Nutrition and Immune Function: Colostrum for immune & gut health

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Key Ideas

- A healthy immune system is central to overall health and longevity
- The immune system can be effectively modulated by nutrition
- Milk derived proteins have significant immune & gut health benefits
Biological Knowledge & Its Application

Levels of Biological Information
- DNA
- mRNA
- Proteins
- Cells
- Organs
- Individuals
- Populations
- Ecosystems

Significance for health & well being
- Genomics
- Transcriptomics
- Proteomics
- Cell Biology
- Anatomy
- Medicine/Nutrition
- Public Health
- Ecology
The immune system consists of a collection of *cells, tissues* and *organs*, that is part of a finely orchestrated combination of *biological systems* and *process* that *protect the integrity of the organism*.
Overview of Immune System

Immune System
Cellular Components & Biological Process

Innate Arm

Cells
- Barriers
- Surveillance
- Inflammatory Process

Phagocytes

Adaptive Arm

Cells
- Phagocytes
- T lymphocytes
- B lymphocytes

Process
- Recognition
- Optimization
- Memory

The gut is the largest immune organ!
Cellular & Humoral Immunity

Why enhance immune health?

CTL (cytotoxic response)

T-cell proliferation

Antibody production

Why enhance immune health?

Bacteria
Virus
Antigen

Phagocytosis

T cell
CD4

MHC II

IL2

cytokines

 APC

B cell

MHC II

T cell
CD4

T help (activation of B cells)

IgA, IgG

Antibody production

IgM

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Life-Stage & Immunity

Th2-Type Bias = lower ability to fight infections, higher allergies
‘Immunity Gap’

• Puppy’s immune system takes several weeks to months to fully develop
• Maternal antibodies from colostrum last for about 10-16 weeks
• Vaccinations are typically not administered during the first few weeks following birth, to avoid interference from maternal antibodies
• For the first 12-16 weeks of age your pup is primarily protected by maternal antibodies!
• Maternal antibodies, however, may not be sufficient even if the pup is weaned appropriately
  - [1] insufficient antibodies produced by the mom
  - [2] inadequate intake of colostrum/breast milk by the pup
  - [3] insufficient absorption of antibodies by the pup
  - [4] movement of pups to a different locale
• ‘Immunity Gap’ makes the puppy vulnerable to infection
Growing Up is Stressful

- Stresses in puppies include:
  - Bathing
  - Going to a new place
  - Meeting new people
  - Being in a crate
  - Playing
Effect of Bathing on Fecal Score

- Fecal Score
  - 48 hr prior
  - 48 hr during
  - 48 hr after

- Score range: 60 to 85

- 48 hr prior: 85
- 48 hr during: 65
- 48 hr after: 80
Stress Depresses Immune System: What Is Happening in the Gut?

**LARGE INTESTINE**

- **Bifidobacteria**
  - Positive Effects
    - Energy for gut cells
    - Help prevent diarrhea
    - pH (more acidic)
  - Helps Mineral Absorption
- **Clostridium perfringens**
  - Negative effects
    - Enterotoxins
    - Potential carcinogens
    - Putrefactive substances

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What Happens in the Gut After Stress

- Shifts in microbial population
- Shedding of pathogenic bacteria [issues with zoonosis]
- Function of protective intestinal barrier
- Negative Nutritional impact at a crucial stage of growth & development
**Key Ideas**

- A healthy immune system is central to overall health and longevity

- The immune system can be effectively modulated by nutrition
  - Milk derived proteins have significant immune & gut health benefits
Modulating Immune System

GENES

LIFE STAGE

Unique Profile

LIFE STYLE
Including diet
Nutritional Modulation of Immunity

Strategy

- **1st Stage**  Complete Nutrition
- **2nd Stage**  Optimizing macro & micro nutrients
- **3rd Stage**  Stimulation using very low levels of nature’s own immunostimulants
  » Whey proteins, bacterial products, probiotics etc.
- **4th Stage**  ‘Personalized Immunomodulation’

Military Analogy

- Personal
- Equipment & technology
- Training
- Tactical Special Forces
Immune Modulation: Health Implications

- Increased phagocytic activity means:
  - “Priming” of the innate immune system
- Increased lymphocyte activity (proliferation) means:
  - Higher activity of T and B lymphocytes
  - “Priming” of the acquired cellular immune system
- Increased antibody (Ig) levels means:
  - “Priming” of the acquired humoral immune system

Priming = Increase of natural defenses
Stronger/faster protection against infections
Healthier immune system = fewer autoimmunity & allergies, foundation for healthier start in life
Key Ideas

✓ A healthy immune system is central to overall health and longevity

✓ The immune system can be effectively modulated by nutrition

➢ Milk derived proteins have significant immune & gut health benefits
Colostrum, Immunity & Gut Health

Milk derived proteins have significant immune & gut health benefits
What is Colostrum?

- Colostrum is early milk produced by cows with a nutrient profile & immunological composition different from ‘mature milk’. Colostrum is available as spray dried powder.
- Colostrum has lower levels of casein and higher levels of proteins collectively called ‘whey proteins’.

Colostrum Composition

Composition of Milk Protein

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History of Colostrum

- Ayurvedic physicians used bovine colostrum therapeutically in India for thousands of years.

- In the west, doctors used it as antibiotic prior to antibiotic era.


- In the past 20 years there are > 2000 publications on colostrum & its health benefits.

Colostrum has long & safe history of use in human/animal health.
Colostrum & Health

- **Antimicrobial Activity**: Lactoferrin is an immunomodulator and inhibits undesirable microflora by sequestering iron in the gut [*Arnold RR et al, Science 1977; 197: 263-5]*

- **Anti-cancer Activity**: Whey proteins protect against chemically induced carcinogenesis in animal models [*Bounous G et al Cancer Lett 1991; 57: 91-4]*

- **Prebiotic Activity**: Whey proteins promote health promoting *Bifidobacterium* species [*Petschow BW & Talbott RD. J Clin Microbiol 1990; 28: 287-92]*.

- **Satiety**: Glycomacropeptide known to regulate appetite and acts as a prebiotic and immunostimulant [*Harper WI. The American Dairy Products Institute, Chicago, 2000]*
Colostrum & Growth Factors

Peptide growth factors in colostrum include:

- **epidermal growth factor [EGF]** – gut wall repair
- **tumor growth factor-α [TGF-α]** – GI growth & maturation
- **tumor growth factor-β [TGF-β]** – gut repair & protection
- **insulin-like growth factors & binding proteins [IGF & IGFBP]** – GI growth & maturation
- **platelet-derived growth factor [PDGF]** – GI growth & maturation
- **vascular endothelial growth factor [VEGF]** – GI growth & maturation
- **growth hormone** – GI growth & maturation
Colostrum & Immune System

- Immune stimulatory molecules –
  - Immunoglobulin, lactoferrin, glycomacropeptide

- Immune modulatory molecules:
  - EGF, TGF-α, TGF-β, IGF, PDGF, VEGF

  - Glutamine is preferred fuel for muscle & immune cells
  - Immune cells cannot synthesize glutamine
  - Exercise, stress can deplete glutamine making immune cells weak
Colostrum & Immune System contd....

- Immune cells are exposed to tremendous oxidative stress & need an effective anti-oxidant system to protect them from harm.
- The glutathione (GSH) antioxidant system is the principal mechanism that protects cells against oxidative stress.
- Whey Proteins are an excellent source of cysteine, an rate limiting amino acid for synthesis of glutathione.

[Glutathione] [Bucci LR & Unlu L in Energy Yielding Macronutrients and Energy Metabolism in Sports Nutrition, p197, 2000]
Colostrum & Enhanced Immune Response

- Mice fed whey protein concentrates [WPC] produced significantly higher serum & intestinal antibodies to several antigens [influenza virus, diphtheria & tetanus toxin, poliomyelitis vaccine, ovalbumin & cholera toxin sub-unit] [Lowe P P L et al 'International Immunopharma. 2, p393, 2003]
- Clearly there is ample evidence from literature to document the general as well as immune and gut health benefits offered by addition of whey proteins to diet
Colostrum, Immune & Gut Health in Dog Response

We could find one report documenting use of colostrum for gut health in dogs Gifford et al have shown that weaned puppies provided with supplemental bovine colostrum for 10 days after arrival in pet shops experienced an improvement in fecal quality [Gifford et al. J Nutr 134: 2126S-2127]
Nestle Purina Dog Nutritional Trial with Colostrum
Nutritional Trial: Effect of Colostrum on Immune & Gut health

- 24 Alaskan sled dog 2-6 years of age
- 2 diets
  - Control
  - Test diet with colostrum
- Trial Protocol
  - 40 wk trials conducted by Dr. Arleigh Reynolds, at our facilities in Alaska
  - Immune and gut health monitored during the study
Study Schematic

CDV Vaccination

Pre-test
-4 Wk  0 Wk

Test
38 Wk

Monthly Sampling

Treatment Groups [n=12]
Control
Colostrum

40 Wk
Immune & Gut Health Measurement

- **Immune Analysis**
  - [A] Evaluation of Systemic Immune Response
    - Response to CDV Vaccine:
      - Plasma Immunoglobulins
      - C-Reactive Protein
  - [B] Evaluation of Local Immune Response (GALT)
    - Fecal IgA Measurements

- **Gut Health Measurements**
  - [A] Fecal Quality
  - [B] Analysis of pathogenic bacteria
  - [C] Gut Microflora Profiles
    - Gut Microflora Diversity
    - Effect of stress on gut microflora

- **Other Biological Measures**
  - [A] Body Weights
  - [B] Blood Profile
Colostrum Enhances Immune Status

Animals fed diet with colostrum demonstrated enhanced immune status – CDV response is stronger & lasts longer
Colostrum Stimulates GALT to Increase Secretory IgA

Animals fed diet with colostrum demonstrated enhanced local immune status – Is enhanced immune response because of over stimulation?

P < 0.05

Treatment Groups (n=12)
Dogs Fed Whey Proteins Had No Overt Immune Stimulation

C-reactive Protein Levels

- C-reactive protein is an acute phase protein that is increased in plasma during inflammation.

Normal CRP levels = 0.8 to 16.4 μg/ml CRP [Otabe K. et al. Vet Res Commun. 1998 22(2):77]

During inflammatory events, such as pancreatitis, CRP levels = 56.1 μg/ml [Holm J L et al., J Vet Emergency & Critical Care 14: 183, 2004]

- NSD

The immune system in animals fed diet with colostrum is not hyperactive -- it responds only when challenged.
Colostrum Enhances Immune Health

- Animals fed diet with colostrum demonstrated significantly enhanced immune status – CDV response is stronger & lasts longer
- Animals fed diet with colostrum demonstrated significantly enhanced local immune status - higher fecal IgA, marker of healthy & active GALT
- The immune system in animals fed diet with colostrum is not hyperactive - it responds only when challenged, a sign of a healthy & active immune system
Immune & Gut Health Measurement

- **Immune Analysis**
  - [A] Evaluation of Systemic Immune Response
    - Response to CDV Vaccine:
    - Serum Immunoglobulins
    - C-Reactive Protein
  - [B] Evaluation of Local Immune Response (GALT)
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    - Gut Microflora Diversity
    - Effect of stress on gut microflora

- **Other Biological Measures**
  - [A] Body Weights
  - [B] Blood Profile
Fecal Quality Was Not Effected By Colostrum

Fecal Score

Control
Colostrum

June  July  Aug  Sep  Oct  Nov  Dec  Jan  Feb  March  April  May

NSD
Stress Depresses Immune System: What Is Happening in the Gut?

**LARGE INTESTINE**

**Bifidobacteria**
- Positive Effects
  - Energy for gut cells
  - Help prevent diarrhea
- pH (more acidic)

**Clostridium perfringens**
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**Helps Mineral Absorption**

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Exercise Model to Evaluate Gut Microflora Stability

- Regular Exercise
- 2 day break
- Exercise: 10 mile run
- Microbial profiling of gut microflora
Whey Proteins Minimized Stress-related Shifts in Gut Microflora

Before & after stress patterns are different

Before & after stress patterns are similar

control

treatment
Dogs Fed Colostrum Had More Stable Microbial Populations

P<0.05
Colostrum Enhances Gut Health

- Colostrum increased gut microflora diversity. A greater level of species diversity reduces the opportunity for potential pathogens to colonize the gut and protect from gastrointestinal bacterial pathogens [Carole J. K et al, Infection and Immunity, 2005, 73(10), 6952] Dogs

- Dogs fed Colostrum had more stable microbial populations following stress. Stable gut microflora will reduce loose stools and GI upsets
Immune & Gut Health Measurement

- **Immune Analysis**
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- **Gut Health Measurements**
  - [A] Fecal Quality
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    - Gut Microflora Diversity
    - Effect of stress on gut microflora

- **Other Biological Measures**
  - [A] Body Weights
  - [B] Blood Profile
Body Weight Was Not Affected By Colostrum

- Control
- Colostrum

NSD
Summary of Key Findings

Diets containing colostrum

- Enhance systemic immune status [protect from infections, help with immunity gap]
- Enhance local immune response in GALT [protect from GI infections, help with immunity gap]
- Do not cause overt immune activation
- Increase gut microflora diversity [protect from GI infections, help with immunity gap]
- Increase gut microflora stability under stress [help with stress associated with growing up]
- Do not effect body weight, fecal quality & blood profiles
Frequently Asked Questions [FAQ]

- How do colostrum antibodies stimulate immune system of dogs older dogs?
- Why was the study done with adult dogs?
- Do findings from a study with dogs age 2-6 years apply to puppies?
- Do heat labile bioactive molecules survive extrusion?
- Do bioactive molecules survive gut environment & interact with the large intestine to induce benefit?
- Does antibodies in diet interfere with routine vaccination?
- How is colostrum manufactured? Is it safe?
FAQ 1

• How do colostrum antibodies stimulate immune system of dogs older dogs?

Antibody Structure-Schematic

ANTIGEN BINDING PART

CELL BINDING PART

The B cell receptor complex (BCR)
(adapted from Janeway 2001)
Ig Stimulates Gut Immune Cells

- Receptors Cross linking
- Activation
- Activated IgA Producing Cell
- Increased cytokine secretion
- Increased IgA secretion
FAQ 2

• Why was the study carried out in adult dogs?
  – Along with immune benefits we wanted to study gut health benefits of colostrum
  – ‘Gut health’ is evaluated by examining the effect of stress
  – We use a ‘exercise stress’ model that can be only carried out with adult dogs
FAQ 3

• Do findings in a study with dogs age 2-6 years apply to puppies?
  – Puppy’s immune system takes several weeks to months to fully develop
  – During this period the puppy’s immune system is being ‘educated’ or ‘trained’
  – ‘Education’ is achieved by exposure to various immune stimuli primarily in the gut [J J Cebra ‘Amer. J of Clin. Nutr., 69 [5], 1046, 1999 ]
  – Optistart with colostrum will help in the ‘education’ process as well support the developing immune system
  – As puppy’s immune system matures, the immune benefits seen in the studies will help them respond to vaccines better & prime their immune system to better fight infections
FAQ 4

- Do heat labile bioactive molecules survive extrusion?
  - Colostrum is added to the coating after kibble is heat extruded, so is never exposed to high temperature
FAQ 5

• Do bioactive molecules survive gut environment & react the large intestine to induce benefit?
  – Igs are partly resistant to degradation in the intestinal lumen, and a majority reach large intestine intact \[Roos N. et al J Nutr '95(125) 238\]
  – Bioactives like lactoferrin, IGFs etc are acid stable
  – When colostrum is delivered with diet like Pro Plan Puppy Optistart there is ample food matrix available for degradation by the stomach enzymes and decreased pH. Igs and other bioactive molecules are small and therefore, survive the stomach before entering the small intestines
FAQ 6

• Does antibodies in diet interfere with routine vaccination?
  – Maternal antibodies from colostrum can inhibit the ability of the pup to generate antibody.

  – Bovine colostrum has antibodies to very different pathogens [*i.e.* cow pathogens]. **Therefore antibodies from the colostrum will not interfere with vaccination in the pup even when the product is fed to a pup beyond week 10-12 when vaccinations are administered.**

  – Colostrum in diet will prime your puppies immune system and help your puppy respond better to a challenge during this ‘immunity gap’.

  – Pro Plan Puppy Optistart does not replace vaccination & routine veterinary care. It will help your puppy respond better to vaccination provided by your veterinarian.
• How is colostrum manufactured? Is it safe?
  - Colostrum used in Optistart certified dairies.
  - Colostrum, is spray dried to ensure the bioavailability of the bioactive components and nutritional factors.
  - Each batch undergoes rigorous QC tests to confirm negative for residual antibiotics, pesticides and pathogenic bacteria.
  - Near infra-red (NIR) is used to assess protein, fat, lactose ash and moisture content. Radial immunodiffusion, ELISA & and HPLC are used to determine bioactive compound content of colostrum.
  - Colostrum from supplier is manufactured for use in human food products

Colostrum is used in Optistart is safe & even approved for human foods
The End