




Lactose and Casein Milk Intolerance or Allergy?

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Milk

- A staple food in our diet
- Milk sugar - lactose - a disaccharide - is a common cause of digestive symptoms
- Milk protein - casein - can also trigger digestive problems
- Young children can usually digest lactose with no problems
- Children have plenty of the lactase enzyme which breaks lactose down to simple sugars

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Dairy allergy

- This is different to lactose intolerance
- Dairy allergy is an immune intolerance to dairy proteins (casein, whey, lactalbumin)
- It involves reactions that affect the GI tract, skin, respiratory tract, multiple systems as in systemic anaphylaxis
- Reactions are mediated by IgE and can cause severe morbidity and death

Bahna SL. Cow's milk allergy versus cow's milk intolerance. Ann Allergy Asthma Immunology. 2002;89:56-60

- Dietary elimination gives a good prognosis

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Food Allergy/Intolerances

- Many factors can trigger food allergies, including increased absorption of poorly digested protein fragments that leak into the systemic circulation across the gut wall

Gardner ML. Intestinal assimilation of intact peptides and proteins from the diet - a neglected field? Biol Rev. 1984;59:289-331

- Dairy may have a "double impact" of lactose intolerance and allergenicity from the casein

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Coeliac disease

- Lactose intolerance has been observed as a secondary feature in coeliac disease, tropical sprue, acute intestinal infections, cystic fibrosis,

Berkow R, Fletcher AJ, Eds. The Merck Manual ed. 16 Rahway, J. Merck 1992:822-830

- alcoholism

Keshavarzian et al. Intestinal-transit and lactose intolerance in chronic alcoholics. Am J Clin Nutri 1986;44:70-76

- pelvic radiation therapy

Henriksson R et al. Effects of active addition of bacterial cultures in fermented milk to patients with chronic bowel discomfort following irradiation. Support Care Cancer 1995;3:81-83

- Crohn's disease

Von Tripitz et al. Lactose intolerance in active Crohn's disease: clinical value of duodenal lactase analysis. J Clin Gastroent 2002;34:49-53

- Treating the underlying condition resulted in restored lactase activity

Kanabar D. et al. Improvement of symptoms in infant colic following reduction of lactose load with lactase. J Hum Nutri Diet 2001;14:359-363

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Undiagnosed lactose intolerance



- Many people suffer from undiagnosed lactose intolerance
- Dairy foods are the exclusive dietary source of lactose
- They are used in the manufacture of many convenience foods

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Symptoms of lactose intolerance



- Diarrhoea
- Bloating
- Abdominal cramps
- Minor dyspepsia and nausea
- Flatulence
- Failure to thrive
- Irritable bowel syndrome

Rusynyk RA, Still CD. Lactose intolerance. J Am Osteopath Assoc. 2001;101:S10-12

- 146 children studied for IBS 24.3% were lactose intolerant; 5 years later 87.5% were still showing benefit from a lactose free diet

Gremsse DA et al. Irritable bowel syndrome and lactose maldigestion in recurrent abdominal pain in childhood. South Med J 1999;92:778-781

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Diarrhoea IBS



- Rana et al found that patients with diarrhoea-predominant IBS have a higher incidence of lactose intolerance (82%) than patients who have either spastic-type IBS or features of both types

Rana SV, et al. Lactose intolerance in different types of irritable bowel syndrome in north Indians. Trop Gastroenterol 2001;22:202-204

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Milk Sugar - Lactose



- Digested in the small intestine by the enzyme lactase
- If lactose is not digested and absorbed in the chyme, the sugars are broken down by bacteria when it reaches the colon
- Gas, bloating, abdominal cramps, and diarrhea ensue.
- Stools may be light coloured and frothy, or covered in mucous

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Loss of lactase



- The vast majority of adults lose their ability to make lactase enzyme as they grow into adulthood
- Some people find it difficult to tolerate a glass of milk

Hertzler SR, Huynh BCL, Savaiano DA. How much lactose is low lactose? J Am Dietetic Assoc 1996;96:243-46

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Lactase - Disaccharide



- Lactase enzymes from the pancreas break down milk sugar lactose in milk to glucose and galactose
- Glucose and galactose can then be absorbed into the blood stream
- Lactase enzymes begin to disappear after infants are weaned
- Many adults have very little lactase left
- This is why a glass of milk may cause them to have problems with indigestion and gas

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Pancreas insufficiency



An endocrine organ

1. Secretes hormones - insulin, glucagon
They regulate carbohydrate metabolism and maintain blood sugar balance

An exocrine organ

2. Secretes enzymes - trypsin, lipase, and amylase

They are necessary for the digestion of specific foods and are produced as the GI tract is stimulated by food

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Pancreatic enzymes



These are released in response to messenger hormones secreted from the stomach

1. Gastrin - from stomach
 2. Secretin, CCK - from small intestine
- Coeliac disease would stop production due to villus atrophy

Green PHR, Jones R. 2006. Celiac Disease. Harper Collins. p180

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Lack of Lactase



- This is not an abnormality or an illness
- Lack of lactase enzyme is a normal part of growing up
- 1965 Baltimore's John Hopkins University tested 60 patients
15% of white adults had digestive symptoms from cow's milk
70% of African-Americans had digestive symptoms from cow's milk

Cuatrecasas P, Lockwood DH, Caldwell JR. Lactase deficiency in the adult: a common occurrence. Lancet 1965;1:14-18

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Ethnic Group % lactose Intol



African blacks	97-100
Asians	90-100
Jewish descent	60-80
Mediterranean	60-80
Mexicans	70-80
Middle Europeans	10-20
North American blacks	70-75
North American Causasian	7-15
Northern Europeans	1-5

Clinical Nutrition IFM. p198

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Obvious sources



- All Cow's dairy products
- All cheeses
- Butter, some margarines
- Goats, sheep, buffalo, camel milks
- Half-half cream, single, double, clotted
- Ice-cream, sherbet, marscapone, crème fraiche
- Milk
- Yoghurts

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Hidden sources



- Artificial sweeteners
- Breading on fried food
- Bread, pizza, cake, biscuits, crackers, donuts
- Breakfast and cereals
- Buttered or creamed foods
- Cakes, biscuits, puddings, pancakes, waffles
- Candies, milk chocolate
- Processed meats
- Non-dairy creamers
- Prescription drugs containing lactose, thyroid medication, GnRH analogues, OCP, HRT
- Nutritional supplements, weight reduction products

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Prescription drugs containing Lactose

- Ativan
- Bumnex
- Coumadin
- Glucotrol
- Imodium
- Premarin
- Sudafed
- Synthroid
- Xanax
- Zoladex
- Always check your medication

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Food labels

- Whey
- Casein
- Caseinate
- Sodium caseinate
- Lactose

Clinical Nutrition: a functional approach 2nd ed., Institute for Functional Medicine. p198

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Lactose Challenge Tests

- Research at Maryland House of Correction tests were done on the inmates
- Lactose challenge tests showed that
- 10% of the white inmates developed symptoms
- 90% of the African-Americans developed symptoms

Bayless TM, Rosensweig NS. A racial difference in incidence of lactose deficiency: a survey of milk intolerance and lactase deficiency in healthy adult males. JAMA 1966;197:968-72

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Primary lactose intolerance

- A genetic lack of lactase
- Normally present at the brush border of the small intestine
- It is normal
- It occurs in 25% of the US population, more in certain ethnic groups
- Single nucleotide polymorphisms C/T-13910 and G/A-13910 contribute to the lactase non-persistence phenotype
- C/T-13910 is the original form

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Secondary lactose intolerance

- This can occur as a result of any disease that damages or destroys the brush border
- e.g. coeliac disease
- OR as a result of parasites (from dogs or cats) or after viral infections
- If mucosal integrity is restored, lactase activity should normalise
- One study on patients with coeliac disease showed that all had recovered after 8 weeks of dairy exclusion

Murphy MS, Sood M, Johnson T. "Use of the lactose H2 breath test to monitor mucosal healing in coeliac disease". Acta Paediatr 2002;91:141-144.

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Alactasia congenital lactase deficiency

- 15% of the Northern Europeans and 80% of Africans and Latin origin peoples, 100% of American Indians and Asians do not maintain the brush border enzyme lactase after the first 5 years of life
- Without lactase, lactose can be considered a toxin because it cannot be digested by humans. It causes fermentation, and produces additional toxins, increasing the burden in the liver detoxification pathways, which may be compromised if the burden continues for a prolonged period of time

Swagerty Jr DL, Walling AD, Klein RM. 2002. Lactose intolerance. Am Family Physician 65, 1845-1850, 1855-1856

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Lactose Tolerance Tests



- Measures your ability to break down lactose
- A. lactose tolerance blood test
- B. hydrogen breath test

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Lactose tolerance blood test



- Avoid strenuous exercise before the test and fast for 8 hours
- Blood is drawn through a needle, you may ask for use of a butterfly needle which is very fine if you wish
- The blood test is considered normal if your glucose level rises more than 30mg/dL within 2 hours of drinking the lactose solution
- 20-30mg/dL is inconclusive
- The blood test is considered abnormal if your glucose level rises less than 20mg/dL within 2 hours of drinking the lactose solution

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Hydrogen breath test for lactose tolerance



Do not eat 8 hours before the test
Avoid fibre for 24 hours before the test, and avoid tobacco smoke
Considered normal if the increase in hydrogen is less than 12 parts per million over your fasting (pre-test) levels
Over 12 ppm the test is considered positive - you have trouble breaking down lactose
The false negative rate is 10% due to use of drugs containing lactose, antibiotics etc..

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Elimination Diet



- A month's exclusion diet - all sources of lactose are to be avoided
- Obvious and hidden sources of dairy food must be sought out
- Some people are also intolerant to fructose, sucrose, and maltose

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Casein Milk Protein



- Casein is the protein in milk
- It can be used hardened to make buttons and shoe heels!
- When the milk is cooked ie. pasteurised the milk protein is cooked
- Some people find it easier to digest un-pasteurised milk and specialist dairies produce this and sell it on-line

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Casomorphins



- Bovine milk from cattle is
- 87% water
- 13% solids
- 'fats, proteins, lactose, minerals, vitamins'
- There are differences between different cows and different breeds
- Holstein/Friesian cows produce milk that is 12% solids
- Jersey cows produce milk that is 13% solids

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Milk Protein



- Casein
- Whey
- “Little Miss Muffet sat on her tuffett eating her curds and whey”
- Whey proteins stay in solution as liquid
- Curds contain the casein protein, they precipitate out as solids
- Casein proteins form the ‘crust’ on rice puddings and custard when cooked

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Casein Proteins



- Alpha-casein
- Beta-casein
- Kappa-casein
- 1 litre Milk contains 9-12 grams (2 teaspoons) depending on the breed of cow
- All proteins are made up from amino acids containing one atom of nitrogen

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Amino Acids



- 20 amino acids are found in human tissues
- 8 are classed as essential
- 10 need to be ingested by infants and the elderly
- 12 can be made internally from the other amino acids which are unbuttoned and rejoined in our cells like coloured popper beads

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Digestive enzymes



- Digestive enzymes from the mouth, stomach, pancreas and small intestines
- They break down proteins in our food into single amino acids in our gut
- Before that stage we get peptide chains of amino acids, like 5 popper bead chains
- Some of these peptide chains may enter the blood stream and are absorbed as a short chain rather than as a single amino acid
- Peptide chains cause the problems once in the blood stream

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Hydrolysis



- Hydro - water
- Lysis - breaking down
- Water molecules are broken down when reacting with proteins and peptides
- Some amino acids just get into the bloodstream singly
- Some amino acids stay in peptide chains and are absorbed in this form
- Then our immune system reacts

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Beta-casein protein



- Beta casein is a folded chain of 209 amino acids
- There are 8 variant forms of beta casein
- A - B - C - D - E - F
- A IN 3 TYPES - A1 - A2 - A3
- The most common forms are
- A1 beta-casein
- A2 beta-casein (shown to be the original one)

Ng-Kwai-Hang KF, Grosclaude F. 2002 Genetic polymorphism of milk proteins. In: PP Fox and Sweeney PLH, (eds). Advanced Dairy Chemistry, 737-814, Kluwer Academic/Plenum Publishers, New York

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A1 and A2 beta-casein



- There is a difference between A1 and A2 beta-casein
- The amino acid at position 67/209 is different
- In A1 beta casein 67 amino acid is
- HISTIDINE
- In A2 beta casein 67 amino acid is
- PROLINE

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ONE TINY AMINO ACID DIFFERENCE YET MAJOR DIFFERENT EFFECTS WHEN DIGESTED



WHY?

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A2 BETA CASEIN



- Proline binds closely to 66 position amino acid - isoleucine
- Position 68 amino acid is also tightly bound to proline
- Digestive enzyme cannot break down this bond

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A1 BETA CASEIN



- Digestion of A1 beta casein can produce a string of amino acids called beta-casomorphin-7 (BCM7)
- The histidine link with position 66 isoleucine and 68 amino acids is easily broken down by digestive enzymes
- The evidence is that this does not happen with A2 beta casein

Hartwig et al (1997), Influence of genetic polymorphisms in bovine milk on the occurrence of bioactive peptides. In: Milk Protein Polymorphisms, International Dairy Federation Special Publication 9702, pp459-460, Brussels, Belgium.
Brantl V, Teschemacher H (1979) A material with opiod activity in bovine milk and milk products. Naunyn Schmiedeberg's Archives of Pharmacology. 306,(3):301-304
Brantl V, Teschemacher H. 1994 Beta casomorphins and related peptides. Weinheim VCH

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Casomorphins



- Are derived from caseins
- They have opiod (narcotic-like) properties
- Caso - casein
- Morphins - morphines
- Morpheus was the Greek God of sleep
- Casein narcotic properties were first reported in 1979 by German scientists

Henschen et al (1979) A, et al Novel opiod peptides derived from casein (beta-casomorphins). II Structure of active components from bovine casein peptone. Hoppe Seylers Z Physiological Chemistry 360(9):1217-1224. (the 1st time BCM7 and its opiod characteristics were identified).

Brantl V, Teschemacher H (1979) A material with opiod activity in bovine milk and milk products. Naunyn Schmiedeberg's Archives of Pharmacology. 306,(3):301-304
Brantl V, Teschemacher H. 1994 Beta casomorphins and related peptides. Weinheim VCH

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BCM7



- Full structure of BCM7
- Tyrosine-proline-phenylalanine-proline-glycine-proline-isoleucine
- Tyr-Pro-Phe-Pro-Gly-Pro-Ile
- The bonds linking the prolines are string-like and gives BCM7 great resistance to breakdown
- Having 3 proline molecules close together is very unusual, very surprising

Woodford K. Devil in the Milk.2007.Craig Potton Publishing. p38

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BCM7



- Japanese and German scientists have reported that they could not get any release of BCM7 from A2 beta casein

Hartwig et al (1997), Influence of genetic polymorphisms in bovine milk on the occurrence of bioactive peptides. In: Milk proteins Polymorphisms, International Dairy Federation Special Publication 9702, pp459-460, Brussels, Belgium.

Jinsmaa Y, Yoshikawa M, 1999 Enzymatic release of neocasomorphin and beta-casomorphin from bovine beta-casein. Peptides 20,(8):957-962

- New Zealand Dairy Research Institute scientists reported in 2001 in a patent relating to A1 milk and autism and related mental diseases that they had investigated whether BCM7 could be released from A2 milk

New Zealand Dairy Research Institute, 2001. Milk containing beta-casein with proline at position 67 does not aggravate neurological disorders, International Patent Number WO 02/19832 A1. (PCT/NZ01/00186).

This patent application was subsequently abandoned.

Beta casein A3 B C D E F



- B - C - F all have Histidine at 67
- Therefore they behave like A1 milk
- Histidine is pro-inflammatory
- A3 - D - E all have Proline at 67 and behave like A2 milk
- Proline is anti-inflammatory

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Human Milk



- Higher in lactose than cows milk
- Similar in fats
- Lower in protein
- Lower in minerals - calcium, sodium, potassium
- Human milk is high in lactose, it is low in minerals. This makes it iso-osmotic with blood in the mammary glands

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Milk Allergies



- These relate to the proteins in milk
- Protein level in human milk is about 1.6% in the first few days after birth, then it drops to 0.9%
- Protein level in cow milk is 3%-4%, depending on the breed of cow
- Human milk major proteins are whey
- Cow milk major proteins are casein

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Human Milk



- Most proteins in human milk are whey protein, they are not the same whey proteins as in cow's milk
- Human milk has no beta-lactoglobulin which is the major whey protein in bovine milk
- Bovine milk has very little lactoferrin, a major whey protein in humans
- Lactoferrin in human breast milk is a protective factor because it has anti-bacterial properties

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Human V Cow's beta casein



- Human beta protein is a shorter protein chain
- All human beta casein is A2 type, the adjacent amino acid
- (58 in humans, 67 in cows) is Proline
- BCM7 in human milk is
- Tyr-Pro-Phe-Val-Glu-Pro-Lle
- 2 amino acids are different to the cow A1 type
- Cow beta casein is a longer protein chain
- Tyr-Pro-Phe-Pro-Gly-Pro-Ile (3 proline)
- The proline and a glycine have been exchanged for a valine and glutamine

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Human V Cow's beta casein



- BCM7 from human milk is not the same as BCM7 from cow's milk
- The opioid properties of BCM7 from human milk are about 10 times weaker than the bovine form
- Human milk releases much less BCM7 and is more like A2 milk, it is a very different BCM7
- The relative opioid effect, human milk has less than one-thousandth the potential potency of A1 cow's milk

Woodford K. Devil in the Milk 2007. Craig Potton Publishing. p40

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Animal dairy beta casein



- Goats' milk contains A2 beta casein and no A1 beta casein
- Sheep milk contains A2 beta casein
- Yak milk contains only A2 beta casein
- Bos indicus cattle in Asia contain only A2 beta casein
- A2 beta casein was the original beta casein
- A1 beta casein is relatively new
- A gene mutation may have triggered it on the 6th chromosome between 5000 to 10,000 years ago after the last ice age, Younger Dryas

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Casein allergy



- With an IgE allergy to casein, whey or lactalbumin all forms of animal dairy foods must be avoided

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Calcium rich foods



- Kelp seaweed 1093 mg per 100grams
- Carob flour 352
- Nuts and seeds, almonds 234, Brazil nuts 186
- Parsley 203
- Corn tortilla with lime 200
- Watercress 151
- Tofu 128
- Dried figs 126
- Ripe olives 106
- Green leafy vegetables, broccoli 103
- Oats, wholegrain cereals 119
- Rhubarb 118
- Salmon 490 /sardines 10000- tinned soft bones
- Legume/pulse vegetables 50

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What can I eat?



- Oat milk, almond milk, hazelnut milk, rice milk, soya milk
- Soft soya cheeses
- Hummous, Guacamole, vegetable pates, poor man's caviar, taramasalata
- Dairy-free foods from FreeFrom, Live-Well ranges
- Plamil dairy-free chocolate

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Menu



- **Breakfast** - Mushroom omelete
- Herb tea - mint, fennel or lemon and ginger
- **Lunch** - Salmon salad, potato salad, lettuce, tomato, spring onion, avocado, Lemon sorbet
- **Dinner** - Chicken curry, broccoli, rice,
- Strawberries and Soya cream
- **Snacks** - nuts and seeds, corn taco and hummus, fresh fruits, plain crisps, popadoms,

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Dairy Pollutants



- Persistent organic pollutants
- Mould aflatoxins from contaminated feeds
Fink-Gremmels J, 2008 Mycotoxins in cattle-feeds and carry-over to dairy milk: A review. Food Additive and Contaminants 25;2:172-180
- Toxins are stored in fat, so high fat dairy products are likely to contain some dioxin, PCB, bisphenol A and phthalates
- Milk 254gms per day = 0.04pg/gm
Schechter A, Ryan JJ, Masuda Y, et al. "Chlorinated and brominated dioxins and dibenzofurans in human tissue following exposure." Environmental Health Perspectives 102, Suppl. 1994. 1:135-47.
- Some cows in the USA have growth hormone
- Anti-biotics are used to fatten cattle so residues may be present in the milk and cheeses

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Gastro-centric support



- Probiotics have a definite role to play in the control of TH17 cell production as, via cytokine IL-27, they produce a key inflammatory cytokine IL-10, required for immunological tolerance through the expansion of Treg cells, which in turn inhibit or control IL-17 production

Awasthi et al 2007 A dominant function for interleukin 27 in generating interleukin 10-producing anti-inflammatory T cells. Nature Immunology 8, 1380-1389

Stumhofer et al 2007 Interleukins 27 and 6 induce SATAT3-mediated T cell production of interleukin 10. Nature Immunology 8, 1363-1371

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Dysregulation of the immune system



- Recognising signals from the trillions of human microflora in order to shape and maintain or destroy human immune tolerance

Gill et al 2006. Metagenomic analysis of the human distal gut microbiome. Science 312, 5778, 1355-1359.

Pennisi 2008. Microbiology. Bacteria are picky about their homes on human skin. Science 320, 5879, 1001

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Saccharomyces boulardii



- Assists improved growth and proliferation of mucosal cells
- Increases SIgA production
- Reduces gut permeability
- Increase brush border enzyme activity
- Neutralises pathogenic toxins
- Suppresses the pro-inflammatory IL-8 Chemokine
- PPARy inducer
- Increases spermines to maintain mucosal integrity
- Inhibits excess zonulin - reducing gut permeability

Lee et al 2005 Saccharomyces boulardii activates expression of peroxisome proliferated receptor-gamma in HT-29 cells. Koren J Gastroenterology 45, 328-334

McFarland et al 1994. A randomised placebo-controlled trial of saccharomyces boulardii in combination with standard antibiotics for Clostridium difficile disease. J Am Med Assoc. 271:1913-1918.

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Probiotics



- Probiotics have many effects on the gastrointestinal immune system:
- Production of antioxidants
- Increased production of SIgA
- Production of antimicrobial bacteriocins etc.
- Transcription of NF-kB
- Induction of pro and anti-inflammatory cytokines
- Bacterial DNA-induced TLR9 signalling
- Anti-inflammatory effect in colitis
- Elevation of serum IL-10 levels

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Probiotics



- Induction of dendritic cell (DC) maturation
- Enhancement of serum antibody response to orally and systemically administered antigens
- Enhanced immuno-reactivity of spleen cells and phagocytes
- Activation of the gene for human beta defensin 2 in intestinal mucosa
- Induction of oral tolerance to beta-lactoglobulin
- Production of beta-galactosidase - improvement of lactose intolerance
- Induction of PPARγ to reduce local inflammation in GIT

Ljungh A, Wadstrom T, 2006 Lactic acid bacteria as probiotics, Current Issues in Intestinal Microbiology 7,73-90
Wallace et al 2009. Clinical use of probiotics in the pediatric population. Nutrition in Clinical Practice. 24, 1,50-59.

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Glutamine, slippery elm, epithelial growth factor



- Reduces inflammation, repairs the epithelial barrier in the gastro-intestinal tract
- Glutamine is an important amino-acid for cellular health

Langmead L, et al, Antioxidant effects of herbal therapies used by patients with inflammatory bowel disease: an invitro study. Alimentary Pharmacology and Therapeutics. 2002;16:2:197-205

Murmin M, et al, Effects of glutamine isomers on human (Caco-2) intestinal epithelial proliferation, strain-responsiveness, and differentiation. J Gastrointestinal Surgery. 2000;4, 4:435-442

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Why should I bother?



- I can take anti-acids and lactulose and lactase enzyme
- Does the immune system suffer long term?
- Does my pancreas react?
- Does it affect my health in old age?
- Does it mean I am more prone to other infections if my immune system is constantly on red alert?
- Does it mean that I won't live a long healthy life?

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End stage allergy



- If not addressed in childhood, if you ignore the warning signs, the problems you experience later on can be quite serious
- Irritable bowel syndrome
- Crohn's disease
- Ulcerative colitis
- Bladder problems
- High blood pressure
- Irregular heart beat
- Arteriosclerosis
- Arthritis

Your bowels talk to you, but few people pay attention! LISTEN NOW

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Wrong Diagnosis?



- Is something else medically wrong?
- Are other foods causing a problem?
- Have you been checked for coeliac disease, Crohns disease ulcerative colitis, endometriosis?
- If dietary compliance is correct and the diagnosis is correct then more checks are needed for associated conditions

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