been shown to have a beneficial effect on lowering serum cholesterol levels**.** Short chain fatty acids such as lactic acid, propionic acid and butyric acid produced by lactic acid bacteria may help in maintaining proper pH and protect against pathological challenge.

Prebiotics

Oligosaccharides function as prebiotic ingredients. A prebiotic is a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, thus improving the health of the host. In the case of dietary inulin, it is preferentially utilized (hydrolyzed and fermented) in the large intestine by the probiotic bacteria (lactobacilli and bidobacteria), thus promoting intestinal health.

A number of studies have also proven that prebiotics such as inulin actually enhance mineral absorption in the colon. These results contradicted the concerns regarding the potential for soluble dietary fiber to bind metal ions. The inulin-

mineral complexes formed are degraded during the hydrolysis and fermentation process, and thus the minerals are made available for enhanced absorbtion in the colon.

Some 13 distinct oligosaccharides have been detected and characterized in bovine milk or colostrum. These compounds comprise up to about 0.1% of bovine milk. Their component simple sugars include glucose, galactose, fructose, N-acetyl glucosamine and sialic acid. They represent a large proportion of the non-protein nitrogen in milk. While the actual mechanism of action and functions of all the oligosaccharides is not known, it is generally accepted that many act to promote lactobacillus growth in the digestive tract. Oligosaccharides also have protective functions against certain potentially harmful bacteria and their toxins. This function is attributed to prebiotics acting as competitive inhibitors for binding sites on the epithelial surfaces of the intestine.

Gastrointestinal Tract Health

Oligosaccharides in the diet are known to enhance the growth of these organisms in the gut. Of particular note is the ability of oligosaccharides to promote the proliferation of bifidobacteria, so they are referred to as bifidogenic or bifidus factors. They achieve this by acting as selective energy or food sources for the beneficial bacteria, but potentially harmful bacteria such as clostridia or Enterobacteriaceae cannot utilize them. For the aforementioned reasons, oligosaccharides are often referred to as ***prebiotics.***

Functional Foods

Oligosaccharides are relatively new functional food ingredients, but the production, range, and range of applications of these complex sugars is rapidly increasing. Currently, the major food applications of oligosaccharides are in beverages, infant formulas, confectionary, yoghurts, dairy desserts, and bakery products. Europe and Japan in particular have experienced rapid increases in consumption of oligosaccharides as functional food ingredients in the last decade. This is largely due to the perceived health benefits derived from their consumption. The main claim

made for these foods is that they are designed to maintain a good gastrointestinal environment and act to increase intestinal bifidobacteria.

Dietary Fiber

Oligosaccharides are most widely incorporated into food formulations in the form of inulin, oligofructose or fructooligosaccharide. Inulin is derived commercially from the chicory root and is classed as a soluble dietary fiber. This dietary fiber classification is based on its specific chemical configuration, which makes it resistant to digestion by mammalian digestive enzymes. The physiological benefits of dietary fiber are well known and widely recognized. These benefits include: relief of digestion, relief of constipation and increased stool volume. Studies have also shown that inulin is non-glycemic in that it improves glucose tolerance and insulin sensitvity. Further, it has been shown to have an affect of lowering serum cholesterol and triglycerides. It has also been shown to have an effect on increasing the HDL/LDL cholesterol (good cholesterol vs. bad cholesterol) ratio, thus having a beneficial affect on overall health.

Complex Lipids

Phospholipids are complex lipids and are the predominant structural element of all physiological membranes. Amphipathic lipid compounds are essential components of all biological membranes. Phospholipids are present in every cell of animals and plants. In animals they are found abundantly in the tissues of the brain, heart, liver, muscle, kidneys, and bone marrow. Though phospholipids function primarily as structural elements, they are also essential in three very critical areas: the growth, maturation and proper functioning of the cells in the body.

Phospholipids are either derived from glycerol or sphingosine and are designated either glycerophospholipids or sphingolipids respectively. The predominate form of phospholipids are the glycerophospholids of which phosphatidylcholine (lecithin), phosphatidylserine, phosphatidylethanolamine, and phosphatidylinositol are the predominant species.

Sphingolipids are specific to animal sources and are not found in plants (such as soy). There are two types of sphingolipids: sphingophospholipids and sphingoglycolipids. As the nomenclature implies, the sphingophospholipids are phospholipids with a sphingosine backbone. Sphingoglycolipids also have a sphingosine backbone, but instead of containing a phosphate group have a sugar group. Prime examples of sphingophospholipids and sphingoglycolipids are sphingomylein and gangliosides respectively.

Phospholipids are an excellent source of choline, which has been shown to increase brain function. Phospholipids, in particular phosphotidylserine, have been associated with improved memory. Phospholipid supplementation has been shown to be beneficial in the treatment of Alzheimer's and similar diseases. Phospholipids have also been shown to reduce mood swings and elevate depression. Phospholipids, in particular phosphatidylcholine, have been shown to have a protective effect on the liver—protecting it against damage caused from toxins including alcohol, drugs and viruses.

Sphingomyelin

The sphingolipid sphingomyelin represents 25–33% of the total milk phospholipids in the milk. Sphingolipids function in variety of physiological roles from initiating cellular defense, tumor suppression and cholesterol mobilization to liposome membrane rigidification.

Milk derived sphingomylein has been shown in ***in vitro*** studies using a human cell line to boost cellular production of interferon-beta, which plays an important role in cellular defense against viral infection. The breakdown products of sphingomylein are sphingosine and ceramide. Sphingosine has been shown to inhibit protein kinase C, an important component in the internalization of growth factors into the cell. Thus it has been theorized that sphingomylein contains components that act as second messengers which are important in The digestive products of sphingomylein have also been shown to highly antimicrobial. They are effective ***in vitro*** against such pathogens as Salmonella, Campylobacter, Vibrio, Listeria, and pathogenic E coli.

Along with other phospholipids in milk, sphingomyelin can protect gastric mucosa against injury caused by acid, pepsin or exogenous irritants. Sphingomyelin, along with phosphatidylcholine, is an important source of choline, which is important for brain function. Sphingomyelin accounts for approximately 10% of the lipids present in the brain.

Considerable research has been undertaken on the functions of phospholipids and, more recently, sphingolipids in health and disease. Recently it has been shown that both sphingolipids and their breakdown products—ceramide and sphingosine—are highly bioactive compounds having a profound effect on various biological functions in the body. Regulation of cell growth, differentiation, signalling, and programmed cell death (apoptosis) have all been attributed to sphingolipids. Further, sphingolipids have also been implicated in playing a vital role in neuronal development. In animal studies it has been revealed that dietary sphingolipids inhibit colon carcinogenesis.

Studies on mice who were administered with 1,2 dimethylhydrazine—a powerful tumor inducing agent—revealed that an up to 70% reduction of tumors was observed after being fed milk derived sphingomyelin. With longer feeding even a greater reduction of tumours was observed. It was revealed that mice fed as little as 25mg of sphingomylein/100g of diet had a 57**%** reduction in incidence of colon tumors. Further studies on mice fed milk-derived sphingomyelin, as compared to a control group fed a standard diet, showed a reduction in aberrant colon tumors, and most importantly revealed a shift from malignant tumors to ones that were benign. Thus it has been postulated that sphingomyelin-containing foods may have anti-cancer activity. Though no clinical trials have been conducted on humans to date, the results of ***in vitro*** studies using human cancer cells lines show great promise. Further, sphingomyelin has been shown to increase the effectiveness of chemotherapy agents in killing cancer cells.

Phosphatidylserine

Phosphatidylserine (PS) makes up approximately 8% of the total phospholipid in bovine milk. There is substantial evidence that indicates that PS improves mem-

ory and brain function. PS is most concentrated in the brain where it functions to support many crucial nerve cell functions. It is the primary component of neuronal cell membranes. In brain disorders, such as Alzheimer's, Parkinson's and multiple sclerosis, there is an association with neuron degeneration and dysfunction. Phosphatidylserine has been shown to stimulate the production of a brain messenger chemical (dopamine) that helps regulate memory. PS has also been shown to stimulate protein kinase C production and help modify mood changes arising from stress. In addition, evidence is mounting regarding the beneficial aspects of PS to elevate mood and reduce the symptoms of depression. PS has also been shown to have positive effects in treating early Alzheimer's and the onset of premature memory loss due to dementia.

Phosphatidylethanolamine

Phosphatidylethanolamine (PE), also known as Cephalin, makes up approximately 30% of the total phospholipid content of bovine milk. Phosphatidylethanolamine comprises the backbone of cell membranes and contributes to the fluidity and structural environment of cells. In regard to the brain and nervous tissue, PE plays an important role in myelin structure and nerve endings in the brain. Phospholipids, particularly PE, have been shown to be beneficial in lowering serum cholesterol levels and thus reducing the risk of heart disease.

Phosphatidylcholine

Phosphatidylcholine (PC), also known as Lecithin, makes up approximately 30% of the phospholipid present in bovine milk. Along with sphingomyelin, PC is a major source of choline. Choline is a major neurotransmitter, Acetylcholine. Dietary PC has been shown to improve neurological malfunctions such as tremors, ataxis and mood swings. Choline is required to sustain tissue growth, and thus a ready supply of this phospholipid is required for the maintenance of good health.

PC is a major building block for all cell membranes, and it supports cellular, tissue and organ function. This is particularly true of the liver with its vast network of cell membranes. Thus the liver is particularly dependent on PC for proper function.

It has been shown in clinical trials that dietary PC has beneficial aspects in helping individuals recover from toxic liver damage. PC has also been shown to protect the liver from damage due to viral infection, medication, alcohol, and nutritional deficiency. It has also been shown to be beneficial in speeding the recovery process resulting from liver damage.

Phosphatidylinositol

Phosphatidylinositol (PI), also known as Inositol, comprises approximately 5% of the total phospholipid present in milk. Inositol is necessary for the proper functioning of the brain, nerves and muscle. Inositol is a lipotropic substance helping to prevent build-up of fatty deposits in the liver. Inositol is also an essential nutrient for proper growth in newborn children.

Phospholipids—Natural Emulsifying Agents

Phospholipids, in particular sphingomyelin, are natural emulsifying agents and are used in a wide variety of applications. The ability of sphingomylein to form very stable micelles and liposomes makes it an ideal candidate in developing drug delivery systems. These delivery systems can be utilized to increase dispersibility and target specific target dissolution. With the advent of new technologies in the isolation and purification of phospholipids, specific phospholipids can now be targeted for end use.

Milk-derived Phospholipids vs Soy Lecithin

The significant difference between plant-based soy lecithin and milk-derived phospholipid is the actual composition of the phospholipids in question. As was mentioned above, only animal-based phospholipid preparations contain sphingomyelin. In addition, milk-derived complex lipids are more similar to human lipids than vegetable sources. The emulsion properties of sphingomyelin are far superior to that of soy lecithin. The actual phospholipid compositional differences are seen below:

Phospholipid Class	Soybean*	Milk*
Phosphatidylcholine	30%	30%
Phosphatidylethanolamine	20%	30%
Phosphatidylserine	3%	10%
Phosphatidylinositol	20%	5%
Sphingomyelin	Not present	25%

*Expressed as total phospholipid present

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PASTEURIZATION

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Named after its inventor, Louis Pasteur, the process of pasteurization is an integral part of the dairy industry. The initial discovery demonstrated that organisms responsible for the spoilage of wine could be inactivated by applying heat. This process has since been applied to milk where it remains the single most important step in the manufacturing of dairy products.

The definition of pasteurization is as follows:

The heating of every particle of milk or milk product to a specific temperature for a specified period of time without allowing recontamination of that milk or milk product during the heat treatment process.

The primary purpose of pasteurization is to destroy potentially pathogenic microbes present in milk thus rendering the milk or milk product safe for human consumption. The secondary purpose of pasteurization is to extend the shelf life of the milk or milk product. It is not only organisms but also enzymes, which are involved with spoilage, that are inactivated by pasteurization.

The Pasteurization Marketing Ordinance (PMO) is a regulatory body founded by the US Public Health Service, in conjunction with the US Food and Drug Agency (FDA) and other agencies and institutions. It is the governing body that

states limits and compliance standards for pasteurization in the United States of America. It should be pointed out that this is the accepted world standard in regard to pasteurization. The PMO has given the following statement regarding health reasons for pasteurization:

The public health value of pasteurization is unanimously agreed upon by health officials. Long experience conclusively shows its value in the prevention of disease which may be transmitted through milk. Pasteurization is the only practical, commercial measure which, if properly applied to all milk, will destroy all milk-borne disease organisms. It has been demonstrated that the time-temperature combinations specified by this ordinance, if applied to every particle of milk, will devitalize all milk-borne pathogens. Compilations of outbreaks of milk-borne disease by the US Public Health Service over many years indicate that the risk of contracting disease from raw milk is approximately 50 times as great as from milk labeled "pasteurized."

The extent to which microorganisms and enzymes are inactivated is directly proportional to the temperature and duration of pasteurization. Thus the higher the temperature and the longer the duration the greater the effect of killing microorganisms and inactivating enzymes.

The two most heat stable pathogens found in fresh milk are ***Mycobacterium tuberculosis*** and ***Coxiella burnetti***. The first is the bacterium which causes tuberculosis, and the second is the bacterium responsible for Q fever. The minimal temperature and duration requirements for pasteurization of milk are based on thermal death time studies on these two organisms. To ensure the safety of all dairy products, these temperature and time combinations are highly regulated. For milk and colostrum, the temperature and duration of pasteurization has been established by the PMO and is as follows:

Milk Pasteurization—PMO Guidelines

Temperature	Time
63°C (145°F)	30 min.
72°C (161F)	15 sec
89°C (191°F)	1.0 sec
90°C (194°F)	0.5 sec
94°C (201°F)	0.1 sec
96°C (204°F)	0.05 sec
100°C (212°F)	0.01 sec

As must be apparent, the higher the temperature utilized, the shorter the time required to destroy all potentially pathogenic microbes. It should be pointed out that for diary products containing 10% or more fat or containing added sweeteners the PMO guidelines stipulate that the specified temperature shall be increased by 3°C (5°F).

The process of pasteurization has undergone many improvements since its inception. In the beginning, milk and other fluids were simply boiled, and unfortunately many of the nutrients and bio-active substances were adversely affected. For a growing number of milk and colostrum manufacturers, the preferred method of sanitizing milk and colostrum is by flash pasteurization, also know as High Temperature Short Time (HTST) pasteurization. By incorporating this method to sanitize or kill microbial contamination, the biological integrity of the milk and colostrum is maintained and any loss of bioactivity is minimized.

Flash pasteurization is performed using a continuous plate and tube or heat exchange system. This counter current method ensures that the temperature of the product is elevated to the exact required temperature, held there for the required time and then swiftly lowered in the shortest possible time. Thus the milk and colostrum is heated to 72 since its inception C in the shortest time possible, held at that temperature for a minimum of 15 seconds and immediately cooled. In this way complete destruction of microbial growth and inactivation of enzy-

matic activity is achieved. Microbiological testing is performed to assure sanitation and product safety. Of significant importance is the fact that this method ensures that maximal biological activity and nutritional benefits are retained.

The thermal stability of immunoglobulin preparations has long been the focus of many research studies. It has been observed that flash pasteurization incorporating high temperature short time (HTST)—72°C for 15 seconds—has minimal effect on protein denaturization and reduction in bioactivity. The following exemplifies the thermal stability of IgG in flash pasteurization.

Thermal Destruction of Immunoglobulins During Processing of Colostrum

Pasteurization is a critical quality parameter used during the manufacture of dairy products. Data collected during processing has shown that minimal loss due to denaturization of immunoglobulins occurs when colostrum is pasteurized (Table 1.).

Table 2. D-Value of IgG in Bovine Colostrum

Temperature (°C)	D-Value (sec)
70	13,038
72	6,456
74	3,960
78	1,122
82	414

D-value = time required to inactivate 90% of the IgG

If a second pasteurization step is a requirement of further processing, research has shown that 65°C for 30 minutes has no effect on the activity of IgG. Previous research conducted at 72°C for 15 seconds found a reduction in IgG activity of approximately 0.5-10%. However, this reduction is likely to be dependent on the precise system into which the colostrum is incorporated and the interactions of the components within this system. For example, salt causes IgG to become

less susceptible to denaturization and aggregation during heat treatment. Further, in a recent investigation it has been reported that IgG values will be only very slightly affected by HTST pasteurization at 72°C for 15 seconds. In fact, what was observed was an approximate drop of 2% in quantified IgG value which is well within the standard error of the assay used in the measurement.

Further antigen binding studies have shown that the bioactivity of antibodies is little affected by the process of flash pasteurization. In determining D-values, the time required to reduce the antigen binding activity of IgG (antibody) by 90% was determined (Table 2.)

Table 2. D-Values IgG Antibody/Antigen Binding in Bovine Bolostrum

Temperature (°C)	D-Value (seconds)
69	8504
72	1387
77	285
81	152

D-value = time to inactivate 90% of the IgG antibody binding to antigen

Thus modern dairy technology has developed to the point where the process of pasteurization, though effective in neutralizing any potential microbial health hazard, has very little negative effect on the bioactivity, biofunctionality, and nutritional composition of the various components found in milk and colostrums.

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FREEZE DRYING VS SPRAY DRYING

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Introduction

The purpose of drying biological material is simple. By removing the moisture from the material, bacteria, yeast and molds cannot grow. Simply, this is a way of preserving food and other biological materials. The basic concept behind food preservation is either to slow down the activity of disease-causing bacteria or to kill the bacteria altogether. Pasteurization is an example of the latter of these two options. In regard to the former, refrigeration and freezing are the most frequently used options. When frozen, bacteria are completely, inactive whereas when refrigerated their action is simply slowed down.

In freezing, biological material is preserved in that microorganisms are prevented from multiplying. However, those that survive the freezing process can reanimate in the thawing material and often grow more rapidly than before freezing. To combat this or to reduce this action, the material is typically sterilized by either pasteurization, sterile filtration or irradiation prior to freezing. Preserving agents can also be introduced prior to freezing. The greatest disadvantage of freezing is that the water in the biological material expands and forms ice crystals during the freezing process. The slower the freezing process, the larger the size of crystals formed and the greater the effect on cellular membranes of the material being frozen. Blast or quick-freezing reduces the size of the ice crystals and thus reduces the damage to the cell membranes. Cryoprotective agents can also be introduced prior to freezing in order to minimize the effect on cellular membranes. In the case of pure protein solutions, sugar is typically used for this purpose, whereas in the case of cells (tissue culture), ethylene glycol or DMSO are typically used.

In both spray drying (warm air drying) and freeze drying, water is removed, thereby preserving the biological material because microorganisms and enzymes require moisture to grow, proliferate, and function. In regard to logistics, the removal of water also decreases both the volume and weight of biological material, thereby reducing transport and storage costs.

The principal difference between spray drying (warm air drying) and freeze drying is temperature. Spray drying employs a higher temperature while freeze drying is performed at low temperature. In spray drying, a liquid in the form of a fine spray is passed through a chamber of warm air where the liquid is dehydrated by evaporation. This is a relatively inexpensive process and is ideal when temperature sensitive materials are not involved. In addition, due to the configuration change involved in the spray drying process, solubility of the final dried product can be affected.

However, it should be noted that recent developments in the spray drying process have come to light where reduced temperature drying is now possible. In this way large-scale spray drying of material that would otherwise be damaged is now not only possible but a reality. A case in point is the spray drying of colostrum. In a recent comparability study conducted in collaboration with Otago University, New Zealand, it was revealed that low temperature spray dried colostrum contained the same amounts of IGF-1 as colostrum which was freeze dried. IGF-1 is a small peptide which is very heat sensitive. Thus it has been shown that low heat spray drying can be successfully used to dry biological material. Further, numerous studies have shown that the process of low temperature spray drying does not adversely affect the various bioactives present in colostrum. These studies include a recent investigation run in conjunction with Otago University showed that the low temperature spray drying process does not discernibly affect antibody function. This information corresponds to earlier investigations in which the efficacy of spray dried colostrum was evidenced.

Freeze drying, on the other hand, is a relatively expensive process and is typically used in the drying of temperature sensitive, high cost materials (e.g. cells, pharmaceuticals). Freeze drying is typically utilized for drying materials that would

be adversely effected by drying temperatures above the freezing point. In freeze drying the material is dried in a frozen state under vacuum. The process of sublimation removes the liquid or water in this manner, that is, ice sublimes directly to gas. Because the material is dried in a rigid frozen condition (stabilized state) the resulting integrity of the dried material remains more or less intact and is readily soluble.

Summary

Freezing and drying of biological material are ways of preservation. In spray drying, a powder is formed when a liquid, in the form of a spray, is subjected to warm air. This is a relatively inexpensive method of drying and is ideal when it involves large volumes of material which are not temperature sensitive or easily oxidized. Due to the configurational change involved in this process, solubility of the final product can be effected. In freeze drying, the moisture is removed from the frozen product directly by the process of sublimation. This is a stabilizing process which has little effect on the configuration of the molecule. Thus the integrity of the product is not effected. In the case of biologically active products, such as proteins, which are heat sensitive, freeze drying is the method of choice. However, it should be pointed out that the recently developed technology of low temperature spray drying has been shown to have a minimal effect on the integrity and bioactivity.

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ADDITIVES VS ACTIVES

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Many colostrum manufacturers are adding extra ingredients to their colostrum products. This is being done for a number of reasons. Unfortunately in only a very limited number of cases does this addition actually improve the colostrum product. In fact, in most cases it is simply to add a new gimmick or to reduce the amount of colostrum being used. The only reasonable thing that should be incorporated into colostrum are actives and specifically actives which improve the effectiveness of the product. The addition of sugar will only make the product sweeter and certainly not more effective. In fact, it will make it less effective as the colostrum is being diluted down. Some manufacturers add vitamins and supplements to their colostrum products. Will these improve the effectives of the product? I think not. Some manufacturers add digestive aids such as enzymes. The only thing this will do is most probably act to destroy the effectiveness of the colostrum.

Colostrum was developed by Mother Nature to be the most important food in the world. It has to be as it is the first food a newborn receives when it is born.

In short, if it doesn't improve the action of the colostrum or if it doesn't improve the effectiveness of the colostrum, why add it?

ATHLETIC PERFORMANCE AND COLOSTRUM

MICHAIL BORISSENKO
Chief Scientist
Institute of Colostrum Research

Introduction

The significance of colostrum in the area of athletic performance lies in several very important features, all of which the athlete can take advantage of to reach a higher level of performance, and most probably a better form of life. It is a highly nutritious food and contains many, many bioactive substances which have been shown to prevent disease and promote overall good health. Of specific interest to the athlete is the fact that colostrum supplementation can be an effective way by which the athlete can increase lean body mass, improve muscular strength, increase endurance and capacity, and at the same time speed recovery. What this means to the athlete is simple: they can train harder, longer and recover faster, thereby increasing their respective level of athletic performance. Of significant importance to the athlete is the simple fact that colostrum is perfectly safe and that the International Olympic Committee (IOC) has designated colostrum to be an accepted and safe dietary supplement. Thus it is recognized as perfectly safe and legal by all the sports regulatory bodies.

Overall Health

One very important aspect of performance is overall good health. This is especially true in the case of the athlete who wants to perform at maximal level. The use of bovine colostrum supplementation has been shown in clinical trials to help

prevent disease. Most infections and disease conditions start in the gastrointestinal tract, and this is exactly where the benefits of colostrum begin—in the gut.

The bioactive molecules in colostrum include such things as immunoglobulins, immune factors, growth factors, and antioxidants. To begin with, immunoglobulins in the form of antibodies and other immune factors act to ward off disease. Antibodies are large protein molecules produced by the immune system to combat and neutralize foreign, potentially disease-causing agents, or antigens. The interesting feature of antibodies is that they are specific in that there is a separate and specific antibody produced for every type of antigen.

Colostrum is produced by the mammary gland of all mammals. It is also known as pre-milk as it is the first milk produced by the mother following the birth of her young. The significance of colostrum lies in the fact that it is the first food the young animal receives after it is born. As such, colostrum is a highly nutritious food. However, of paramount importance is the fact that colostrum is involved with a phenomena known as passive transmission of immunity. This is a life-supporting function and is best exemplified in farm animals such as the horse, cow, dog, sheep, goat, etc. Unless these animals receive colostrum in the first day or two of life they most likely will die. Unlike humans, who are passively immunized in the womb via the placenta, these animals are born without any defense mechanism (immune system) by which they can fight off infection. Colostrum contains antibodies produced by the mother against all the disease-causing agents she has been exposed to during her lifetime.

At the time of birth the gut of these animals is not yet sealed, and whole antibody molecules can be absorbed through the gut wall directly into the blood system. By ingesting colostrum, the newborn is able to obtain antibodies from the mother to help them survive until their own immune system is sufficiently developed to fight off disease. After a day or two of life the gut seals, and the antibodies present in the colostrum function in local immune protection of the gut. This local immune protection is not species-specific, and as such we as humans, and all other animals, can use bovine colostrum for its various health benefits.

In addition to antibodies, colostrum also contains many other substances which help promote good health in the form of growth, maturation and development. These include growth factors and immune factors. Growth factors include epidermal growth factor (EGF), transforming growth factor (TGF), insulin-like growth factor (IGF), and fibroblast growth factor (FGF). These factors function primarily in the growth, development, and maturation of cells, organs, nerves, muscle, and tissues. Immune factors include lactoferrin, cytokines, lysozyme, lactoperoxidase, and transfer factor (PRPs). These factors have a very wide range of actions and include augmenting the action of antibodies and modulating the actions of the immune system.

Antibodies belong to a group of bioactive molecules who as a group are referred to collectively as immunoglobulins. Antibodies function to hunt down, fight, and destroy disease-causing agents or pathogens. Colostrum supplementation has been shown to be an effective means by which infections of the gastrointestinal tract and other areas can be prevented. It has been shown n the form of clinical trials that colostrum supplementation can be effective in preventing and treating diarrhea (scours) and other infections. In a recent investigation conducted in collaboration with the Department of Microbiology, Otago University, New Zealand, it was revealed that colostrum derived from non-immunized pasture fed cows had significant specific antibody potency (titer) to a very wide variety of potentially pathogenic (disease-causing) microbes. Bovine colostrum has been shown in clinical trials to have a safe, protective effect in a variety of animals, including humans.

In addition to immunoglobulins, colostrum also contains other immune factors which help ward off disease and promote overall health, including bioactive peptides, lactoferrin, secretory component, lysozyme, lactoperoxidase, cytokines, oligosaccharides, complex lipids, many others. Colostrum also contains growth promoting substances collectively referred to as growth factors which help to accelerate the growth or healing process thus aiding the athlete to train harder and recover faster.

It has recently been discovered that colostrum is a significant source of antioxi-

dants. One such antioxidant, glutathione, has been described as the ultimate antioxidant. In this capacity glutathione and glutathione precursors play an important part in colostrum's role in overall health. Glutathione, also referred to as GSH, is a naturally occurring peptide or small protein, which has a primary function as an antioxidant. Linus Pauling was a leading advocate of antioxidants and their respective role in prevention of disease and the promotion of overall good health. Antioxidants for the most part are naturally occurring compounds that possess the ability to neutralize unstable free radicals. Unchecked, these free radicals have been linked, at least in part, as the causative agents of a number of disease conditions, including cancer, heart disease, stroke, and improper nervous and immune system function. A growing number of scientific and medical research studies have shown that that antioxidants can deactivate free radicals and thus limit the spread of certain disease states. Further, it has been shown that glutathione enhances athletic performance by increasing muscle strength and weight gain.

The direct benefits of colostrum that have been observed to date are numerous and include overall good health, prevention of disease, improved performance, reduced healing time, increased recovery, and improved immune protection. These benefits are obvious and can be explained through biochemical pathways and various specific actions of specific components present in colostrum. However, the indirect effects of colostrum are not so clear cut. What is clear is that all the wonderful things in colostrum work together in such a way as to increase the effectiveness of each component.

Colostrum and Athletic Performance

The beneficial aspects of colostrum on athletic performance is well documented in clinical trials. It has been shown that colostrum supplementation in athletes improves running, jumping, rowing, swimming and cycling performance. It has also been shown that colostrum supplementation has a positive effect during periods of heavy training and improves physical work capacity. Of major significance is the fact that the athletes who received colostrum supplementation experienced a greater capacity for endurance. Thus the athletes who received colostrum were shown to run further, jump higher and longer, cycle and row faster and lon-

ger. Further, they where shown to recover faster as compared to the placebo group. In an investigation into the effects of bovine colostrum supplementation on body composition in association with exercise, it was revealed that the colostrum group experienced a significant increase in lean body mass as compared to the placebo group. Thus the results to the athlete must be obvious—colostrum supplementation can increase lean body mass, improve muscular strength, increase endurance and capacity, and at the same time speed recovery. What this means to the athlete is simple—they can train harder, longer, and recover faster, thereby increasing their respective level of athletic performance.

How Does It Work?

It has long been established that both milk and colostrum contain peptide growth factors, which stimulate growth and differentiation of mammalian cells. The predominant growth factor activity is typically concentrated in the colostral phase. A number of growth factors have been described in bovine colostrum. These include insulin-like growth factor (IGF-1, IGF-2), transforming growth factor (TGF-β_1 and TGF-β_2), and epidermal growth factor (EGF).

Insulin-like growth factor-1 (IGF-1) is found in relatively high concentrations in colostrum and is of specific interest in regard to athletic performance. Specifically, this growth factor mediates the growth or metabolic effects of growth hormone. On a molecular level, IGF-1 functions to stimulate muscle and bone cell proliferation and development, i.e., helps to build muscle and strong bones. In a recent study it was shown that oral supplementation with bovine colostrum enhances the recovery process following physical exercise or exertion. Thus it allows for harder training with improved recovery. Two further studies have shown that bovine colostrum has positive effect on maximal power output—increases vertical jump performance and improves rowing performance in elite female rowers.

Improves Recovery

Physical exercise and training cause muscle damage. Recovery from this damage is necessary or subsequent exertion will be limited. Bovine colostrum has been

shown to help in this recovery process. It has been demonstrated in laboratory studies that IGF-1 can promote an increase of up to 15% in muscle mass and a 14% increase in strength.

Oxidative stress in the form of training and exercise contributes to muscle fatigue. Glutathione and its precursors, present in colostrum, have been shown to increase the capacity of exercise prior to the onset of fatigue. There is an ever increasing amount of evidence that suggests free radicals play a very important role in muscle damage and inflammation. Glutathione is a powerful antioxidant and as such a powerful scavenger of free radicals.

In a study involving Olympic skiers it was shown that athletes taking colostrum were less fatigued and showed improved performance compared to their counterparts who were given a placebo. Creatine kinase is a critical enzyme involved with muscle metabolism and has been shown to be a marker of muscle cell damage. Elevated circulating (blood) creatine levels are often associated with significant muscle damage. In this study, the athletes who consumed colostrum had, following exercise, approximately half the circulating creatine levels of the control group.

Speeds Healing

Transforming growth factor and epidermal growth factor are also found in relatively high amounts in colostrum. Both these growth factors stimulate tissue repair and wound healing. Digestive disorders are associated with a number of contributing factors: stress, medications, infectious agents, diet , and, in the case of the athlete, overtraining. The use of bovine colostrum has been proven effective in the treatment of gastrointestinal disorders caused by aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs).

Anti-Inflammatory Properties

Associated with physical exertion and strenuous exercise is inflammation. In fact, at the Sydney Olympics the second most common medication taken by the

athletes were anti-inflammatories, being only surpassed by vitamins. Though typically this inflammation is centered in the joints, it is also observed in the digestive tract. In colostrum and milk there are two principle molecules (proteins) that have been implicated as natural anti-inflammatory agents: lactoferrin and secretory component of the secretory IgA molecule. Both proteins are abundant in bovine colostrum

Inflammation is a complex localized event in response to either injury, an invasive foreign substance (pathogen), or in some instances to internally produced substances (e.g., rheumatoid arthritis). This is a protective adaptation that serves to isolate, destroy, and rid the infected area of both the injurious agent and the injured tissue. Prostaglandins and leukotrines play an important role in mediating the process of inflammation by increasing histamine-mediated vascular permeability. It is predominately this action which causes the discomfort associated with inflammation.

The common anti-inflammatory analgesic and antipyretic drugs, such as corticosteroids, aspirin and indomethacin, inhibit prostaglandin and/or leukotrine synthesis. In fact, most, if not all, of the anti-phlogistic actions of steroidal and non-steroidal anti-inflammatory drugs' action involve the inhibition of prostaglandin synthesis. The anti-inflammatory effect of aspirin and indomethacin is inhibition of cyclooxygenase, whereas those of corticosteroids are thought to inhibit the release of fatty acids from phospholipids either by inhibition of phospholipase-A2 or by interfering with the release of membrane phospholipids. It has been shown by ***in vitro*** studies that the secretory component of secretory IgA inhibits phospholipase-A2 activity and therefore prostaglandin and leukotrine synthesis by limiting the release of arachidonic acid.

The fact that colostrum is a natural food that has no contraindications or negative side effects suggests that it is an ideal supplement to be used to counter inflammation. The adverse side effects associated with certain anti-inflammatory agents limits their use. In the case of corticosteroids, the potential side effects include the elevation of blood pressure, water and salt retention, increased calcium and potassium excretion, gastric upset and possibly peptic ulceration. In addition, the

use of these compounds may also aggravate diabetes mellitus. The non-steroidal anti-inflammatory compounds (salicylates) are synthetic biochemical substances that can be toxic at high doses. The possible side effects associated with these substances include gastric upset and gastric bleeding, prolonged clotting time, and hepatic injury. Though the number of various anti-inflammatory agents is great, so are the potential side effects and adverse reactions associated with these compounds. It is in this regard where colostrum has also been shown to be of direct benefit. NSAIDs are very effective agents for treatment of inflammation, but unfortunately they cause gastric injury. Colostrum has been shown to be beneficial in the prevention and treatment of gastrointestinal injury caused by NSAIDs. Further, colostrum has been shown to be beneficial in treating not only ulcerative conditions but also other diseases of the gut.

Supplementation

It has recently been reported that for top class Olympic athletes the variation in their respective performance of as little as 1% can be the difference between winning and losing. Colostrum, in conjunction with proper nutrition and training, can just be that little extra edge that not only helps the athlete perform better but also keep them healthier.

In a recent survey involving 463 sports coaches in the USA, it was revealed that 87% of the coaches believe that "dietary supplements are a safe and effective means of improving performance." It was also reported that some 80% of these coaches routinely advised their athletes on nutrition and some 40% recommended specific products. Dietary supplementation has long been associated with sport and athletic performance. The increasing number of research and clinical information on the benefits of colostrum is substantiating the fact that colostrum supplementation enhances athletic performance.

Colostrum and the International Olympic Committee

Colostrum is a completely natural substance that has been used as a food for hundreds of years. Everything in colostrum is also found in milk, although at a

much lower level. As such colostrum has been labeled by the IOC as being a "strong" milk, and the IOC does not consider colostrum to be a prohibited substance. Further, bovine colostrum supplements are not on the banned drug lists of the IOC or any other sports governing body.

Safety of Colostrum

The efficacy and safety of colostrum supplementation in humans and animals has long been established in clinical trials. Currently there are a growing number of either colostrum or colostrum derived products available that are registered for therapeutic use. There are no known contraindications to use of bovine colostrum supplements in athletes. As with all supplements, individuals who are pregnant, lactating, or who have an intolerance to dairy products should consult with their health professional.

In Summary

Colostrum is a very complex mixture containing many bioactive substances that have yet to fully appreciated. Among these substances so far identified are immunoglobulins, growth factors, immune factors and antioxidants. An important feature, which must be pointed out, is the synergistic actions of a highly complex mixture like colostrum. The general belief is that this synergism is paramount for the true benefits of colostrum to be experienced. In regard to the athlete, it has been shown that colostrum is an effective, safe, and legal supplement which can have a very positive influence on performance.

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COLOSTRUM VS CREATINE

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Colostrum

Colostrum, also known as pre-milk, is a natural product and is produced by the soon-to-be mother just before and for several days following the birth of her young. It is the first food available to the newborn

The use of bovine colostrum for its associated health benefits, though known for centuries, has only recently gained much attention.

The significance of colostrum in the area of **athletic performance** lies in several very important features, all of which the athlete can take advantage of to reach a **higher level of performance**, and most probably a better form of life. First, it is a highly nutritious food, and second, it contains many bioactive substances which have been shown to prevent disease and promote overall good health. Of specific interest to the athlete is the fact that colostrum supplementation can be an effective way by which the athlete can increase **lean body mass**, **improve muscular strength**, **increase endurance and capacity, and at the same time speed recovery**. What this means to the athlete is simple—he or she can train harder, longer, and recover faster thereby increasing his or her respective level of athletic performance. Of significant importance to the athlete is the simple fact that **colostrum is perfectly safe and has no known side effects.** Further is the fact that the International Olympic Committee (IOC) has designated colostrum to be an accepted and safe dietary supplement. Thus it is recognized as perfectly safe and legal by all the sports regulatory bodies.

At the cellular level, colostrum contains many bioactive substances which function in a variety of ways. The direct benefits of colostrum that have been observed to date are numerous, and they include overall good health, prevention of dis-

ease, improved performance, reduced healing period, increased recovery, and improved immune protection. These benefits are obvious and can be explained through biochemical pathways and various specific actions of specific components present in colostrum. However, the indirect effects of colostrum are not so clear cut. What is clear is that all the wonderful things in colostrum work together in such a way as to increase the effectiveness of each component.

Creatine

Creatine is also a natural substance and is a normal constituent of our normal diet. It is found in meat, fish, and poultry. Most of the creatine—up 95%—is found in skeletal muscle. Creatine is produced naturally by the body in the liver, kidneys and pancreas from the amino acids arginine, glycine and methionine. The benefits of creatine in regard to athletic performance lay in its role in muscle contraction. Creatine plays a critical role in the replenishment of anaerobic energy stores in muscle. Muscle contraction requires energy, and this is derived from adenosine triphosphate (ATP). As this energy is being used up, it needs to be replenished or regenerated, and this comes from phosphocreatine stored in the muscle. In order for this to happen, creatine must be available to replenish phosphocreatine stores. This is especially true during intense, short duration exercise. There is a growing amount of evidence which indicates that creatine supplementation may help to increase phosphocreatine stores, thus delaying the onset of exhaustion during heavy exercise. There is also evidence that creatine supplementation helps to improve the recovery process and thereby reduce recovery time required between training sessions. Thus in regard to athletic performance, creatine supplementation may give those individuals in activities involving intense, short bursts an edge.

It should be noted that there are certain side effects associated with creatine supplementation, and certain precautions should be observed. It has been noted that a weight gain of 1-2 kg is typically seen when initiating creatine supplementation. This has been attributed to an increase in fluid stores. It has also been reported that creatine supplementation is associated with muscle cramps and tightness—most probably also due to the increase in water retention.

Creatine in its pure form is permitted in sport and poses no problems in healthy individuals. It should be pointed out that no large long term studies have been performed to evaluate the safety of creatine. However, creatine is not a food but rather a preparation and as such may contain impurities. As such the IOC has indicated that athletes should seek a written guarantee of the supplement's purity from the respective manufacturer to ensure that the material does not contain any harmful and possibly banned substances.

M. Borissenko
3 February, 2002

NEW RESEARCH

A Comparison of IgG and IgG1 Activity in an Early Milk Concentrate from Non-Immunized Cows and a Milk from Hyperimmunized Animals.

McConnell, M. A., Buchan, G. A. A., Borissenko, M. V., Brooks, H. J. L.
Food Research International 34:255-261 (2001)

A recent investigation was conducted in collaboration with Otago University, Department of Microbiology. In this study we compared the antibody specificity of a hyperimmune milk product with that of a colostrum product derived from non-immunized, pasture-fed cows. Specific antibody titers (concentration) to a panel of 19 of the same 22 pathogenic bacteria and yeast that were used as immunizing antigens, were determined by immunoassay. Three of the pathogens used as immunizing antigens were not available due to regulatory import restraints by the New Zealand Ministry of Agriculture and Fisheries (MAF). The following specific antibodies to the following microbes were identified:

PATHOGEN	DISEASE CONDITION
Bacillus cereus	Food poisoning, mastitis
Campylobacter jejuni	Food poisoning
Candida albicans	Thrush, yeast infection
Clostridium difficile	Food poisoning
Escherichia coli	Commensal bacteria
Escherichia coli 0157:H7	Food poisoning
Haemophilus influenzae	Bacterial meningitis, can be fatal
Helicobacter pylori	Stomach ulcers
Klebsiella pneumoniae	Pneumonia, urinary tract infection
Listeria monocytogenes	Food poisoning, can be fatal
Propionibacterium acnes	Acne
Salmonella enteritidis	Food poisoning, can be fatal
Salmonella typhimurium	Food poisoning, can be fatal
Staphylococcus aureus	Pneumonia, osteomyelitis, carditis,
	Meningitis, arthritis, toxic shock syndrome,
	Antibiotic Resistant—MRSA
Staphylococcus epidermidis	Multiple antibiotic resistance (MAR)
Streptococcus agalactiae	Mastitis, bacteremia, meningitis, pneumonia,
	can be fatal
Streptococcus mutans	Periodontal disease, tooth decay,
	Arteriosclerosis, endocarditis
Streptococcus pyogenes	Strep throat, flesh-eating bacteria, myositis,
	toxic shock syndrome, rheumatic fever,
	kidney disease
Yersinia enterocolitica	Food poisoning, septicemia, can be fatal

The results indicated that both the hyperimmunized milk and the non-immunized High IgG colostrum possessed high levels of specific IgG antibodies to all the 19 pathogens tested. It was also indicated that compared to the hyperimmunized product, High IgG colostrum is at least equipotent and is of greater specific antibody titer to that of hyperimmunized equivalent. As compared to the

hyperimmunized product, High IgG colostrum consistently exhibited significantly higher titers to all 19 pathogens tested. Even when based on equivalent IgG concentration, High IgG colostrum had a higher level of specific antibody titer to all the pathogens tested.

The significance of these findings lies in the fact that this was a comparative study involving both a natural pasture fed colostrum versus a hyperimmunized equivalent. The results suggest that pasture fed grazing and environmental factors far outweigh the benefits of active hyperimmunization. It is of further interest that the specific antibody titer, even at equivalent IgG concentration, was significantly higher in the non-immunized pasture fed colostrum. Add to this all the other bioactives found in colostrum—immune factors, growth factors, hormones, etc. It is true that for the most part these bioactives are also present in milk, but only in minute amounts. Thus from the information given it appears obvious that the High IgG colostrum product is a far superior product to that of a commercially available hyperimmunized equivalent.

LEPTIN

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Derived from the Greek word, ***leptos,*** meaning thin, leptin is a naturally occurring peptide hormone which is involved with body composition through metabolic regulation, appetite control, and even reproduction. First discovered in 1994, leptin has been hailed as the cure-all and end-all in regard to the prevention and treatment of obesity principally because of its actions in regulating energy expenditure, food intake, and storage of fat.

There is a very close association between obesity and Type-2 diabetes, a potentially serious disease affecting some 15 million individuals in America alone. Type-2 diabetes is characterized by the body's inability to properly use sugar. If left un-

checked, diabetes can cause a variety of conditions associated with deteriorating health, including blindness, heart disease, kidney disease, and even death. It has been estimated that in America obesity affects some 58 million and contributes to between 280,000 and 325,000 deaths per year. Because of this, researchers have been trying to unravel the mystery of leptin since its discovery.

Leptin is a small protein (16,000 Daltons) produced by the ob (obese) gene. It was found that mice that have had the ob gene knocked out, missing, or defective produced no leptin. It was also observed that these same animals had voracious appetites and ate continually, becoming grossly obese, sterile, and diabetic. When leptin was administered to these animals by injection, they stopped overeating and rapidly lost weight. These animals also experienced a lowering of percentage body fat, serum insulin, and glucose levels. In addition, their metabolic rate, body temperature and activity levels were increased subsequent to administration of leptin. Even non-obese, normal weight mice injected with leptin lost body weight. It has been reported that this phenomenon was due at least in part to a reduction in fat synthesis and an increase in the burning of fat. It was postulated that leptin is a neurotransmitter that turns the appetite signal off in the brain.

Naturally this attracted enormous excitement throughout the world, the reasoning being that obese people simply do not have enough leptin and thus get fat. Would it not be wonderful if by simply administering leptin and increasing the body's leptin levels obesity could be treated and prevented? The significance and the commercial potential of such a discovery is illustrated by the fact that the California based biotechnology company, Amgen, spent $70 million (US) to obtain the commercial rights to the ob gene and its product, leptin.

However, in clinical trials with leptin on obese humans, the observed results were not so clear-cut. Only a small percentage of obese humans have the mutant ob gene, so most obese individuals produce leptin. In fact, it has been suggested that only some 5% of the obese population can truly be considered leptin-deficient and as such can benefit from leptin therapy alone. Even more surprising is that obese individuals typically produce 20 to 30 times higher levels of leptin as compared to lean individuals. Researchers thus speculated that the obese human

body was insensitive to leptin's signal, and thus no trigger or signal to the human brain to stop eating.

Leptin is produced by adipose or fat cells. In the normal rodent model with a properly functioning ob gene, leptin is produced when the fat cells have stored enough fat. The leptin then travels through the blood to the brain where it signals the brain that the body has stored a healthy amount of body fat. The brain then signals the body to down regulate (reduce) food intake in order to maintain normal body mass. Rodents which possess the defective ob gene do not produce leptin when they have ingested sufficient enough food, some of which is stored as fat. Thus they have no leptin to signal the brain to stop eating, so they stay hungry and continue to eat and eat and eat. Various studies have shown that leptin acts as a signal of satiety (fullness) to the brain, thus stimulating feeding behavior. One important study revealed that there exists a leptin receptor at the blood-brain barrier of humans that mediates saturable, specific, and temperature-dependent binding and thus internalization of leptin into the brain.

Like all hormones, leptin must first bind to its receptor so it can be internalized and perform its function. It has been theorized that at least some obese individuals have defective leptin receptors, and thus the brain does not hear the signal to stop eating. It has been hypothesized that obesity in humans is associated with leptin resistance. The results from an investigation to determine whether leptin resistance is related to leptin binding by a serum component other than the leptin binding protein showed that affinity and binding of leptin to the leptin binding protein was specific and that no binding was observed for growth hormone, insulin, IGF-1 or 2, LH, FSH, TGF-beta1, IL-6 or leukemia inhibiting factor. It was also demonstrated that the leptin/leptin binding protein complex had a molecular weight of approximately 450 kDa. Further, it was determined that an inverse relationship exists between concentration of serum leptin and quantity of leptin binding protein. This information provided further evidence that binding of leptin to the leptin binding protein does indeed influence the biological function of leptin. Genetically obese rodents who have mutations of leptin or the leptin receptor are defective in leptin signaling and thus become obese and develop diabetes. In these animals, the circulating levels of both leptin mRNA and leptin receptor

mRNA are increased some 20-fold. This gives further evidence that there exists a biofeedback mechanism that controls the leptin concentration in the circulation.

Many hormones circulate bound to proteins found in the blood serum. The belief is that these binding proteins (BP) modulate ligand bioavailability and bioactivity. In a recent study it was revealed that two such proteins are found in humans and three in rodents. Of specific interest is the fact that in humans, free leptin in serum increases proportionally with increase in Body Mass Index (BMI). In lean rodents and humans, a large proportion of circulating leptin was found to be bound to the leptin binding proteins. However, in normal non-ob obese rodents and humans, the predominant form of leptin is in the free form, i.e., not bound to the leptin binding protein. It was also shown that both obese rodents and obese humans lack or have a much reduced expression of leptin binding protein. Thus it has been postulated that leptin binding protein may modulate the bioactivity, transport and clearance of leptin.

It has been reported that a lowering of serum leptin levels was associated with dieting and reduction of body fat in obese humans. It has also been reported that serum leptin levels correlated with Body Mass Index (BI) in lean and obese humans with weight loss due to food restriction. In a six month clinical weight reduction trial involving 38 healthy obese women it was found that the average weight loss for this group was 8.4 kg with corresponding plasma leptin decrease of 22.3% under baseline.

Significant increase in circulating leptin levels has been observed in glucose tolerance test (OGTT) experiments on obese individuals. Interestingly enough, no such increase was observed in normal non-obese subjects. It has also been shown that leptin gene expression and thus secretion is increased by insulin but blocked by inhibitors of glucose metabolism. This indicates that leptin synthesis is modulated by insulin and is mediated through glucose uptake and metabolism. Thus it has been postulated that a decrease in glucose metabolism may be responsible for the fact that dieting and fasting decrease serum leptin levels, and in turn increased glucose metabolism is responsible for an associated increase in circulating leptin after resuming food intake. It therefore appears that insulin and leptin interact in

a biofeedback system by which insulin up regulates (increases) leptin expression (secretion) which in turn down regulates insulin secretion.

It is also of interest that in mice circulating leptin levels rise some 20-40 fold during pregnancy. Pregnant mutant mice that have the ob/ob gene have no detectable circulating leptin. However, normal mice have very high levels of circulating high molecular weight leptin complex of leptin bound to the leptin binding protein. This may indicate that there is over expression of the leptin binding protein in pregnancy. These studies revealed that the placenta is a source of leptin, leptin receptor and leptin binding protein. Leptin and leptin receptor have also been identified in colostrum and milk where it has a role in neonatal development, especially in regard to energy metabolism, digestive function, thermogenesis, and regulation of growth. Leptin is involved in the development of gastrointestinal tract structure and function (motility and absorption) in the newborn.

The appetite controlling effects alone cannot explain the metabolic response elicited by leptin. A recent study involving the underlying mechanism of leptin's metabolic actions showed that leptin represses the expression and activity of hepatic stearoyl-CoA desaturase-1 (SCD-1). This enzyme is involved with biosynthesis and catalysis of monounsaturated fatty acids. Leptin thus acts at the cellular level and affects the actual mechanism by which fat is stored.

It is becoming obvious that leptin in the treatment of obesity and eating disorders is far from simple. In the first place, it appears that only 5% of the total obese population is actually deficient in leptin. Therefore leptin therapy on its own may be of little use to the other 95% of obese individuals. Also, most obese individuals in fact over produce leptin. It is clear that not only leptin but also leptin binding protein and leptin brain receptor and their respective expression are all linked with obesity in humans.

As previously stated, only some 5% of the obese population can possibly benefit from leptin therapy. In fact, a recent 6 month study involving 54 normal or lean individuals and 73 obese patients showed that exogenenous leptin may affect weight loss. The objective of this study was to determine the relationship

between the increased dosage of recombinant human leptin administered daily subcutaneously and weight loss in both obese and lean adults. The lean subjects consumed their normal staple diet while the obese patients were placed on a restricted caloric diet. The results of this study indicate that weight loss was increased with increasing dose of leptin. It should mentioned that at the highest dose more than 95% of the weight loss was due to loss of fat with eight of the patients on the highest doses losing an average of 8.5 kg in weight as compared to the placebo group (36 patients) who lost an average of 2 kg each. It appears that exogenous leptin injected subcutaneously daily may indeed induce fat and weight loss in some obese subjects with only minor side effects. The major drawback of this treatment is that leptin, due to its peptide nature, has to be injected daily in high doses to be even slightly effective for only a small percentage of obese people.

The annual expenditure on weight loss programs in America has been estimated to be approximately $35 billion (US). Of the total 58 million obese Americans it has been estimated that approximately 5% of these individuals are actually deficient in leptin. Thus exogenous leptin therapy could potentially help some 2.9 million obese individuals in America. Though the results to date are far from conclusive, they are promising and warrant further study into the actual mechanism and role leptin, leptin receptor and leptin binding protein play in obesity.

It should be pointed out that recently a number of dietary supplement manufacturers have jumped on the leptin bandwagon and are actively advertising that their leptin-containing elixirs taken orally will cause fat "to literally melt away." The current method of leptin exogenous delivery is by subcutaneous daily injection, and little if any clinical evidence currently exists indicating the efficacy of orally ingested leptin in weight loss. To date, little, if any, information is available regarding the efficacy of using bovine leptin in the treatment and or prevention of obesity in humans.

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DISCLAIMER:

The statements contained herein have not been evaluated by the Food And Drug Administration. It is not intended to diagnose, treat, cure or prevent disease. The statements are for informational purposes only and is it not meant to replace the services or recommendations of a physician or qualified health care practitioner.

Those with health problems or pregnancy are specifically advised that they should consult their physician before taking colostrum or any nutritional supplement.

FAQS FROM THE INSTITUTE FOR COLOSTRUM RESEARCH INSTITUTE WEB SITE

Michail Borissenko
Chief Scientist
Institute of Colostrum Research

Albumin in Colostrum

There are two types of albumin in both milk and colostrum: lactalbumin; and milk albumin. In colostrum they represent approximately 2% of total solids.

Animals and Colostrum—Can They All Benefit?

It's kind of like the Oscar Mayer hot dog jingle—everyone can benefit from taking colostrum, including pets. In fact, I have come across papers on the use of bovine colostrum in the treatment of birds, elephants, mice, even fish.

Arthritis and Colostrum

There are actually two types of arthritis—osteoarthritis and rheumatoid arthritis. In the case of osteoarthritis, this is caused by the actual grinding down of the cartilage due to use, or rather overuse. It is perfectly normal and comes with getting older. Having played rugby, etc, as a youth doesn't help. The other form, rheumatoid arthritis, is an autoimmune disease in which the bodies own immune system attacks the joints and can afflict anyone at any age.

I suspect that you are referring to the former, osteoarthritis. The biggest problem

here is inflammation and pain come hand in hand. The degradation of the cartilage causes inflammation, which in turn causes the pain. Now, how can colostrum help? Well, first off, colostrum contains several very keen natural antiinflammatory agents, and these function to reduce and possibly stop the swelling. Secretory IgA and lactoferrin are the bioactives in colostrum which have this anti-inflammatory action. Secondly, there are numerous drugs out on the market which act as anti-inflammatory agents, and this includes aspirin. As a general heading, these drugs fall under the heading non-steroidal anti-inflammatory drugs (NSAIDs). These NSAID drugs, for the most part, are very good in their action to inhibit the resulting inflammation associated with osteoarthritis. The problem is that for the most part NSAIDs also effect the stomach and the rest of the gut in a very adverse way. Basically they eat the gut, causing ulceration, etc, when used for long periods of time. Guess what? Colostrum has been shown to help prevent and treat the damage done to the stomach and gut by NSAIDs.

Apolipoprotein Levels and Colostrum

Briefly, there are actually two major types of cholesterol—one is good, and one is bad. The bad form of cholesterol is called Low Density Lipoprotein (LDL), also known as Apolipoprotein B-100. This is the one that binds onto the walls of blood vessels and causes causes atheriosclerosis or heart disease. The good form of cholesterol is High Density Lipoprotein (HDL), also known as Apolipoprotein A1, and it functions in preventing the LDL from binding to the vessel wall.

Optimally, you want a high ratio of HDL vs LDL. What colostrum does is reduce LDL levels and increase HDL levels. That is very good. The mechanisms involved include insulin-like growth factor-1 (IGF-1), antioxidants (such as glutathione) present in colostrum, and cytokines, also present in colostrum. Colostrum growth factors promote the repair and regeneration of heart muscle and the regeneration of new blood vessels for collateral coronary circulation.

Athletic Performance and Colostrum

The significance of colostrum in the area of athletic performance lies in several

very important features—all of which the athlete can take advantage of to reach a higher level of performance, and most probably a better form of life. First, it is a highly nutritious food, and secondly it contains many, many bioactive substances which have been shown to prevent disease and promote overall good health. Of specific interest to the athlete is the fact that colostrum supplementation can be an effective way by which the athlete can increase lean body mass, improve muscular strength, increase endurance and capacity, and at the same time speed recovery. What this means to the athlete is simple: they can train harder, longer, and recover faster, thereby increasing their respective level of athletic performance. Of significant importance to the athlete is the simple fact that colostrum is perfectly safe, and further is the fact that the International Olympic Committee (IOC) has designated colostrum to be an accepted and safe dietary supplement. Thus it is recognized as perfectly safe and legal by all the sports regulatory bodies.

Atopic Skin Allergy and Colostrum

In regard to skin allergies, colostrum contains a very interesting bioactive known as proline-rich polypeptide (PRP), also called Colostrinin or transfer factor. This is a very interesting modulator (controller) of the allergic response. Briefly, this substance has been shown to reduce the allergic reaction. You may also try applying colostrum topically to the allergic area. Use any cream as a base and simply dissolve some colostrum in it.

Atopic Dermatitis and Colostrum

Also known as atopic eczema. The word "atopic" refers to a tendency for excess inflammation in the skin, lining of the nose, and lungs.

It may be of interest that this condition often runs in families in which family members are affected with allergies such as hay fever and asthma. In approximately 20% of the cases only a single family member may be affected by this condition. It should be noted atopic dermatitis is very common throughout the world and approximately 10% of infants and 3% of all people in the USA are affected. The

most common cause of this condition is allergy, and it may involve environmental conditions, though rarely food allergy.

In regard to colostrum, it may possibly be of benefit, and this is due to a component in colostrum called colostrinin, also referred to as proline-rich polypeptides, or PRP for short. Very briefly, colostrinin are small polypeptides which have regulatory activity—stimulating or suppressing the immune response. In the case of allergies, the immune system is over-stimulated, hyper-stimulated. PRP has been shown to reduce the stimulation and thus help alleviate the symptom.

When my kids had dermatitis, I just added some colostrum (1 capsule) to the nappie cream we were using at the time and applied it topically. The results were magic. Virtually overnight the redness, etc, disappeared. You also might try giving the child half a capsule in their bottle. However, as always, it may pay to discuss options with a trained health professional, such as dermatologist. This is especially true as it is not our position to give medical advice. You also might want to check the following Web site for more details on eczema: www.eczema-assn.org .

Babies—Is Colostrum Safe to Feed Babies

The area of infant formula is a very sensitive one and involves controversy—breastfeeding vs bottle feeding. It is also tightly regulated, and as such I would suggest due caution be observed in this respect and a disclaimer be included. In regard to the feeding of colostrum to infants and babies—though numerous clinical trials have been conducted involving colostrum in the treatment and prevention of enteric infection, it is still classed as a dietary food supplement. As with any dietary food supplement, it is generally agreed that in regard to feeding colostrum to babies, especially ones less than 6 months old, individuals consult with their healthcare professionals first.

There are numerous cow's milk infant formulas currently being used wordwide to not only feed babies under the age of 12 months but from the time of birth, and I thus must question the nurses' motives. I think everyone will agree that breastfeeding is best, but not all mothers are able. Infant formula is an option,

and colostrum will most probably improve the associated health benefits if this option is taken. Infant formula companies such as Nutricia, Nestle, Wyeth, and Mead have been investigating just this for some time, the biggest hurdle being manufacturing costs.

The final decision to use or not to use colostrum lies with the parents. We can supply the scientific and medical evidence to them or their chosen representative, but the final decision is theirs. The fact is that colostrum does work!

Babies—Feeding Colostrum to Babies

Colostrum is an ideal supplemental food for the infant in that it supplements the digestive tract with various things that protect against disease. Disease starts in the gut, and so does health. However, in the case of a infant please discuss this with your health care professional if there are any concerns.

Barley, Alkaline pH, and Colostrum

I really cannot see how an increase in pH will effect weight loss, unless somehow you expect to increase the pH of the lower intestine thereby affecting the digestive processes of the friendly bacteria there. Thus no digestion and no absorbtion of food, and what you eat goes right down the toilet. You would certainly need to ingest a lot of barley for that. Why not try sensible diet with exercise. supplemented by colostrum? I think this will serve you better.

From the chemical point of view, barley is simply grass. Yes, it is an insoluble fiber and might work as a prebiotic. Stick with the colostrum, but if you so desire, by all means mix it with colostrum.

Benefits of Colostrum—How Long Before I See Them After Starting

Colostrum is a wonderful thing produced by mother nature for the primary purpose of supporting the newborn. It does this by helping the newborn to fight dis-

ease (passive transmission of immunity) and promote development and maturation of various tissues. Further, as the first food the newborn receives, colostrum is very nutritious. For us humans its main function is that it promotes overall good health—you don't get sick. This is very hard to measure. The degree of our health is often masked by our level of fitness, diet, lack of excercise, lack of sleep, alcohol intake, etc. A friend of mine just turned 50 years old, and he told me that he felt great—like a teenager with a hangover.

We as humans come in all kinds of sizes and shapes, and because of this, the time it takes for the various benefits of colostrum to take hold varies. Further, these positive effects may appear subliminally without us noticing them. One classic question I get is, "After taking colostrum for several weeks I noticed my muscles were sore." This typically comes from a sedentary person who after taking colostrum becomes more active and as it turns out starts using muscles they haven't used in years. The best way to determine if the beneficial effects of colostrum are being achieved is to measure them by objective determination. This can be done by keeping a diary and rating how you feel on a daily basis, say, 1-10 (with 1 being close to to death and 10 being the first time you fell in love). I think you will shortly find that with colostrum you will be achieving the higher numbers.

In regard to weight loss, I want to emphasize that colostrum is not the magic bullet in losing weight. You can't simply take colostrum and watch the fat melt away. Colostrum, however, augmented with proper diet and exercise, can help you burn fat and build lean body mass, which has been shown in clinical trials.

Body Building and Colostrum

First, I have written a paper I recently wrote on Athletic Performance and Colostrum. It basically explains how colostrum works as an aid in athletic performance, its safety and its acceptance by the International Olympic Committe (IOC) as an acceptable dietary supplement.

Briefly, in conjunction with proper diet and exercise, colostrum has been shown to help build lean muscle mass and reduce body fat. It has also been shown by

way of clinical trials to help improve athletic performance. This is accomplished in two main ways. First, by maintainence of overall good health, second, by improving capacity to train harder, and third, by improving the recovery and healing process. Thus the athlete can train longer, harder and recover faster.

One important substance implicated in these actions is insulin-like growth factor-1 (IGF-1), a substance normally found in our bodies, in milk and colostrum, also in red meat. The use of pure or recombinant (gentically engineered) IGF-1 is banned by the IOC, as is the use of pure Growth Hormone. The reasoning is that this material can be injected intramuscularly (IM) for local action. However, since normal milk, colostrum and even red meat contain IGF-1, its use as a dietary supplement or food cannot be banned. In fact, our bodies produce IGF-1 on their own, and it has been shown that exercise will increase our circulating IGF-1 levels. The normal IGF-1 level for the human adult is approximately 15-500 ug/l in blood. With 6 liters of blood, the human adult will thus have approximately up to 3000ug (3mg) of IGF-1. Colostrum contains approximately 1ug/g of IGF-1 or 1/3000 of what our bodies normally have already. In addition, I would like to point out that IGF-1 is not an anabolic steroid hormone but is a growth factor. How it functions is two-fold: it helps in our utilization of foods; and it controls the metabolic effects of growth hormone which is also normally present in our bodies. In this capacity it helps to build strong muscles and bone.

Breastfeeding

Please consult with your health care provider, but we can quote science and what has been shown to be true in clinical studies. Primarily there is the fact that colostrum has been shown in clinical trials to prevent enteric disease—diseases of the gut. The leading cause of infant disease, as in adults, is gut infection. This is where colostrum can help. There are no contraindications involving colostrum as far as I am aware. It is very simple, really—colostrum will help you stay free of disease, and in turn your baby will be free of disease. I know this is a very simple concept, but it is actually is true.

BSE AND COLOSTRUM

Safety of Milk

The WHO Consultation of 2-3 April 1996 concluded that milk and milk products were safe. This statement was based on unsuccessful attempts to transmit the agent from cows clinically affected by BSE by inoculation of their milk into mice by intracerebral or intraperitoneal routes or by feeding milk.

More recent data from a suckler herd study in the UK further support the conclusions concerning the safety of milk. No BSE cases out of 132 offspring born to BSE-infected cows have occurred so far (minimum age was 20 months in August 1996).

The present Consultation concurs with the view that milk is safe.

CATEGORY III Low infectivity

Peripheral nerves, nasal mucosa, thymus, bone marrow, liver, lung, pancreas.

CATEGORY IV No detectable infectivity

Skeletal muscle, heart, mammary gland,milk, blood clot, serum, faeces, kidney, thyroid, salivary gland, saliva, ovary, uterus, testis, seminal testis, foetal tissue, [colostrum, bile, bone, cartilaginous tissue, connective tissue, hair, skin, urine]*.

*Tissues in brackets were not titrated in the original studies, but relative infectivity is indicated by other data on spongiform encephalopathies.

Cancer and Colostrum

Regarding colostrum and pancreatic cancer, the article below may be useful.

From the ***American Journal Of Natural Medicine:***

"The 1985 Steven Rosenberg book, ***Quiet Strides in the War on Cancer***, first popularized the benefits of cytokines in the treatment of cancer. Since that time, the same cytokines found in colostrum (interleukins 1, 6, 10, gamma-interferon, and lymphokines) have been the single most researched protocols in scientific research for the cure for cancer.

"Colostrum lactalbumin has been found to be able to cause the selective death (apoptosis) of cancer cells, leaving the surrounding noncancerous tissues unaffected. Lactoferrin has similarly been reported to possess anticancer activity.

"The mix of immune and growth factors in colostrum can inhibit the spread of cancer cells. If viruses are involved in either the initiation or the spread of cancer, colostrum could prove to be one of the best ways to prevent the disease in the first place."

Cancer (Leukemia) and Colostrum

In regard to your enquiry regarding leukemia and how colostrum can help, I should initially state that leukemia is a serious medical condition, and it is advised that the individual's healthcare professional should be consulted.

First, leukemia is a type of cancer, of which there are several types. Colostrum can most probably help in some areas, such as following chemotherapy, reducing the incidence of infection caused by secondary or opportunistic pathogens. Case in point is the use of colostrum for the prevention of fungal infection (Candida or yeast) following bone marrow transplant. Finally, in promoting overall health, disease starts in the gut, and colostrum acts to imunosupplement the gut, that is, protect the gut from infection.

Cancer and Colostrum

The IGF-1 controversy is really overplayed to the point of being ridiculous. It is based on the fact that IGF-1 on the molecular level helps make certain cell types divide faster. All normal cells require growth factors for proper cell division. How-

ever, when a cell undergoes mutagenesis and becomes cancerous, it loses this requirement for growth factors in cell division.

Insulin-like Growth Factor-1 (IGF-1) is a normal constituent in the milk and colostrum of all mammalian species, including humans. It is also found in the blood, saliva, urine, skeletal muscle and other areas of the body. An adult healthy male will typically have approximately 1-3 million nanograms (0.000000001–0.000000003 grams) of IGF circulating through their blood system. In order to replenish these circulating levels and maintain this concentration, the body produces approximately 1 million ng of IGF daily.

The food we eat and drink is the main source of exogenous or external IGF, and this comes from dairy products, meat, poultry (chicken and eggs) & fish. The IGF-1 concentration found in bovine milk is approximately 500 ng per 100 milliliter (ml) while bovine colostrum contains approximately 30,000 ng per 100 ml.

Produced by the liver and other tissues, IGF-1 plays a very important role in a wide range of actions within the body. This includes various transport processes such as ion transport, RNA and DNA synthesis, protein and lipid metabolism, and glucose and amino acid (food) uptake by cells. IGF-1 is also involved with cell division and differentiation in that it is stimulates muscle and bone cell development. It is because of these actions it was postulated that IGF-1 could play a significant role in various sporting activities. This includes building lean body mass while functioning in improving the healing process. A significant body of clinical evidence suggests that IGF-1 can, among other things, help the athlete train harder, longer, and recover faster. In these studies IGF-1 has been shown to help increase lean body mass (muscle) and burn fat.

Relatively recently the field of biotechnology has developed the technology to produce sufficient quantities of recombinant human IGF-1 to make it economically viable to make pure recombinant human IGF-1 available to the public. It is because of this the International Olympic Committee has designated IGF-1 a banned substance and has placed it on their list of Prohibited Substances. This material is typically administered intramuscularly where there is a local mode

of action. On this topic very little information is available but sure to grow. In regard to Growth Hormone (GH), it appears that its inclusion on the Banned Substances list is justified as it has clearly been shown that its use significantly increases circulating IGF-1 levels in test subjects. In fact, it has been shown that the administration of growth hormone by injection can elevate IGF-1 levels by up to 700%.

In regard to the ingestion of naturally occurring foods containing IGF-1, however, the information is well established, and all the evidence indicates that the ingestion of colostrum and or milk will not increase circulating IGF-1 or GH levels. One very early study investigating the effects of colostrum supplementation on athletic performance did suggest that ingestion of colostrum may cause a negligible increase in serum IGF-1 levels. However, in this same study it was also reported that this change in IGF-1 level could also be attributed to the exercise itself. Heavy resistance exercise has been shown to increase circulating IGF-1 levels by up to 25%. It should also be reported that the same researcher who originally reported a possible increase due to colostrum now supports the fact that the ingestion of colostrum has no significant effect on circulating IGF-1 levels.

Clinical trials involving athletes using as much as 60 grams of colostrum per day (60 times the normal dose) showed that no significant increase in IGF-1 and GH levels, as compared to the control group. Typically a good quality colostrum contains approximately 1,000 to 2,000 ng of IGF-1 per gram powder. These 60 grams of colostrum powder corresponded to 60,000 to 120,000 ng of IGF-1 being taken daily. Thus the ingestion of colostrum containing the equivalent of as much as approximately 10% of the total circulating level of IGF-1 had no effect on elevating existing levels.

Further, it has been shown that diet has a very important role in regulating circulating IGF levels. In fact, it has been determined that processed starchy foods, such as white bread and junk food, elevate IGF levels. If IGF did indeed cause cancer, then physical exercise must also be regarded as a potential cancer risk—I don't think so! Further, could it be that an athlete who consumes high amounts of junk food be at the highest risk of developing cancers? I really don't think so! The

controversy may continue, but common sense must prevail. Does colostrum and IGF cause cancer? Definitely no!

Just to kill this thing once and for all I should also point out that there are a number of papers giving evidence how substances in milk and colostrum actually help prevent cancers.

Candida (Yeast Infection) and Colostrum

New Zealand colostrum has been shown to possess very high levels of specific antibody to a wide variety of microbes, and this includes Candida. We have shown that this colostrum will actually inhibit growth of Candida.

Children and Colostrum

Children, like adults, can benefit from colostrum. The age at which one gives colostrum to children is up to the parents. It should be pointed out that there is a registered therapeutic based on colostrum and designed for prevention of rotavirus infection that is designed for children. It should also be noted that there are no known ill side effects associated with colostrum, and it is generally recommended that colostrum is safe to give children over the age of 6 months. This is not a recommendation but rather a rule of thumb as in some countries this age limit does vary. Further, if there is any doubt whatsoever, please consult with a healthcare professional.

Colostrum—What is it?

The significance of colostrum in the area of overall health lies in two very important features. Firstly, it is a highly nutritious food, and secondly, it contains many bioactive substances that have been shown to prevent disease and promote over-all good health. The use of Bovine Colostrum supplementation has been shown in clinical trials to help prevent disease in a number of species, including us humans.

The bioactive molecules in colostrum include such things as immunoglobulins, immune factors, growth factors, and antioxidants. To begin with, immunoglobulins in the form of antibodies and other immune factors act to ward off disease. Antibodies are large protein molecules produced by the animal's immune system to combat and neutralize foreign, potentially disease-causing agents (antigens). The interesting feature of antibodies is that they are specific in that there is a separate and specific antibody produced for every type of antigen. During our lifetime we continually add to the complement of antibodies that are formed in response to the various infectious agents we are exposed to. Antibodies are found in the blood and many other bodily fluids, such as saliva, colostrum and milk.

Colostrum is produced by the mammary gland of all mammals. It is also known as pre-milk as it is the first milk produced by the mother following the birth of her young. The significance of colostrum lies in the fact that it is the first food the young animal receives after it is born. As such, colostrum is a highly nutritious food. However, of paramount importance is the fact that colostrum is involved in a phenomenon known as "passive transmission of immunity." This is a life-supporting function and is best exemplified in farm animals such as the horse, cow, dog, sheep, goat, etc. Unless these animals receive colostrum in the first day or two of life they most likely will die. Unlike humans, who are passively immunized in the womb prior to birth via the placenta, these animals are born without any defense mechanism—immune system—by which they can fight off infection. Colostrum contains antibodies produced by the mother against the disease-causing agents she has been exposed to throughout her lifetime.

At the time of birth, the gut of these animals is not yet sealed, and the whole antibody molecule can be absorbed through the gut wall directly into the blood system. By ingesting colostrum the newborn is able to obtain antibodies from the mother to help them survive until their own immune system is sufficiently developed to fight off disease. After a day or two of life the gut seals, and the antibodies present in the colostrum and milk function in local immune protection of the gut. This local immune protection is not species-specific, and as such we as humans, and all other animals, can use bovine colostrum for its various health benefits.

Antibodies belong to a group of bioactive molecules who as a group are referred to collectively as immunoglobulins. Antibodies function to hunt down, fight, and destroy disease-causing agents or pathogens. Colostrum supplementation has been shown to be an effective means by which infections of the gastrointestinal tract (gut) and other areas can be prevented. It has been shown in clinical trials that colostrum supplementation can be effective in preventing and treating diarrhea (scours) and other infections. In a recent investigation conducted in collaboration with the Department of Microbiology, Otago University, New Zealand, it was revealed that colostrum derived from non-immunized New Zealand pasture fed cows had significant specific antibody potency (titer) to a very wide variety of potentially pathogenic (disease-causing) microbes. Bovine colostrum has been shown in clinical trials to have a safe protective effect in a variety of species, including humans, dogs, cats, horses, and pigs.

In addition to immunoglobulins or antibodies, colostrum also contains other immune factors which help ward off disease and promote overall health—including bioactive peptides, lactoferrin, secretory component, transferrin, lysozyme, lactoperoxidase, cytokines, oligosaccharides, complex lipids, and many others. Colostrum also contains growth promoting substances collectively referred to as growth factors which help to accelerate the growth or healing process.

Colostrum, in addition to antibodies, also contains many other substances which help promote good health in the form of growth, maturation and development. These include growth factors and immune factors. Growth factors include epidermal growth factor (EGF), trophoblast growth factor (TGF), insulin-like growth factor (IGF), and fibroblast growth factor (FGF). These factors function primarily in the growth, development, and maturation of cells, organs, nerves, muscle, and tissues. Growth factors are also involved with the healing and recovery process. Immune factors include lactoferrin, transferrin, cytokines, lysozyme, lactoperoxidase, and transfer factor (PRP). These factors have a very wide assortment of actions and include augmentation (helping) of the action of antibodies and modulation (controlling) of the actions of the immune system.

The direct benefits of colostrum that have been observed to date are numer-

ous, and they include overall good health, prevention of disease, improved performance, reduced healing period, increased recovery, and improved immune protection. These benefits are obvious and can be explained through biochemical pathways and various specific actions of specific components present in colostrum. However, the indirect effects of colostrum are not so clear cut. What is clear is that all the wonderful things in colostrum work together in such a way as to increase the effectiveness of each component.

Compositional Changes in Colostrum Over Time

Yes, the composition of colostrum does change over time. Colostrum is produced for the first 5 days following birth, as defined by the US FDA and NZ MAF. It is highest in concentration in the first milking and then diminishes rather rapidly to form transitional milk, then final regular milk. For example, in the first milking the IgG value is approximately 45mg/ml, dropping to approximately 10 mg/ml at 48 hours and then finally to approximately 0.5mg/ml for regular milk. In New Zealand, colostrum is typically collected in the first three milking only.

Chronic Fatigue Syndrome and Colostrum

Thank your for your enquiry regarding colostrum and salmonella poisoning and Irritable Bowel Syndrome (IBS). One of the most common occurrences following course of antibiotic treatment is secondary infection caused by opportunistic microbes, such as Candida (yeast), etc. The antibiotics typically kill not only the causative agent of the original infection but also the good bacteria which populate the gut, lactobacillus, bifidobacteria, etc. These good bacteria, also known as probiotics, help keep the gut in check. They have numerous functions, including antimicrobial properties. Thus the natural environment of the gut is disturbed and the opportunistic microbes are allowed to colonize. This can lead to chronic infections of the gastrointestinal tract. Irritable Bowel Syndrome, leaky gut syndrome, fibromyaglia, and other disease states have been attributed to this type of chronic infection. This is exactly where colostrum can possibly be of help. Colostrum functions to immunosupplement the gut and thus can help in fighting the infection.

Diabetes and Colostrum

I would like to point out that we do not give any medical advice and suggest that you consult your healthcare provider for medical advice. Also I need to point out that colostrum, at the moment, is still considered by the Ministry of Health to be a food supplement, and as such, no claims can be made as to its use in the treatment or prevention of any disease.

Untreated diabetes can cause extremely high blood sugar levels which, if left untreated, can place great strains on other organs. As such this should be treated seriously. If you suspect you have diabetes, then it would be most wise and prudent to consult with your health care professional.

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Type 2 diabetes or non-insulin dependent diabetes typically appears in adults over 40 years of age and is linked to diet. Obesity or overweight is most often linked with this condition. Most individuals with Type 2 diabetes can regulate their condition by proper diet and exercise. Type 1 diabetes is insulin dependent.

In regard to colostrum, I would like to quote Dr David Henderson in his book, **Colostrum: Nature's Healing Miracle**: "Colostrum contains growth factors that help your body better utilize the food you eat and burn more fat. These growth factors (in particular, IGF-1 or insulin-like growth factor 1) are normally produced by the body, but their numbers can be severely reduced be aging, lack of exercise, exposure to environmental toxins, and poor nutrition. Colostrum restores the body's level of IGF-1 which, along exercise and a nutritious diet, can result in better destabilization ("burning") of fat, increased rate of growth of muscle mass, better strength and endurance-leading to a leaner, healthier body and appearance."

Further he states that, "Insulin-Like Growth Factor 1 and 2 (IGF-1 and IGF-2) are the most abundant growth factors in bovine colostrum. These proteins affect how the body uses fat, protein, and sugar."

Dosage for Children

Colostrum has been shown in clinical trials to prevent disease in not only adults but also children. Children should half the daily adult dose. In other words, adults 2 capsules per day, children 1 capsule, and infants half a capsule per day. My kids won't take capsules, so I either give them chewables or dissolve the powder in a drink or even sprinkle on top of ice cream. It should be noted that this is only a rough guideline.

Daily Recommended Dosage of Colostrum

As of yet there is no recommended daily allowance (RDA) for colostrum. As I am sure you aware, there are a wide variety of colostrum products in the marketplace worldwide. These products vary in composition, potency, and quality, and as such it would be very difficult to assign one therapuetic daily dose for all of them. Most manufacturers suggest 1 to 2 grams per day for maintainence of overall good health and up to 10 grams per day for therapuetic dose if under stress or ill. The high doses of up to and surpassing 60 grams a day are for specific purposes, such as extreme sport performance where the test subjects in several clinical trials received 60 grams of colostrum a day—this equates to 120 capsules. It has been determined that 2 grams of colostrum per kilogram body weight can be taken very safely. This would correspond to a person weighing 110 lbs (50kg) can safely take 100 grams (200 capsules) safely every day.

Colostrum is a wonderful thing. It helps to keep us in good health, and it helps our bodies to keep in balance. To take advantage of all the benefits of colostrum requires that it be taken every day. Most probably 1 gram a day for an adult is the minimum while the maximal amount to take to achieve desired effect depends on what outcome is desired, and to a point what one can afford. In regard to how much colostrum to take for specific desired outcomes, you might want to do a search of the ICR Web site for outcome, disease state, action, etc, and look for clinical trial information. This will give you the amount of colostrum that was administered.

Dosage—Why on an Empty Stomach?

The theory behind taking colostrum on an empty stomach is that this method of delivery will maximize the beneficial effects of colostrum. Whether you take it on an empty stomach with a glass of water or any other way, the most important thing is to take it every day. Build a routine so you take it every day to achieve the benefits, as an ounce of prevention is worth a pound of cure.

Drug Interactions with Colostrum

In regard to drug interaction and negative effects, no drug interaction are known. This is because colostrum is a food. However, it is always advised that individuals taking medication prescribed by a physician first seek medical advive. Further in a just completed clinical trial in which I was involved, we showed that the use of colostrum improved the survival rate of young piglets during a course of antibiotic treatment.

Epilepsy—Can Colostrum Help ?

I have done a pretty thorough search and could not come up with any research involving the use of colostrum and epilepsy directly. But what I have come out with is various things in colostrum which may have a beneficial effect for people with epilepsy. For example, antioxidants may be of help and colostrum contains the ultimate antioxidant, glutathione. Folic acid present in colostrum has been shown to help protect the brain from disease and degenerative disorders. Cystine, glutamic acid and other amino acids present in colostrum could be beneficial. Phospholids present in some colostrum products are known as brain food. Growth factors have been shown to protect and repair adult brain. A group of small peptides (PRPs) found in relatively high amounts in colostrum has been shown to have a very beneficial effect in Alzeimer's patients. Colostrum contains two proteins that have anti-inflammatory function, lactoferrin and secretory IgA. Anti-inflammatory agents have shown to be beneficial in slowing the onset of brain disorders.

In short, there are alot of things in colostrum that may help and probably also important they certainly won't hurt. Further, colostrum will certainly help with overall good health and it will promote well being. Colostrum has been shown in clinical trials to prevent disease. This alone should be a good reason to give it a go! However, as in all conditons which involve medical intervention, it is suggested that you consult with your healthcare provider.

Fat—Why is Fat Removed From Colostrum?

In regard to fat removal, most colostrum is reduced in fat from 4% down to 2%. Though stability may be increased, the major reasoning is processing—whole fat colostrum tends to clog pasteurizers, UF units, etc. Also the growth factors are found in the skim portion, not the fat. The reduction from 4% down to 2% does not lower the complex lipids content significantly.

Freeze Drying versus Spraying Colostrum Products

For the most part colostrum powder is manufactured by spray drying. This is true worldwide of not only colostrum powders but also other milk powders. Freeze drying (lyophilization) is a more gentle form of drying but very costly—something like 30X more costly than spray drying. In addition, economies of scale limit the use of freeze drying as only relatively small volumes can be dried effectively using this technique. Probably the most important point, however, is the fact that dairy processing technology has developed to such a point that the spray drying process can now be performed at reduced temperature and any damage caused by heat is minimal.

Can a Child Suffering G6PD Consume Colostrum?

G6PD stands for glucose 6 phosphate dehydrogenase, which is an enzyme present in the red blood cells in the blood. Individuals suffering from this illness are deficient in this enzyme. G6PD deficiency is one of the most common human enzyme deficiency syndromes affecting some 400 million people wordwide.

Red blood cells carry oxygen in the body, and the enzyme G6PD in normal individuals protects the red blood cells from natural oxygen chemicals that may build up in response to infection, medications or even certain foods. If there is a build up of these chemicals, it can cause destruction of these cells and lead to hemolytic anemia. Medications that should be withheld from individuals suffering from G6PD deficiency include asprin. Though colostrum has no known ill side effects, I think it would still be most wise and prudent for this individual's physician to be consulted first.

Just to make a point, this condition is a very tricky one considering that diet and even aspirin can effect treatment. Further, vitamin K is also implicated in causing anemia in individuals suffering from this disorder, and colostrum is relatively high in vitamin K. Once again, it would be most wise and prudent that the individual's health provider be consulted.

Growth Hormone versus Colostrum

Growth Hormone has definite anti-aging properties, but one thing the manufacturers of these products do not mention are the side effects. First all, GH needs to be injected intramuscularly for it to work or otherwise it will be quickly metabolized by the liver and made inactive. Second, no long-term health studies have been conducted on its use. Third, GH does act to build muscle and lean body mass, but it does cause an increase in organ and bone weight—not a good thing. Fourth, GH administration needs to very controlled as too much can cause gigantism (Acromegaly). You can always tell when body builders or weight lifters are on GH as they usually have wide gaps in between their teeth—the skull has grown! Colostrum, however, has been shown to be a safe alternative.

The good news is colostrum is nature's perfect answer to hGH. Extensive research shows that colostrum is unique because it is the only substance that offers anti-aging hormones in perfect balance, the way nature intended. According to Zoltan Rona, MD, (***Bovine Colostrum, Immunity and the Aging Process***, Nature's Impact), when colostrum is taken as a supplement, "skin appears more youthful, age

and 'liver' spots disappear, bone mass and density increases and sexual function is improved and restored." In other words, it appears colostrum works similarly to hGH with none of the known dangerous side effects.

Guillian-Barre & Colostrum

First of all, I hope you can appreciate the seriousness of this disease state and that we do not provide medical advice—your physician is best suited for that. What we would like to do is give you some scientific information on the subject.

Guillian-Barre syndrome is a relatively rare dissorder in which the body's own immune system attacks the peripheral nervous system. It frequently follows viral infection. The incidence of this disorder is approximately 1-2 cases per 100,000 with most patients recovering with no or minimal long-term effects. However, in some cases this disorder can be very serious and can cause total paralysis and the need for ventilatory assist. Death occurs in less than 5% of the cases.

In approximately 70% of the cases, Guillian-Barre is preceded by a mild respiratory or digestive tract infection. One organism in particular has been singled out as being associated with development of Guillian-Barre—***Campylobacter jejuni***. It is of interest that this microbe has become the leading cause of enteric (gastric) infection in the developed world. It has been theorized that Guillian-Barre arises as result of the immune system producing antibodies to the surface coating proteins (antigen) of ***C. jejuni***.

In other words, the infecting ***C. jejuni*** stimulates the immune system to produce antibodies to help fight the infection, and these antibodies are directed to the surface coating proteins. The unfortunate thing is that these surface coating proteins are very similiar in structure, composition, and configuration to the myelin sheath surrounding the axons of nerve cells. Thus the antibodies initially directed towards ***C. jejuni*** also attack the individual's own nervous system. Guillian-Barre is called an autoimmune disease, and the extent and duration of the syndrome is most probably due the extent and duration of the initial exposure to ***C. jejuni*** infection. Once stimulated to produce antibodies, the immune system continues

production as long as the antigen is present. In this case, the antigen becomes the individual's own nervous system, and thus Guillian-Barre can be a chronic illness.

The use of plasmaphoresis and high immunoglobulin therapy has been shown to reduce the severity and duration of Guillian-Barre. Principly this method of treatment involves injection of pooled human plasma and involves the passive transmission of systemic immunity, the reasoning being that a pool of human plasma would have a complement of antibodies to a wide variety of microbes, including ***C. jejuni***. Given early on, this extra boost of antibody can thus nuetralize and reduce the level of infection and minimize the body's own autoimmune response mechanism, thus reducing the severity of the disease. It is important to note that this is passive transmission of immunity which in this case functions systemically.

In regard to bovine colostrumm the following information may be of interest. I was involved in a study conducted at Otago University in which we investigated the presence and potency of specific antibodies to a wide variety of microbes. The results indicated that New Zealand colostrum contains very high levels of specific antibody to ***C. jejuni***. This is attributed to the fact that the enviromental conditions here combined with our dairy farming practice of free range pasture feeding allows the cows to be exposed to a very large variety of microbes.

Bovine colostrum has been shown in clinical trials to help prevent and treat enteric (gastrointestinal) infections. This includes Campylobacter infection.

Health Benefits of Colostrum

In regard to the health benefits associated with colostrum, there are many. Immune factors in the form of antibodies, lactoferrin and others that help in the immunosupplementation of the gut, growth factors which help in the healing and recovery process, prebotics in the form of oligosaccharides which help promote the growth of beneficial bacteria (probiotics), antioxidants in the form of glutathione and others that not only help in preventing disease but also have certain anti-aging properties. In other words, many things that have many beneficial properties.

Heart Medications and Colostrum

In regard to anyone under the present care of a health professional, it would be both wise and prudent to have them consult on what is best for their respective patient. This is especially true in cases such as high blood pressure and heart disease. Only the prescibing physician knows the whole story including the underlying causes of the symptoms. All that said, colostrum may possibly be of help, and this would probably be due to insulin-like growth factor-1 (IGF-1), which has been shown to help burn fat and build lean body mass, also to have a beneficial apsect in regard to helping the lowering of bad cholesterol (LDL) and raising the good cholesterol levels (HDL). Also IGF-1 has been shown to stabilize elevated blood sugar levels. Phospholipids have been shown to have a beneficial effect on lowering blood pressure also.

Herxheimer Reaction and Colostrum

I have heard of a few people experiencing a Herxheimer reaction when first starting with colostrum. Herxheimer reaction is basically detoxification and is sometimes associated with soreness. It is important to note that this occurs in only a very few people and is short-lived. It is very important to drink a glass of fresh and clean water when one experiences this type of adverse reaction, to help prevent toxins to being redeposited body tissue.

High Blood Pressure and Colostrum

If anything, colostrum should help in lowering blood pressure. Colostrum contains many things that contribute to lowering blood pressure—phospholipids and IGF in particular. Phospholipids have been shown to lower blood cholesterol levels while IGF has been shown to lower and stabilize blood sugar levels.

Colostrum and Horses

The significance of colostrum in the area of the competing horse lies in several very important features, all of which one can take advantage of to reach a higher

level of performance, and most probably afford the animal a better quality of life. First, it is a highly nutritious food, and second, it contains many, many bioactive substances which have been shown to prevent disease and promote over-all good health. Of specific interest to the trainer is the fact that colostrum supplementation can be an effective way by which the performance horse can increase lean body mass, improve muscular strength, increase endurance and capacity, and at the same time speed recovery. What this means to the horse is simple—they can train harder, longer, and recover faster thereby increasing their respective level of performance. Of significant importance to the athlete is the simple fact that colostrum is perfectly safe and further is the fact that the International Olympic Committee (IOC) has designated colostrum to be an accepted and safe dietary supplement. Thus it is recognized as perfectly safe and, legal by all the sports and racing regulatory bodies.

Insulin-like Growth Factor (IGF) and Weight Loss

The primary substance in colostrum associated with weight loss is insulin-like growth factor (IGF). IGF is found in relatively high concentrations in bovine colostrum. IGF regulates the metabolic effects of Growth Hormone, which is naturally produced by the body. In so doing, IGF functions to increase lean body mass (muscle) and the burning of fat. As its name indicates, IGF is very similiar in structure and function to insulin and is thus involved with regulating or balancing blood sugar levels. Of utmost importance, however, is the fact that simply taking colostrum doesn't mean you will lose fat. Colostrum augmented with proper diet and excercise will, however, most surely help you loose the flab.

Johnie's Disease and Colostrum

In regard to Johnies disease or Mycobacterium paratuberculosis, this is in fact a bad news kind of disease—no cure, major problem in USA. Fortunately not transmittable to humans. In regard to testing for Johnies disease, the New Zealand dairy industry regularly tests for the presence of the disease. In addition the method of pasteurization in New Zealand ensures that this pathogen is destroyed

Lactating Mothers

As with all supplements, medications, and even diet, individuals who are either lactating or pregnant should advise their healthcare provider.

Lactose Intolerance and Colostrum

Thank you very much for your recent enquiry regarding colostrum and lactose intolerance. Unfortunately to date we haven't been able to remove lactose from colostrum. However, colostrum is reduced in lactose, and the amount present in a daily colostrum is negligible. In fact, the amount of lactose present in 2 capsules (1gram) of colostrum would be equivalent to approximately 1.5 ml of milk.

Did you know that even individuals who are lactose intolerant can for the most part tolerate 240ml of milk per day quite nicely? Did you know that hard cheeses have virtually no lactose as it is degraded during the aging process? The same is true of most yogurts. So if you tolerate hard cheese or lactose, colostrum should present no problem at all. However, if in doubt, by all means consult with your healthcare provider. Also you might want to try the old police trick by just placing a very little bit (~10mg) on the tongue to see how it goes.

Lactose intolerance is a food allergy, and creates an imbalance in specific cytokines in the body. The peptides or PRPs in colostrums actually normalize or modulate the levels of cytokines in the body, so the body does not recognize the lactose as a food allergin.

Does the Addition of Lipid Have a Negative Effect on Colostrum?

In regard to lipid, I suspect you are referring to complex lipids in the form of phospholipids, sphingolipids, and glycolipids which are added to the Alpha Lipid colostrum. Quite the opposite, these complex lipids actually add to the biofunctionality of Alpha Lipid colostrum. The phospholipid forms are phosphatidylserine (PS), phosphatidylcholine (PC), phosphatidylethanolamine (PE). The sphingolipid is in the sphingomylein form while the glycolipid is in the ganglioside GD3 form. The

unique benefits these complex lipids add to Alpha Lipid colostrum include added bioavailability due to the delivery system so that all the colostrum is available. Furthermore, the complex lipids function in improving brain function, improve memory, and elevate mood. They have also been shown to help in protection of the gut and aid in liver function.

Colostrum and Lupus

Systemic lupus erythematosus (SLE) is an autoimmune disease which primarily attacks women of childbearing age. It should be pointed out that this is potentially a very serious condition, and as such, individuals who suffer from this disease should consult with their healthcare professional prior to taking any supplement or medication. In lupus the immune system is over-reactive and produces antibodies that attack the patient's own tissues. Lupus can effect many different parts of the body, including joints, organs, heart, nervous system, and blood vessels. Patients that take a PRP supplement for a few weeks may have there Antinuclear Antibody Test (ANA) readings stabilized.

SLE is associated with Antiphospholipid Syndrome (APS), a condition associated also with recurrent miscarriage, coronary disease, preeclampsia, and many other conditions. In APS the individuals produce antibodies to their own phospholipids—the primary structural element of all membranes. Current treatment includes the use of immunosuppresants, NSAIDs, aspirin, and prednisone.

In SLE the patient's immune system is over-stimulated in producing autoantibodies. Colostrinin, also known as proline-rich polypeptides (PRP), is an immunomodulator (regulates the immune response) present in colostrum. Thus colostrinin may be of value in slowing down the production of autoantibodies. Also the autoantibodies that are being produced are directed towards phospholipids. As such, the ingestion of phospholipids, such as Alpha Lipid colostrum, may be of value in that the antiphospholipids may bind to the free phospholid instead of membranes. Further, colostrum has been shown to reverse the damage caused to the gastrointestinal tract by NSAIDs.

Mineral Content of Colostrum?

Thank you very much for your enquiry regarding mineral content of colostrum. I hope you can appreciate that the absolute value for each mineral will most likely vary based on end product—skim vs whole vs whey, etc. The general values in a powder are as follows:

Sodium ~ 3.44mg/1000mg
Phosphorus ~ 4.94mg/1000mg
Magnesium ~ 1.19mg/1000mg
Potassium ~ 8.39mg/1000mg

Pregnant Dogs & Cats

Thank you for your recent enquiry regarding feeding colostrum to pregnant dogs and cats. First, colostrum is a food and has been shown to be free of any known side effects. Second, colostrum has been shown in clinical trials to help prevent disease and promote overall good health. This being the case, why not? If you have any doubts, then please consult with your veterinarian—I am sure he or she will concur.

Radiculopathy and Colostrum

I have attached some information regarding this condition just in case for your information. The direct effect of colostrum in regard to this condition is most probably minimal. However, the indirect effects may be of interest, especially as colostrum contains natural anti-inflammatory agents which may be of benefit. Please discuss this with your physician. Colostrum is a natural food that possesses many health benefits -all of which contribute to overall health

Taste of Colostrum

One thing to remember is the sense of taste and smell are very powerful and sensitive indicators—if it smells bad and tastes bad it most probably is indeed bad.

On the other hand, colostrum powder, unless it contains a flavor additive, should have little taste.

Urticaria and Colostrum

Thank you for your enquiry regarding urticaria and colostrum. Urticaria, commonly called hives, is an inflammation of the surface layers of the skin. It is commonly characterized by small, itchy white or red welts. Urticaria is commonly caused by an allergic reaction. However, the allergen or causitive agent has not been identified.

In regard to colostrum, it may possibly be of benefit, and this is due to a component in colostrum called proline-rich polypeptides, or PRP for short. Very briefly, PRPs are small polypeptides which have regulatory activity—stimulating or suppressing the immune response. In the case of allergies, the immune system is over-stimulated and PRP has been shown to reduce the stimulation and thus help alleviate the symptom.

Whey Type Products vs Colostrum

The IgG type products are for the most part derived from the whey of milk and not from colostrum. In that sense they are isolates and as such usually are lacking in certain bioactives found in whole colostrum, such as growth factors, cytokines, immune factors, etc.

Both milk and colostrum can be seperated into whey and curd. By removing the curd you increase the concentration of things like IgG or immunoglobulins. However, some other very important bioactives are either lost in the curd or they are simply not present in milk.

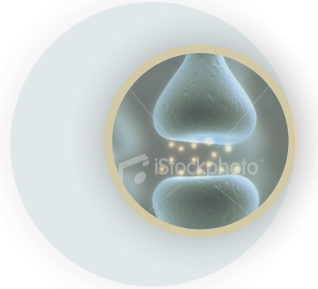
The major differences in milk vs colostrum:

Colostrum / Milk
IgG 50mg/ml 0.6 mg/ml

IgA 6 mg/ml 0.06 mg/ml
IgM 7 mg/ml 0.07 mg/ml

Protein 50%/30%

The major difference is the simple fact that all the bioactives in colostrum act in such a way as to make the overall effect or benefit greater than the sum of the individual components. This is called a symbiotic effect. The milk-derived whey IgG products simply do not possess this.



APPENDIX D

CAN COLOSTRUM ASSIST AIDS PATIENTS?

A commentary by Thomas E. Stone, ND, CNHP

In 1995, an article in ***Scientific American*** concluded that ***traditional*** disease fighting methods were not effective in fighting the HIV virus - otherwise know as AIDS. Instead, this author recommended that we focus on finding ways of stimulating the immune system and reducing the viral load. Colostrum can be very effective in both of these ways. Colostrum stimulates and strengthens a weakened immune system and those who take it on a regular basis have a heightened ability to resist and fight infection - exactly what the AIDS patient needs. Colostrum activates or "turns on" the immune system in the newborn and it can do the same thing for the AIDS patient - or anyone, for that matter. It contains over 40 different immune factors which work in harmony to support a stronger defense mechanism. This is so critical for the AIDS patient, who dies —not from the HIV virus—but from secondary infections which the immune system is no longer able to control.

One of the immune components in colostrum falls into a category called ***immunoglobulins***. These are "functional antibodies," ready to combat a host of bacterial pathogens. In this way, colostrum can actually be a sort of secondary immune system for the AIDS patient.

Colostrum and colostral components can also be effective in reducing viral populations. A 1995 study conducted in the Netherlands indicated that the

immune factor, lactoferrin, is one of the best ways to reduce viral levels in the body. It inhibited the HIV virus of certain body cells and was able to completely block Cytomegalovirus infection. This same study concluded that bovine (cow) lactoferrin was up to 2.5 times more effective than human lactoferrin. Several other immune factors contained in colostrum have been shown to have antiviral activity as well.

One of the most serious problems with AIDS is something called "wasting." It is brought on by chronic diarrhea and results in a loss of vital nutrients and fluids. It also depletes the supply of intestinal antibodies, leaving the patient even more vulnerable to dangerous pathogens. A 1992 study showed that out of 37 immunodeficient patients with chronic diarrhea, 72% experienced significant improvement with the use of immunoglobulins from colostrum. Another study stated that colostral immunoglobulins have been able to treat diarrhea-causing infections associated with AIDS where no other treatment was effective.

Wasting occurs when the AIDS-infected body begins burning muscle for fuel. Here again, colostrum can help. The growth factors, contained in colostrum, also play a big role in supporting AIDS patients. Treatment with IGF-1 and growth hormone (GH), both contained in colostrum, produce an increase in muscle mass, preventing the severe weight loss associated with wasting. If colostrum were used for no other reason than to reduce the diarrhea-induced wasting and to prevent the loss of muscle mass, it would greatly enhance quality of life for those who suffer from AIDS. However, in my experience, colostrum can do so much more than this.

Eight months ago I treated a patient with full-blown AIDS, who had been sincerely searching and doing everything in his power to regain his health. When I initially met with him, he had a T cell count in the high teens, despite the fact that he had been following a strict health regime for a matter of months. With megadoses of colostrum (60 capsules/day) and a herb called Maca, we eliminated many of the other things he was doing. He continued to eat healthfully and take ample amounts of green juices. Within two weeks, both he and his medical doctors were shocked to find that his T cell count had risen to 350! His doctor even insisted

on a retest to verify these results. Now, eight months later, he has been declared HIV-free, and doctors are saying that they must have misdiagnosed him in the first place. This man is so dedicated to helping other people that he now owns a health food store and is sharing his knowledge with hosts of other people.

A ***desire*** to get well is a critical factor in healing. This man was totally dedicated and when he found the additional nutritional help of colostrum, he made fast progress. Can colostrum assist AIDS patients? In a variety of ways, the answer is a resounding, Yes!

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GLOSSARY

Adaptive immune system—the defensive system of the body that produces specific antibodies to a particular antigen.

Apoptosis—programmed cell death. It is the normal process by which unneeded cells in the body are removed, such as the resculpting of body tissues during development.

Autoimmunity—a pathologic condition in which the body makes antibodies against its own tissues.

B-lymphocytes (B cells)—a type of lymphocyte produced in Bone marrow and that is mainly responsible for producing antibodies (immunoglobulins). They are also known as Plasma Cells.

Cell-mediated (Th1) immunity—immune defense mediated by cells such as cytotoxic lymphocytes, natural killer cells and macrophages to fight infections and cancer.

Chemokines—small cytokines that mobilize and activate white blood cells, usually by acting as a chemoattractant to attract cells of the immune system to the site of an infection.

Colostrum—the first milk, or pre-milk, produced a mammalian mother following the birth of her newborn. Technically it is only the milk in the mammary glands at the time of birth. It is a normally a thin, yellowish fluid.

Cytokines—regulatory proteins that regulate many bodily processes, including reproduction, growth and development, homeostasis, blood clotting, and the immune response. They generally fall into six groups: interleukins, colony-stimulating factors, interferons, tumor necrosis factor, growth factors and chemokines. They can be produced by a variety of cells.

Dendritic cells—antigen presenting leukocytes (white blood cells) of the immune system. Found primarily in the skin, mucosa and lymphoid tissues, they function to initiate the immune response by activating lymphocytes and secreting cytokines.

Humoral (Th2) immunity—immune defense mediated by antibodies secreted by B lymphocytes to fight infections and toxins.

Immunoglobulins—also known as antibodies, immunoglobulins are the principal components of the adaptive immune system which has the capacity to make antibodies to specific antigens (proteins recognized as foreign by the body). Mammals have five basic types of immunoglobulins: immunoglobulin G (IgG), responsible for systemic immunity to a specific antigen; IgA, responsible for localized immunity to antigens, such as in the gut; IgM, basically five IgG molecules bound together, IgM is the first immunoglobulin produced during an infection; IgE, involved in the allergic reaction in response to the allergen (protein that sets off the allergic response); IgD, binds to the surface of B lymphocytes and appears to play a role in antigen recognition.

Innate immune system—the first line defense system of the body that provides non-specific defense against invaders, such as bacteria, viruses, protozoa and tumor cells. Consists of both cells (NK cells, mast cells, eosinophils, basophils, neutrophils, macrophages, dendritic cells) and proteins (lactoferrin, lysozyme, lactoperoxidase)

Lymphocytes—a type of white blood cell that composes the main cells of the immune system. They are of different types, some which produce antibodies (B cells), some which locate and identify antigens in the body (helper

T cells), some which attack and kill pathogens (NK cells and cytotoxic T cells), some which inhibit the activity of other immune cells in order to shut off the immune response and avoid damage to healthy tissue (suppressor and regulator T cells), and some which retain a memory of encountered antigens to speed the response time in case of reinfection (memory T cells).

Macrophages—scavenger cells of body tissue spaces that phagocytize (eat) foreign material, such as bacteria, protozoa, viruses and tumor cells. They are formed when blood monocytes migrate into the tissue spaces.

Mast cells—cells of the innate immune system that are found in connective tissues and mucous membranes. They release histamine and heparin when activated, part of the inflammatory response.

Monocytes—phagocytic cells of the blood which remove foreign material, such as bacteria, viruses, protozoa and tumor cells, from the bloodstream. When they leave the bloodstream and enter the tissue spaces they are known as macrophages.

Natural killer (NK) cells—lymphocytes whose primary function is to kill cells in the body infected by viruses or other pathogens or neoplastic (cancer) cells.

Peptides—short strings of amino acids with no tertiary (three-dimensional) structure. Polypeptides are longer strings of amino acids but still with no tertiary structure.

Phagocytes—literally "eating cell" in Greek, these are scavenger cells, like macrophages and monocytes, which ingest foreign material in the body. The material is then broken down and either assimilated or discarded.

Plasma Cells—see B cells.

Proline-rich polypeptides (PRPs)—short strings of amino acids that lack

the tertiary (three-dimensional) structure of proteins. They act as intercellular signaling molecules. In the case of the PRPs found in colostrum, they act to modulate the activity of the immune system, either stimulating it in the case of an underperforming system, as may be found in the case of a severe infection, or inhibiting it in the case of an overperforming system, such as is found in allergies and autoimmune conditions.

Proteins—large, often very complex molecules composed of amino acids and usually having intricate tertiary (three dimensional) structures. Most of the functions in the body are carried out by proteins, and most structural components of the body are composed of proteins.

Signal transduction—the process by which a message is passed from cell to other cells through the use of signaling molecules, usually peptides or polypeptides, that interact with specific receptors on the surfaces of the target cells, setting off a chain of intracellular events that typically result in a specific protein being produced by the cell.

T lymphocytes (T cells)—lymphocytes which are produced in bone marrow but mature in the Thymus gland, located in the neck. There are a number of subsets of T cells:

- Helper T cells—lymphocytes that act to regulate the immune response by secreting cytokines when activated. They are further broken down into Th_1, Th_2, Th_{17} and other subsets depending on the types of cytokines they produce.
- Cytotoxic T cells—also known as CD8+ T cells, these lymphocytes actively seek out and kill virally infected cells and tumor cells, as well as tumor rejection.
- Suppressor T cells—lymphocytes which suppress the immune response to prevent damage to healthy tissues once the infection is controlled or neutralized. They are thought to be formed through interaction of cytotoxic T cells with helper T cells.
- Memory T cells—lymphocytes that provide a memory of antigens pre-

viously encountered and capable of quickly multiplying in the event of reinfection.

- Regulatory T cells—lymphocytes which act to suppress the immune response toward the end of the immune reaction. They are very similar to suppressor T cells but have a different origin.
- Natural Killer (NK) T cells—lymphocytes which form a bridge between the adaptive immune system and the innate immune system. They are activated by recognizing a certain type of antigen, after which they perform as cytotoxic cells.
- γδ (***gamma delta***) T cells—a small subset of T lymphocytes which tend to concentrate in the gut mucosa. They seem to be able to respond to whole proteins rather than peptides presented by antigen-presenting cells. They appear to be part of the first line of defense against infection.

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