

Systemic Inflammation, Food Intolerance, and Autoimmunity

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Disk 1 Introduction

Introduction

Outline

Cases

Treatment vs Cure

Inflammation

Diseases

C-reactive protein

Outline of the seminar: Day 1

- Cases of severe inflammatory conditions cured with natural methods.
- Pathology and processes of inflammation
- Vitamin D, barrier function, and inflammation
- Leaky gut syndrome and systemic inflammation
- Drugs and the leaky gut syndrome
- Other causes of chronic inflammation
- Fasting and inflammation
- A materia medica of anti-inflammatory herbs

Cases

Case 1 and 2

- A farmer in his 60s with diabetes and congestive heart failure, given one year to live, was treated by a nature cure practitioner. Twenty years later, in his 80s while still running the farm, he wrote a testimonial to his cure.
- A woman with congestive heart failure in her 50s was scheduled for a heart-lung transplant. After several months of treatment, she was removed from the transplant list.
- What was the common factor in their treatment?

Case 3 and 4

- A woman in her 40s with systemic lupus had been on medications for 8 years. She developed a cancer, and was told that the drugs were causing the cancer, but that she would die of lupus if she stopped taking them. Fifteen years later she remains medication-free, and one HMO doctor told her that her previous conditions had been misdiagnoses.
- A woman in her twenties had her first onset of lupus symptoms, which recurred in a cyclic pattern 4x per year. After treatment no further attacks occurred.
- What was their common treatment?

Cases 5 and 6

- A woman in her twenties had acute glomerulonephritis, and presented with pitting edema all the way up her leg, and severe abdominal edema. Twelve years later she is usually symptom-free, with occasional mild recurrence.
- A woman in her early 50s had ITP, and presented with bruising around mosquito bites, and blood dripping when bitten by black flies. Ten years later she is usually symptom-free, with occasional mild recurrence.
- What triggers the occasional recurrence in both these patients?

Case 7

- A woman with severe rheumatoid arthritis could not sit comfortably in a chair. She also had hypertension, and was an insulin-dependent Type I diabetic taking 30-36 units of insulin per day with frequent episodes of hypoglycemia.
- Six years later she is free of arthritis and hypertension, and manages her diabetes with 18-24 units of insulin, with few episodes of hypoglycemia.
- What was the treatment?

Case 8

- A woman with disabling migraines 1-2 times per week because migraine-free with a simple treatment protocol.
- Four weeks later she had a relapse
- What triggered the relapse?

Case 9

- A woman with mild eczema underwent a protocol which cleared it completely.
- 3 years later she had a severe relapse with eczema on about 25% of her body with large patches of it severe and scabbed.
- What triggered the relapse?

Case 10

- A woman in her twenties was on disability with severe fibromyalgia, and also on mental disability
- After six months of treatment she was off disability for both conditions and attending school
- Six years later she has completed undergraduate pre-med with high grades and is applying to medical school.
- What was the treatment?

Cases 11 and 12

- A man in his 40s with severe ulcerative colitis was scheduled to have his colon removed
- A woman in her teens with ulcerative colitis and polyps was told she would need her colon removed in 12-18 months.
- Both patients became free of symptoms of colitis after 3 months, and both avoided colon removal. Pt 12 polyps no longer present.
- What was the treatment?

Case 13

- A woman in her thirties had chronic swollen lymph nodes throughout her body.
- She was certain that she had ruled out a possible cause of the swollen glands
- After treatment, that cause was found in fact to be the cause, and 18 months later she remains free of lymphadenopathy.
- What was the cause?

Case 14

- Six patients met the criteria for disability because of panic disorder or severe anxiety.
- All six were cured with a similar treatment.
- What was the treatment?

Case 15

- A young male college student was diagnosed with rapid-cycling bipolar disorder, and trouble concentrating on his homework, and was unable to meditate. He was also morbidly underweight.
- 3 months later he was free of mood swings, getting good grades, sitting meditation, and had gained 10 pounds of healthy weight
- 12 month later he was still calm and focused, had completed a course of occupational training, and had gained 25 pounds entirely as lean muscle mass.
- What was the treatment?

Case 16

- A woman in her forties began experiencing neurological symptoms, and was diagnosed with multiple sclerosis
- 2 years, later many symptoms have regressed, and she has no progressive symptoms at all, and is engaged in a busy professional life.
- What was the treatment?

Case 17

- A woman who had previously survived two bouts of cancer with chemotherapy could not sleep for more than 4 hours a night for the last 2 years. She had a constantly cycling migraine, she was scheduled to have all her teeth removed due to severe gum disease. She was a Type II diabetic progressed to insulin dependence. In 21 days she was migraine-free, sleeping through the night, and her doctor took her off her insulin.
- What was the treatment?

Case 18

- A woman suffered potential constant and potentially fatal intestinal inflammation due to a lactase-isomaltase deficiency, a genetic condition. The enzyme is necessary to break down starch, and its lack leads to intestinal inflammation. Patients need to follow a difficult and strict starch and sugar free diet. The chronic inflammation frequently leads to the necessity to remove parts of the intestine.
- The woman could not strictly follow her diet and maintain her nutritional status, and occasionally had severe enteric inflammation.
- She was able to manage this completely with an herbal formula, delivered in a medium. What herbs and medium?

Inflammation

Stages of inflammation

- Injury or infection
- Chemical trigger
- Dilation of blood vessels
- Leakage of plasma
- Infiltration with white blood cells and *fibrocytes*

Chesney J, Metz C, Stavitsky AB, Bacher M, Bucala R. Regulated production of type I collagen and inflammatory cytokines by peripheral blood fibrocytes. J Immunol. 1998 Jan 1;160(1):419-25.

- Tissue changes, healing, scarring

- Inflammation is not pathology
- Inflammation = Immunity
- Pathology: may be chronic or excessive
- Pathology #1: Fuel on the fire, chronic infection, antigen exposure, or injury
- Pathology #2: Inadequate endogenous quenching of inflammation.

Diseases of chronic inflammation

- **Atherosclerosis.** Systemic inflammation is a factor in the development of arterial plaques, and also in the instability of those plaques that lead to thrombotic/ischemic events
- **Neoplasm and cancer.** Chronic systemic inflammation is a factor in cell changes that lead to cancer.
- **Autoimmunity.** Systemic inflammation is involved in autoimmunity on the spectrum from low grade generic processes to full-scale diagnosable disease
- **Tissue damage/aging.** Chronic inflammation leads to tissue changes, scarring, aging. “itis” proceeds to “osis”
- **Endocrine system exhaustion.** Progression loss of adrenal capacity to secrete anti-inflammatory hormones.
- **Alzheimer’s disease/dementia.**

Process

CRP as inflammatory accelerant

- C-reactive protein is best simple test for systemic inflammation. (hsCRP)
- Was originally viewed simply as a marker for systemic inflammation rather
- Is now understood to stimulate preexisting inflammation throughout the body when levels are elevated.
- Chronic local exposure to infectious agents or food antigens can result in elevated CRP which in turn promotes inflammation in where it pre-exists.

Disk 2 Nutrition I

Nutrients

Trace elements

Barrier function

Plants with trace elements

Oils

Broad spectrum micronutrient malnutrition

- Vitamins, minerals and trace elements.
- Nutrient dense herbal decoctions or powders may supply critical minerals and trace elements declining in the food supply. Roles in inflammatory processes and immune barrier integrity.
- Silicon and copper have critical role in connective tissue.
- Herbal “green drink” powders.

Copper in selected foods, 1948 to 1997

Snap Beans	1948 (high)	1948 (low)	1992 (average)
• copper (mg/ 100 g)	6.9	0.3	0.069
Cabbage			
• copper	4.8	0.04	0.023
Lettuce			
• copper	6	0.3	0.028
Tomatoes			
• copper	5.3	0	0.074
Spinach			
• copper	3.2	0.5	0.13

Plants containing silicic acid

Highly water soluble, highly bioavailable source of silicon

- *Equisetum arvense* L. Plant 80,000 ppm
- *Symphytum officinale* L. Leaf 40,000 ppm
- *Borago officinalis* L. Plant 22,000 ppm

Calcium and magnesium Mg/Oz

	Calc	Mag
• Kelp	1013	289
• Nettle Leaf	966	286
• Horsetail	630	145
• Comfrey leaf	600	23
• Peppermint	540	220
• Oatstraw	476	400
• Red Clover	436	116
• Red Rasp.	403	106
• Chickweed	403	176
• Alfalfa	299	76
• Licorice	292	321
• Marshmallow	272	172

Trace elements Mg/Oz

	Iron	Chrom	Mang	Sel	Sil
● Red Rasp.	3.3	0.04	4.8	0.08	0.04
● Catnip	4.6	0.09	1.25	0.41	0.00
● Nettle Leaf	1.4	0.13	0.26	0.07	0.34
● Kelp	0.5	0.02	0.25	0.06	0.03
● Horsetail	4.1	0.01	0.23	0.04	1.29
● Red Clover	0.0	0.11	0.20	0.03	0.04
● Burdock	4.9	0.01	0.20	0.05	0.75
● Comfrey leaf	0.4	0.06	0.19	0.04	0.30
● Chickweed	8.4	0.04	0.18	0.14	0.19
● Licorice	2.9	0.06	0.16	0.00	0.53
● Skullcap	0.8	0.02	0.16	0.03	0.16
● Marshmallow	3.8	0.05	0.15	0.11	0.10
● Alfalfa	0.87	0.03	0.08	0.00	0.00
● Peppermint	2.0	0.00	0.02	0.04	0.00
● Oatstraw	0.4	0.13	0.02	0.04	0.61

Mineral content of a plant is entirely dependent on the soil from which it came

There is no one set amount of a mineral in any plant

Process: good oils/bad oils

- Pro-oxidative refined oils. Commercial food oils usually undergo a final step of “deodorization” through steam distillation above 400 degrees F under vacuum.
- Excessive omega-6 oils relative to omega-3 promote inflammatory prostaglandins.
- Deficiency of anti-inflammatory omega-3 oils.
- Neutral oils: Olive, butter, ghee, sesame as tahini, coconut

“... A number of randomised controlled trials of marine n-3 PUFAs have been performed in patients with RA. A systematic review included 23 studies. Evidence is seen for a fairly consistent, but modest, benefit of marine n-3 PUFAs on joint swelling and pain, duration of morning stiffness, global assessments of pain and disease activity, and use of non-steroidal anti-inflammatory drugs.”

Miles EA, Calder PC. Influence of marine n-3 polyunsaturated fatty acids on immune function and a systematic review of their effects on clinical outcomes in rheumatoid arthritis. *Br J Nutr.* 2012 Jun;107 Suppl 2:S171-84.

The Oil Change

- The “black bag” treatment. Take a black garbage bag, go through the entire kitchen and pantry, and remove all the inflammatory oils and the foods containing them.
- Consume neutral oils ad-libitum
- Take 1-3 grams equivalent of combined EPA and DHA per day from oil, seafood, or grass fed animals.

Disk 3 Pathophysiology I

Vitamin D

Vitamin D protocol

Vitamin D toxicity

Leaky Gut syndrome

Gut associated immunity

Microbiome

Probiotics

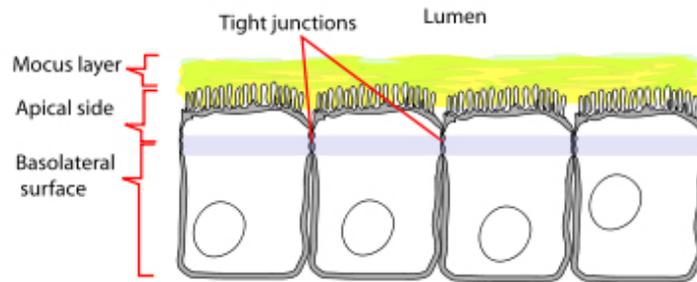
Teas in chronic

Vitamin D

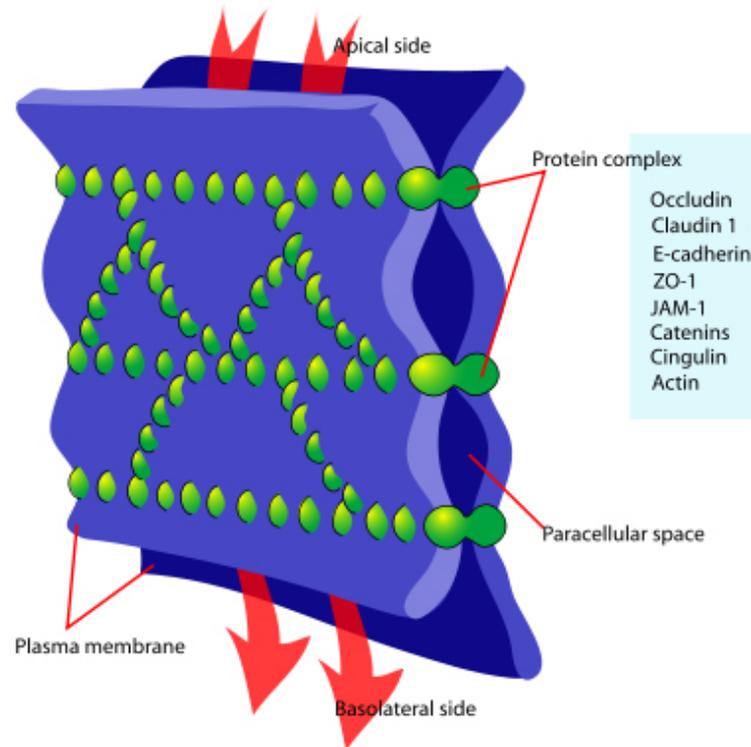
- Participates in junction dynamics
- Promotes local immunity
- Puts a brake on systemic inflammation

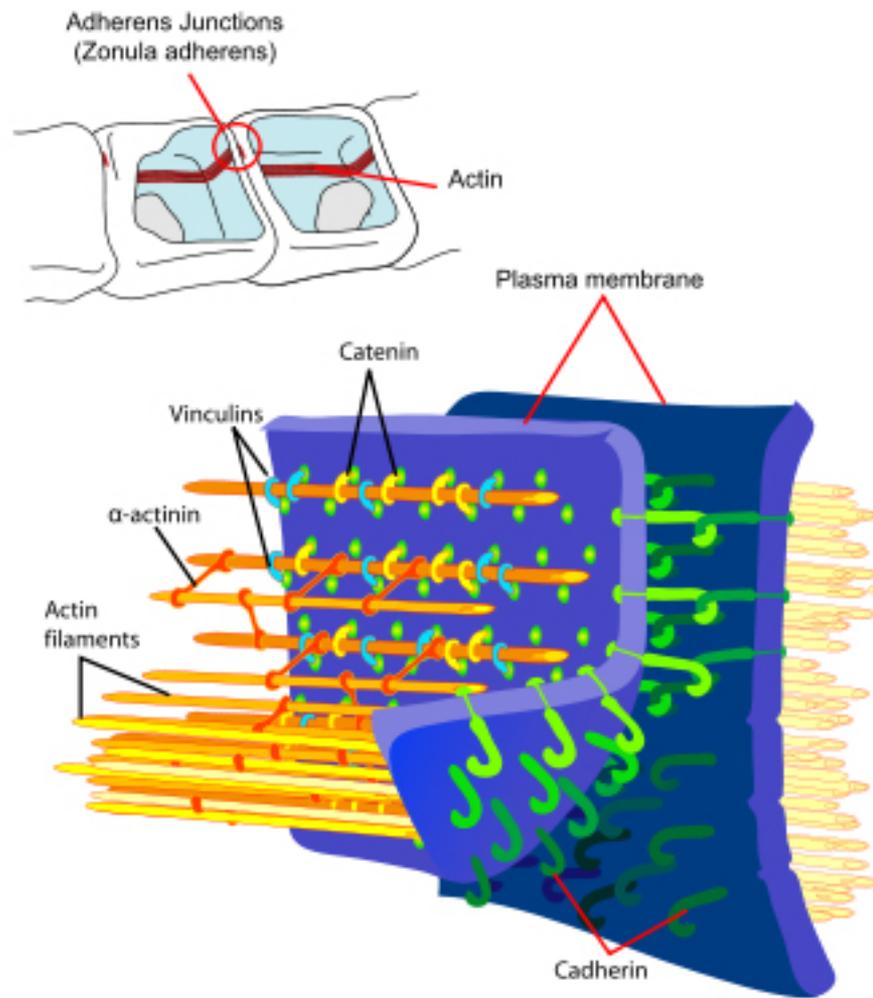
Vitamin D and barrier function

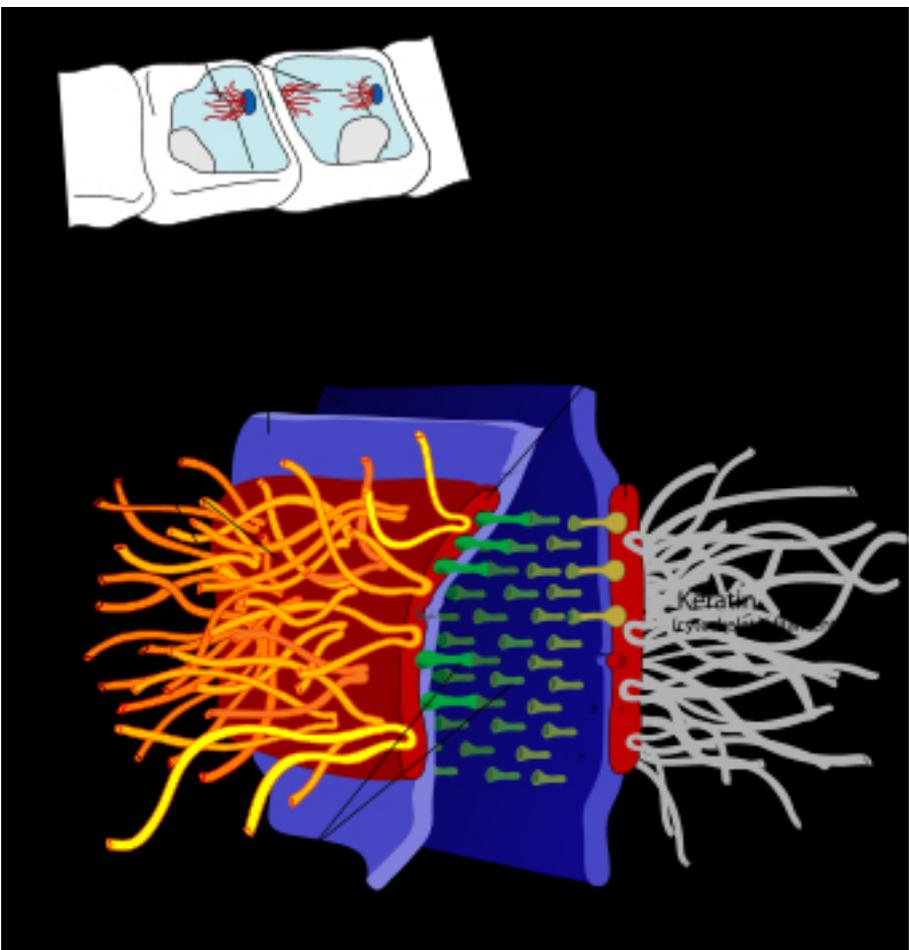
- Protein and peptides of the epithelial cellular junctions are Vitamin D dependent.
- 25(OH)D₃ enters cell
- It is transformed to 1,2 (di-OH)D₃
- The molecule binds to the RXR receptor on the DNA
- The cell is induced to produce the binding proteins or the junctions.

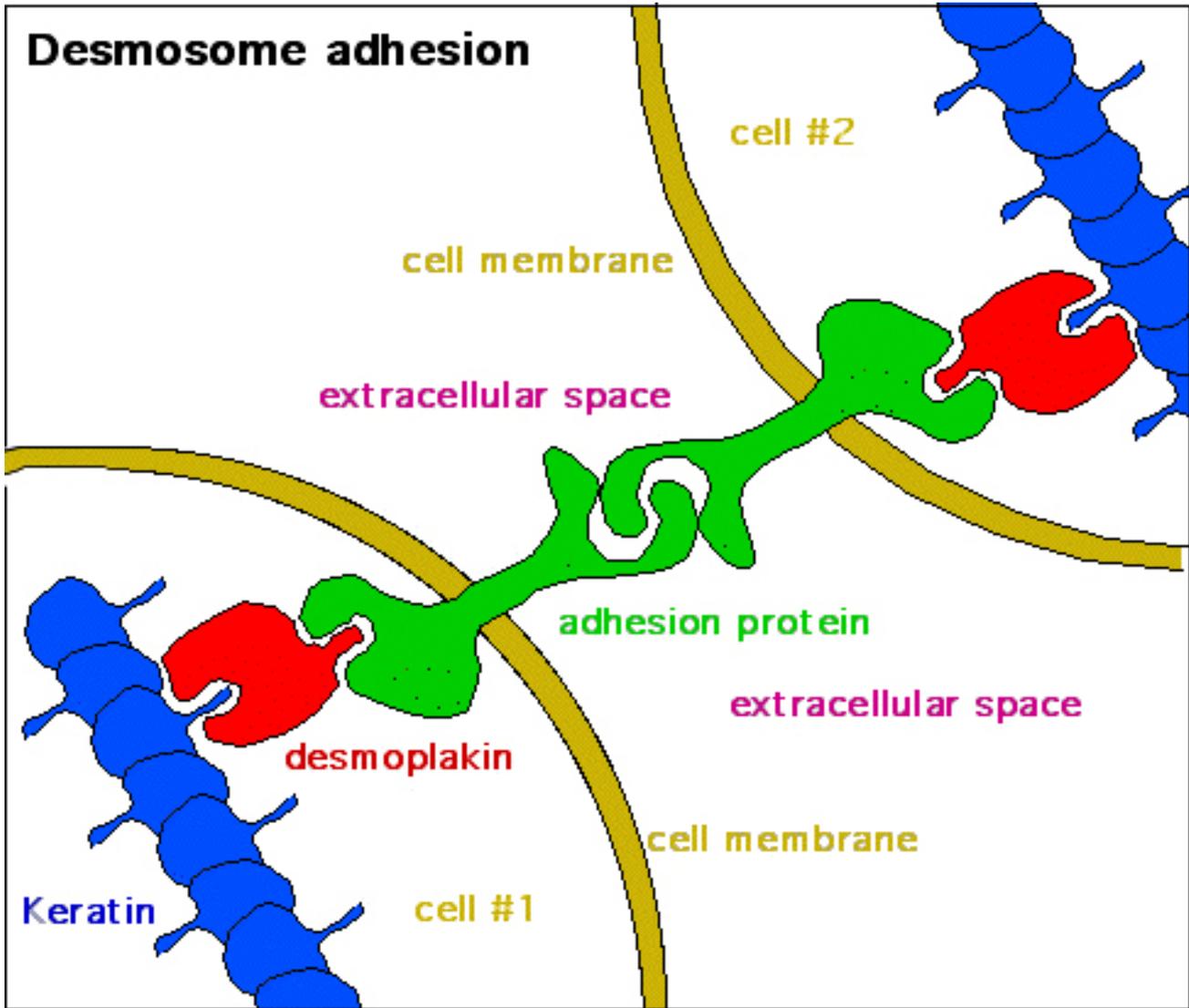


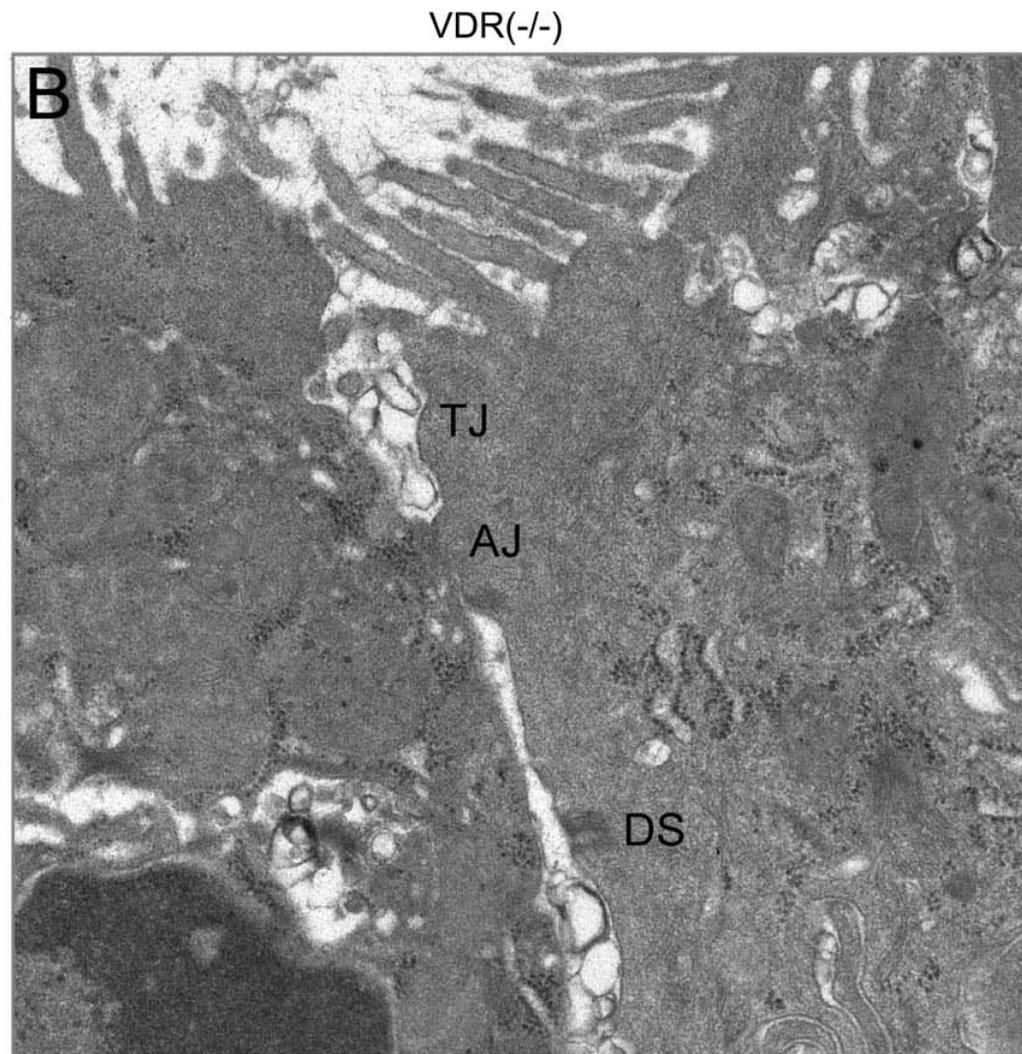
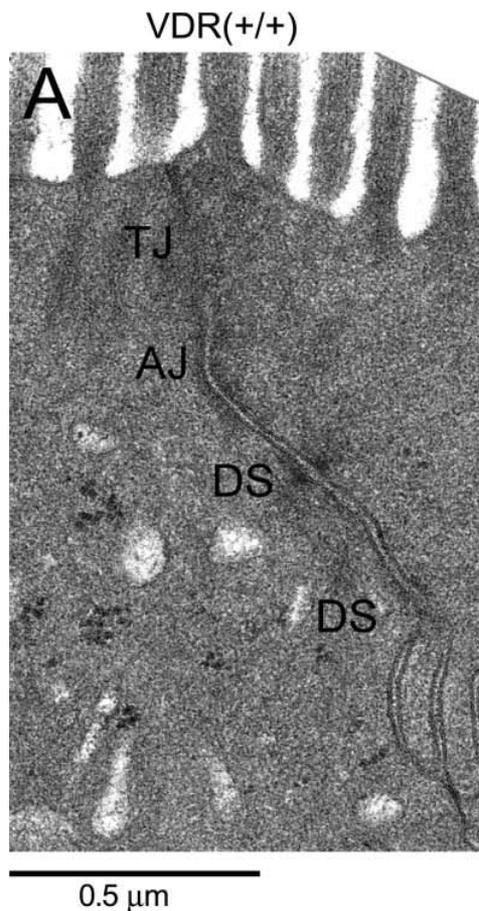
Tight junction







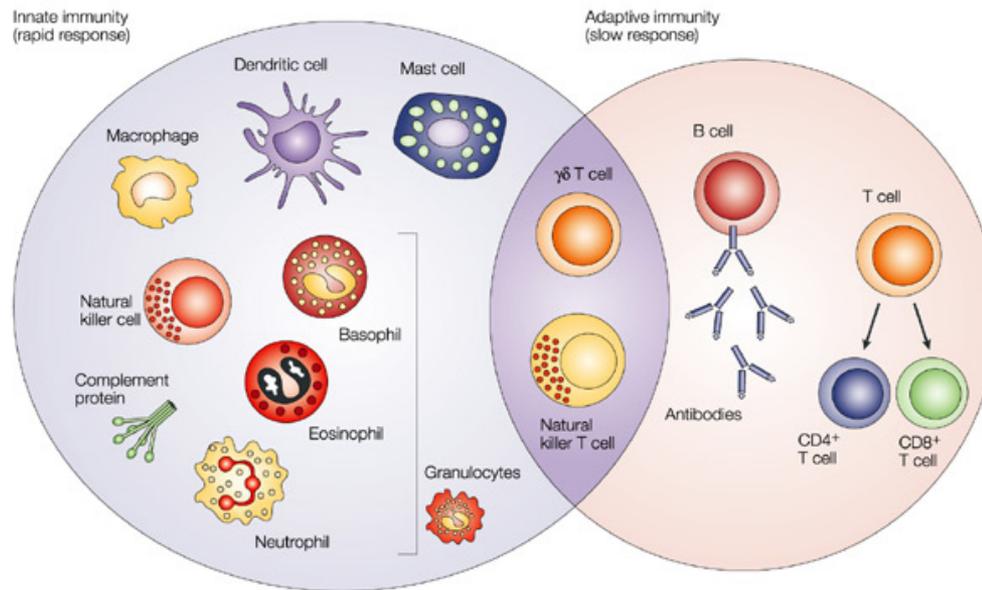




Tight junctions (TJ) Adherens junctions (AJ) and Desmosomes (DS) in colonocytes of normal and vitamin-D receptor-negative mice after inflammatory challenge

Sander GR, et al. Rapid disruption of intestinal barrier function by gliadin involves altered expression of apical junctional proteins. FEBS Lett. 2005 Aug 29;579(21):4851-5.

Vitamin D and systemic inflammation



Nature Reviews | Cancer

Enhances local and non-specific immunity

Put a brake on specific systemic immunity

Vitamin D protocol

- Measure laboratory value 25(OH)D3
- Supplement with D3, or in summertime, sunbathe during the hours around true noon. 20 minutes for white skin; up to 3 hours for very dark skin. Others intermediate.
- D3 in dose of 4000 (summer) to 7000 (winter) IU. 10,000IU is considered a safe upper limit by vitamin D experts.
- May combine doses for 50,000/wk, but do not exceed 50,000 at a time.
- Aim for serum levels of D3 above 50 ng/mL. Upper normal is 80-100 ng/mL. Toxicity occurs only over 200 ng/mL

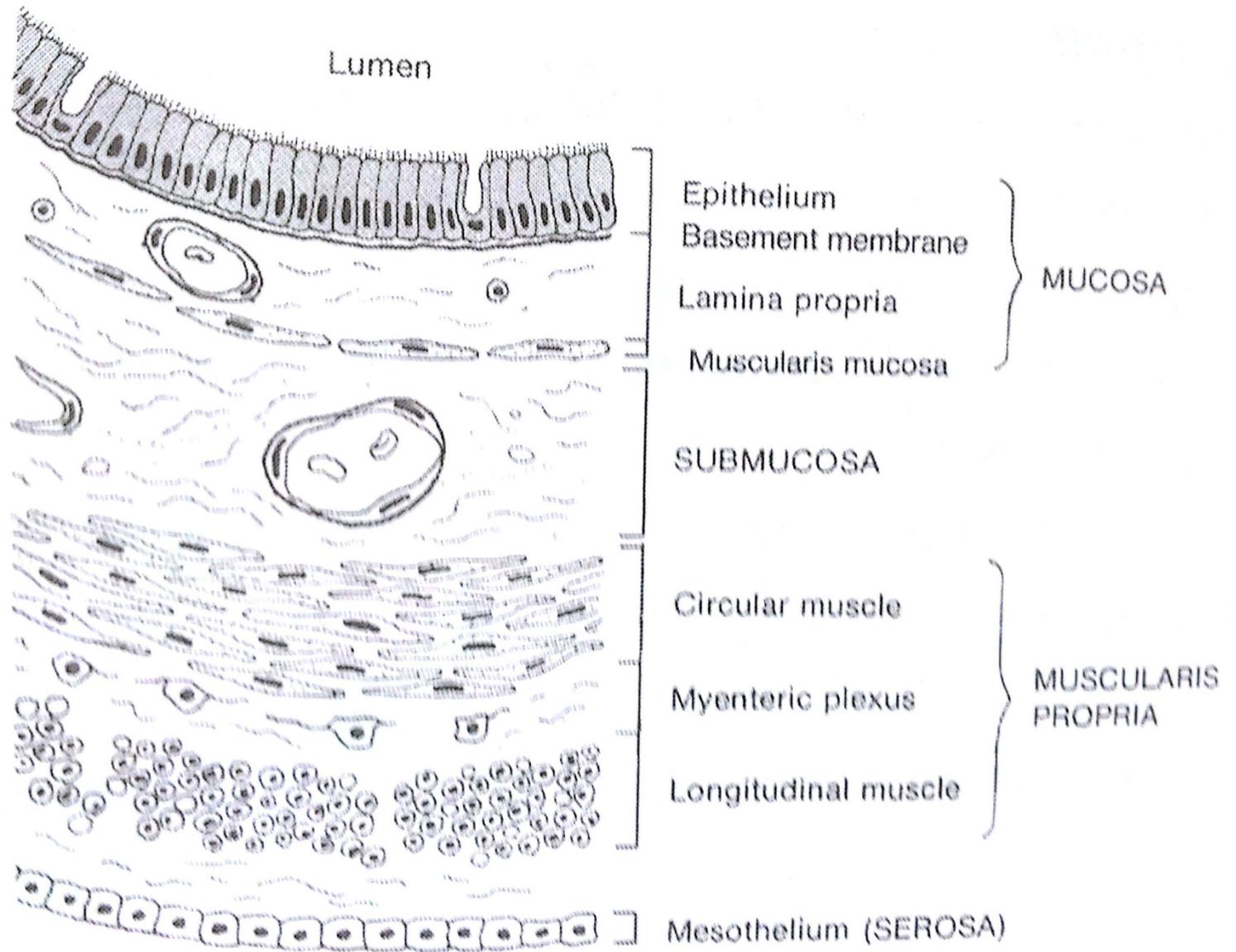
Granulomatous conditions

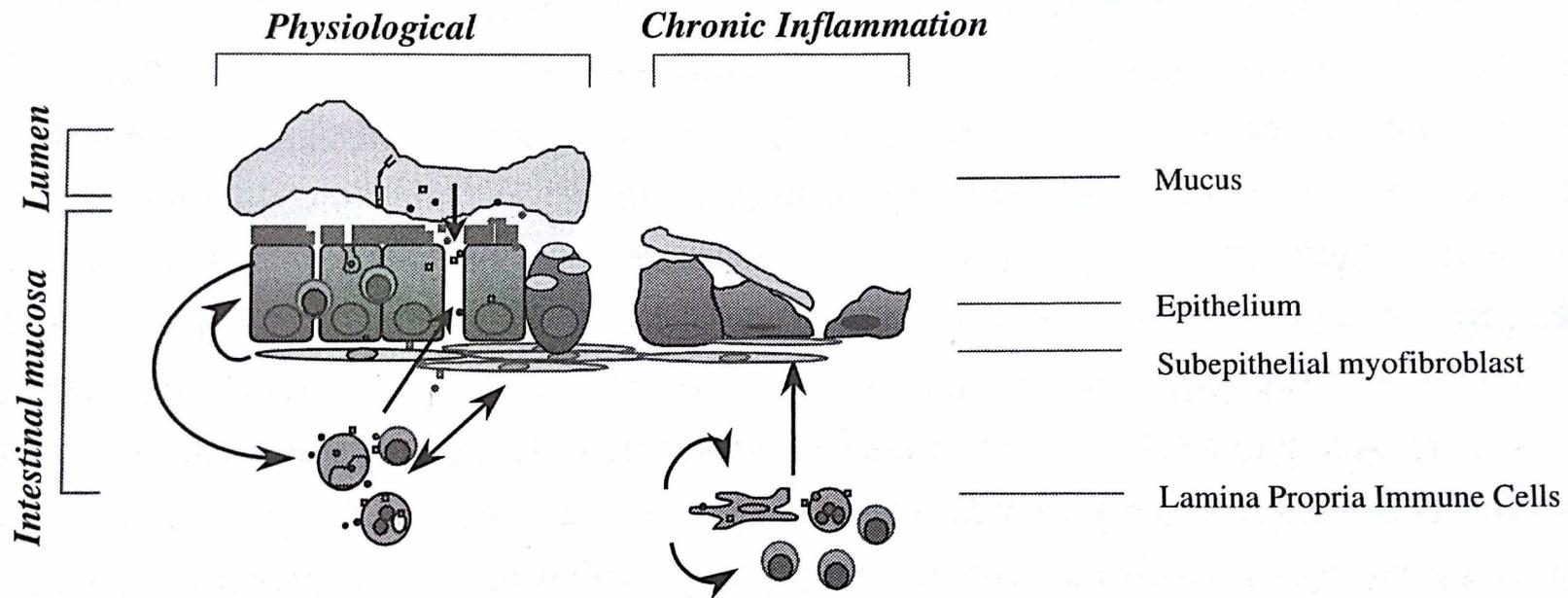
- In sarcoid, some cancers, and other granulomatous diseases, normal levels of vitamin D may cause toxicity. When supplementing must measure and monitor both 25(OH)D₃ and 1,25 di-hydroxy D₃ (calcitriol) and watch for elevated calcitriol levels.
- Research all autoimmune, neoplasia, and chronic infectious diseases for possible granuloma involvement. Consult with physician if necessary.

“Leaky gut” syndrome and systemic inflammation

Abnormally increased permeability of the gut barrier

Systemic immune signaling from the Gut Associated Lymphatic Tissue

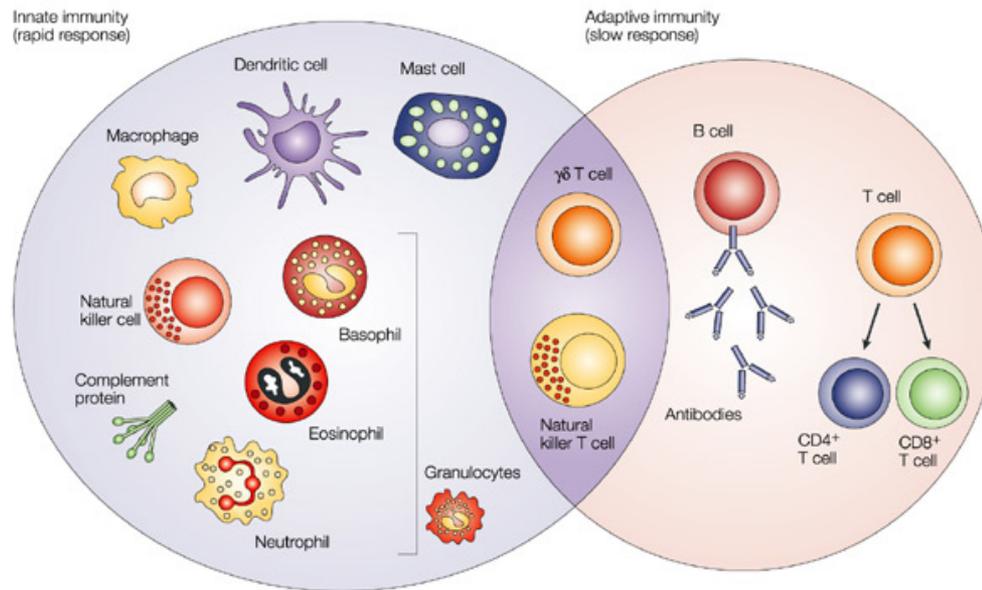




Myofibrocytes in basement membrane below enterocytes are antigen-presenting and cytokine-secreting cells.

Chesney J, Bacher M, Bender A, Bucala R. The peripheral blood fibrocyte is a potent antigen-presenting cell capable of priming naive T cells in situ. *Proc Natl Acad Sci U S A.* 1997 Jun 10;94(12):6307-12.

Vitamin D and systemic inflammation



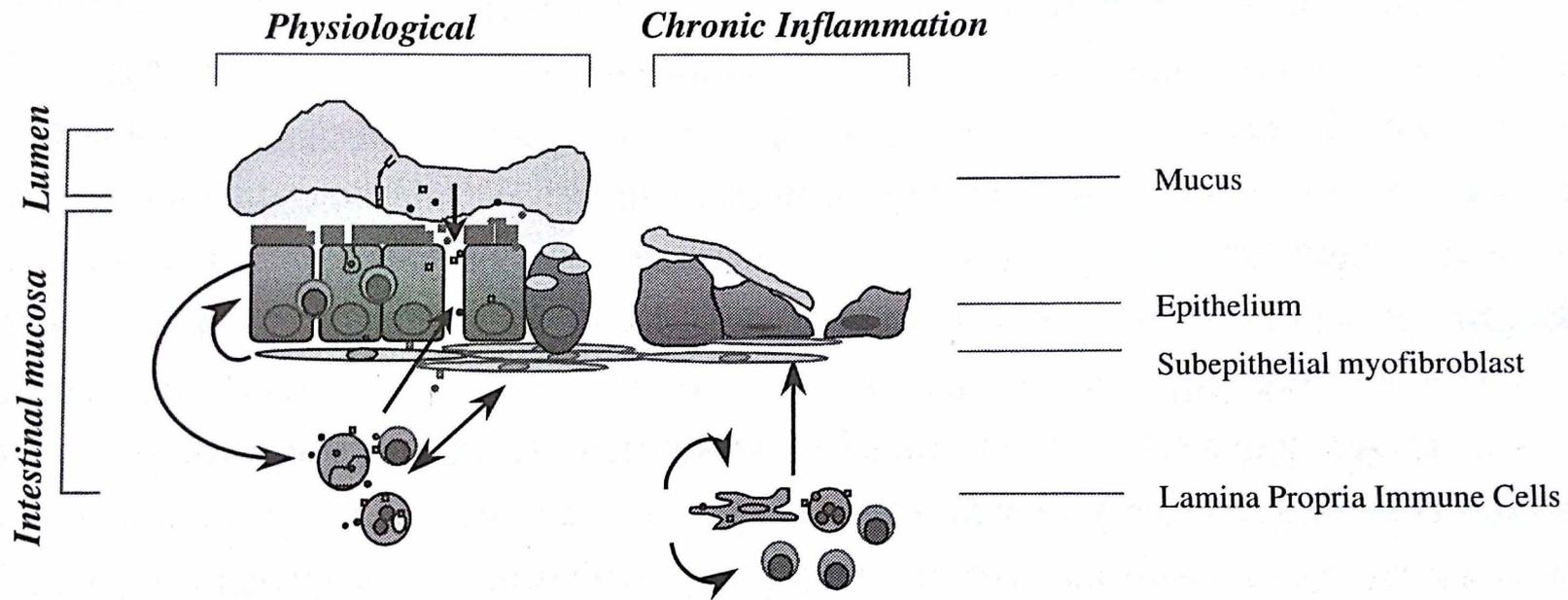
Nature Reviews | Cancer

Enhances local and non-specific immunity

Put a brake on specific systemic immunity

Gut lumen and microbiome

- The lumen contains a robust and diverse bacterial civilization, and a bacterial biofilms line the mucin layer.
- The bacterial colony collectively metabolizes fiber, starch, pectin, inulin, and cellulose to short-chain fatty acids which are required by the enterocytes for *fuel* and *and immune signaling*. They local and **systemic anti-inflammatory** properties
- *Acidophilus* and *Bifidobacterium* species (and other) are **adherent** friendly bacteria and contribute a layer of protection to the gut, and also produce SCFA as above.



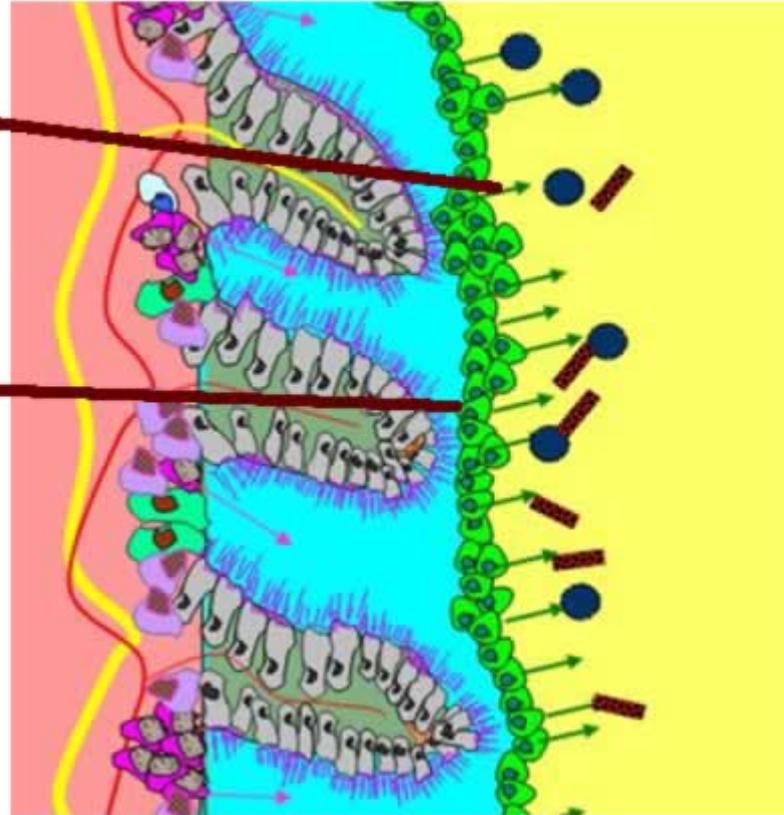
- Myofibroblasts at the base of the enterocytes control gut lining regeneration and tight junctions through chemical triggers.
- The initiating trigger of control is the presence of short-chain fatty acids from the microbiome, mediated by prostaglandins.

Probiotic Benefits

ACIDOPHILUS AND OTHER PROBIOTIC BACTERIA SECRETE: ANTIVIRAL ANTIBACTERIAL AND ANTIFUNGAL CHEMICALS.

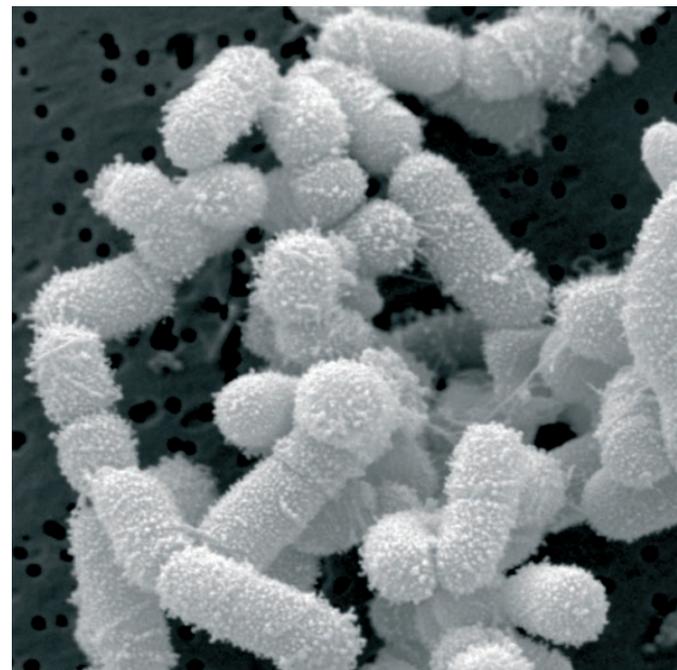
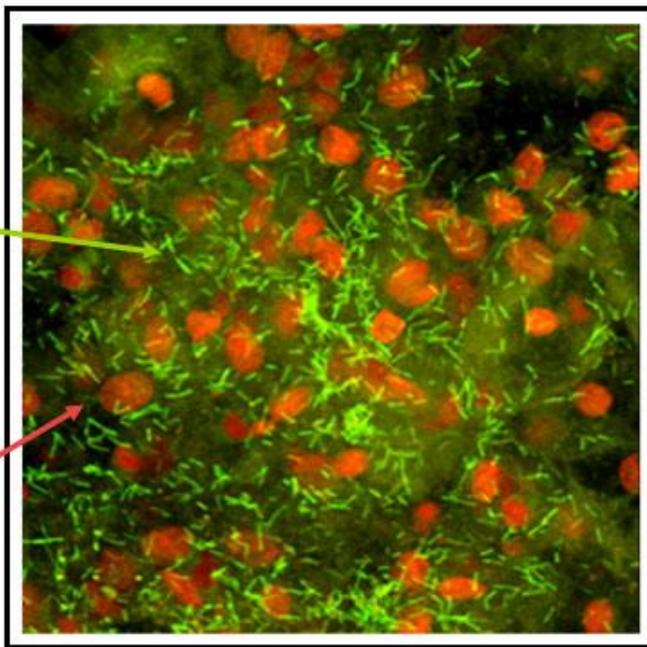
PROBIOTICS FORM A PHYSICAL BARRIER TO HINDER INVASION OF BACTERIA AND YEASTS

PROBIOTICS LIKE ACIDOPHILUS CREATE AN ACIDIC MICROENVIRONMENT WHICH PROMOTES IRON AND OTHER MINERAL ABSORPTION.

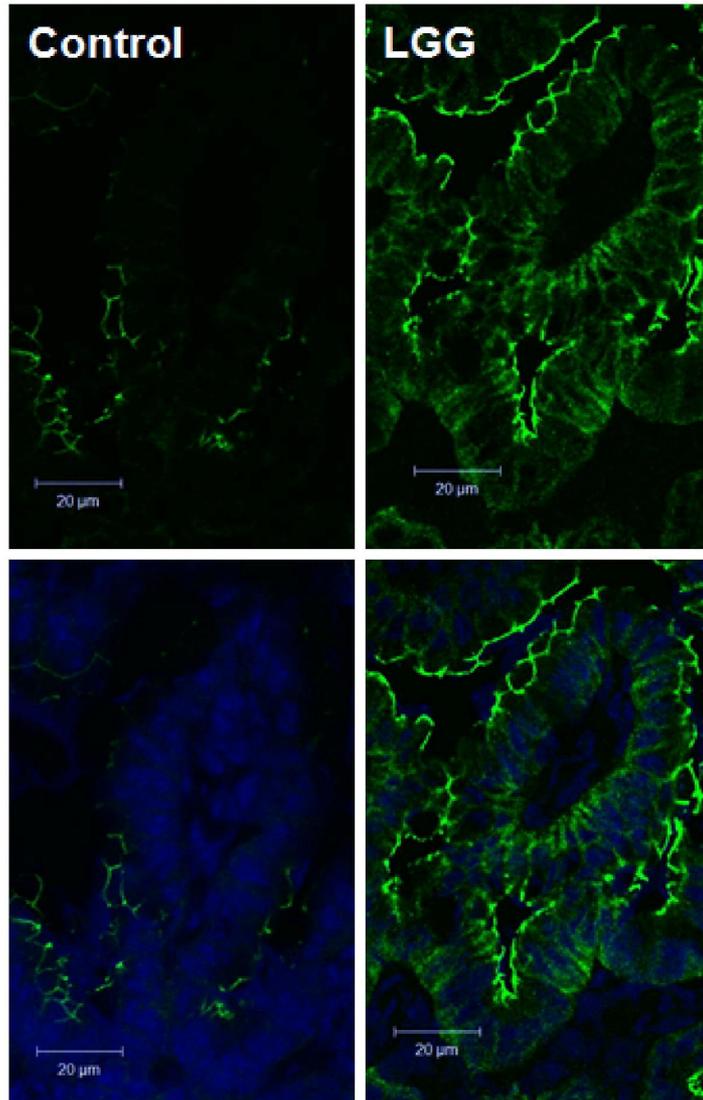


Lactobacillus sp.

Vaginal epithelial
cell



Lactobacillus



- Images of intestinal *Lactobacillus* biofilms in humans are difficult to find. More common are images in mice and birds.
- In this scan of a mouse intestine, before and after treatment with a *Lactobacillus* species (LGG), the effects of the LGG mucosal colonization on the expression of junction protein claudin-3 is shown with the luminescent dye.

Patel RM, Myers LS, Kurundkar AR, Maheshwari A, Nusrat A, Lin PW. Probiotic bacteria induce maturation of intestinal claudin 3 expression and barrier function. *Am J Pathol.* 2012 Feb;180(2):626-35.

Disk 4 Pathophysiology II

Gut Lymphatic system

Villous lymphatics

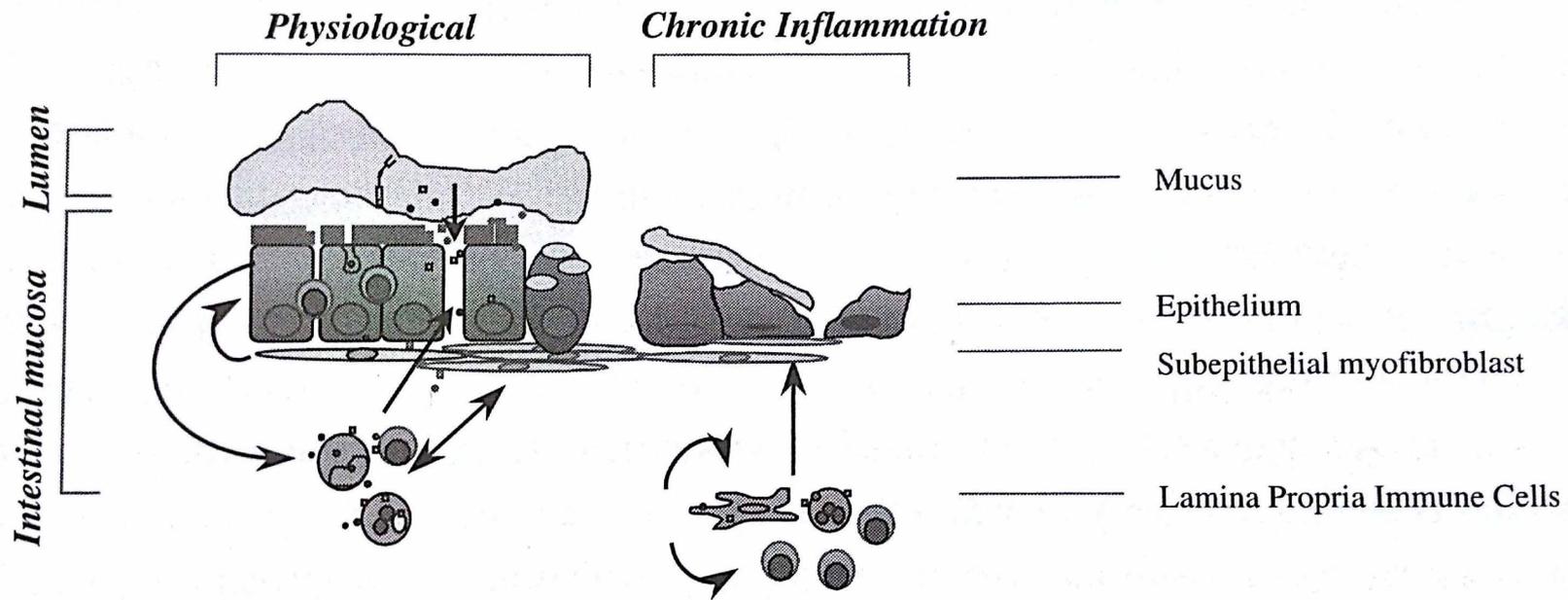
Systemic effects

Migrating plasma cells

Outgrowing allergies

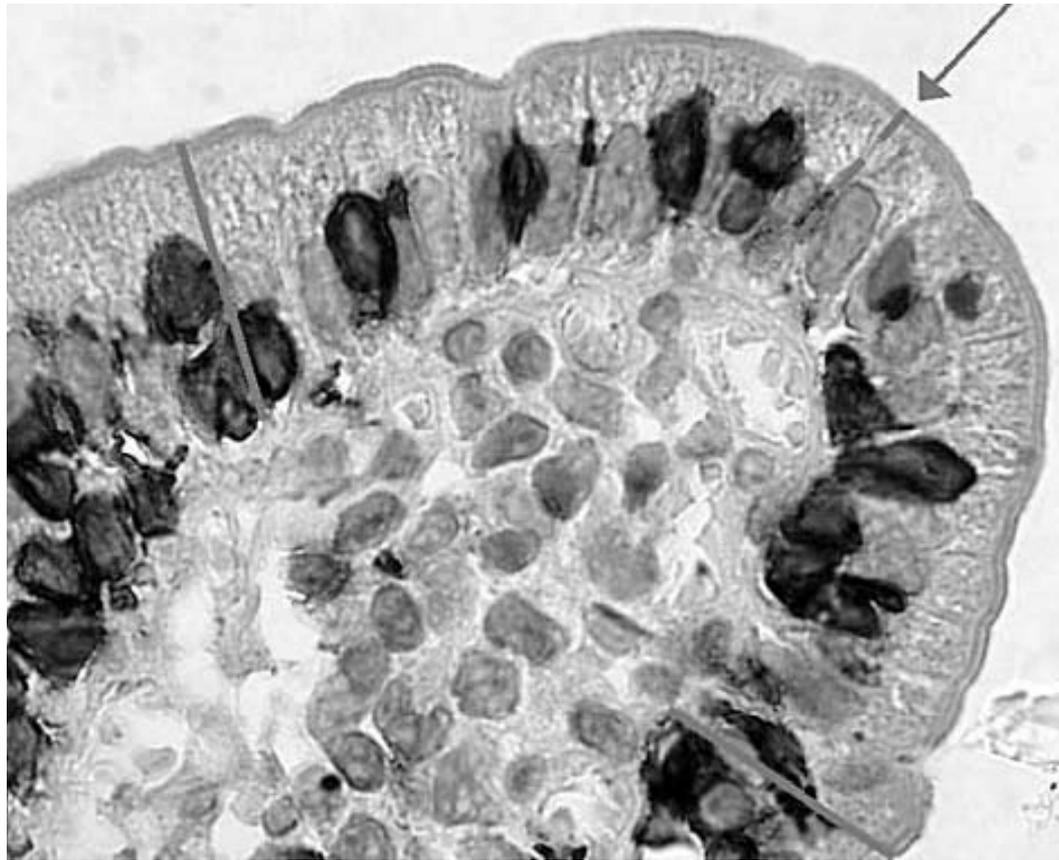
Molecular mimicry

The villus as a lymphatic organ

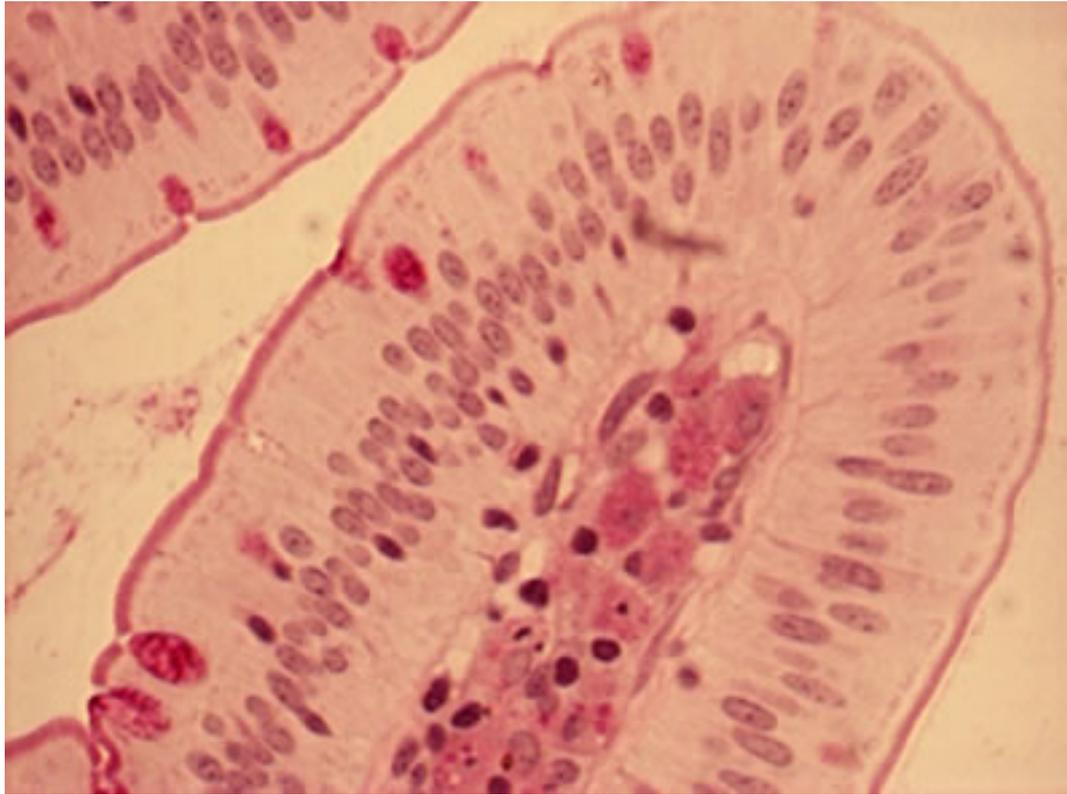


Myofibroblasts at the base of the enterocytes control gut lining regeneration and tight junctions through chemical triggers.

The initiating trigger of control is the presence of short-chain fatty acids from the microbiome, mediated by prostaglandins.

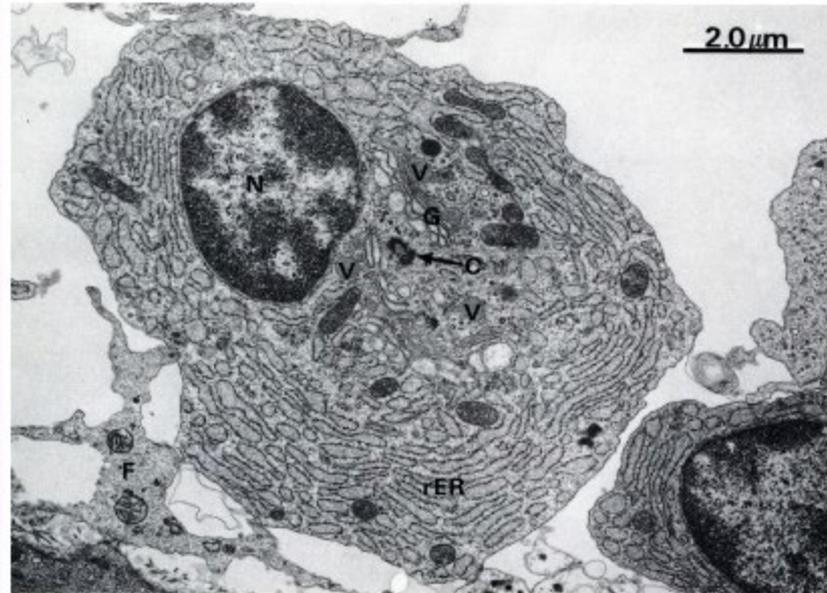
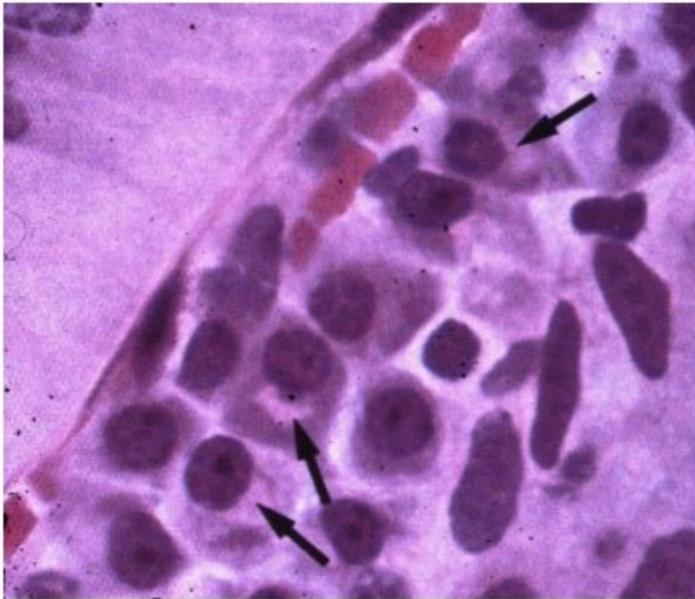


Lymphocytes in villus tip are stained in black



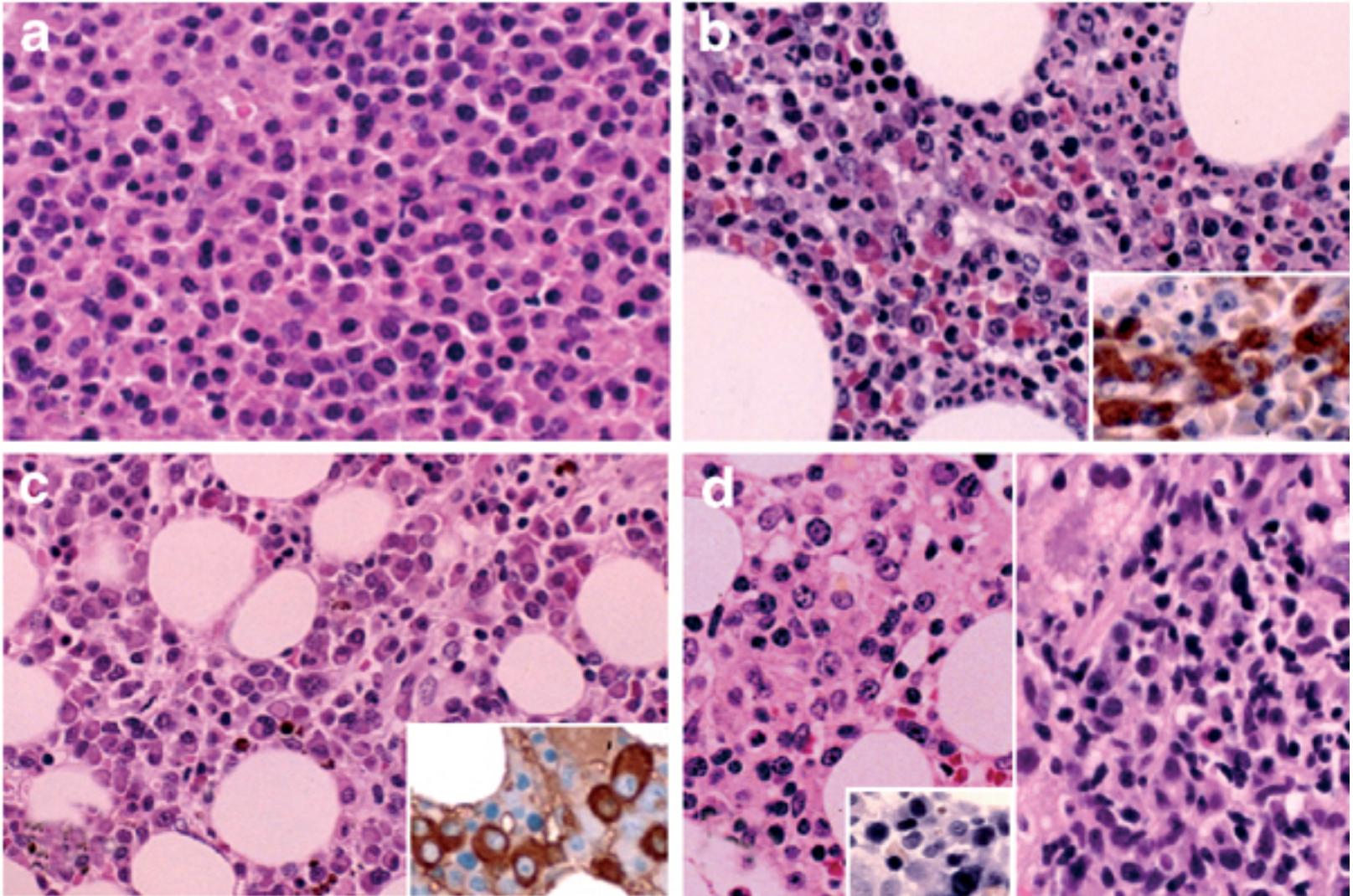
Macrophages in villus are stained pink

Plasma cells are immigrant, antibody-producing cells

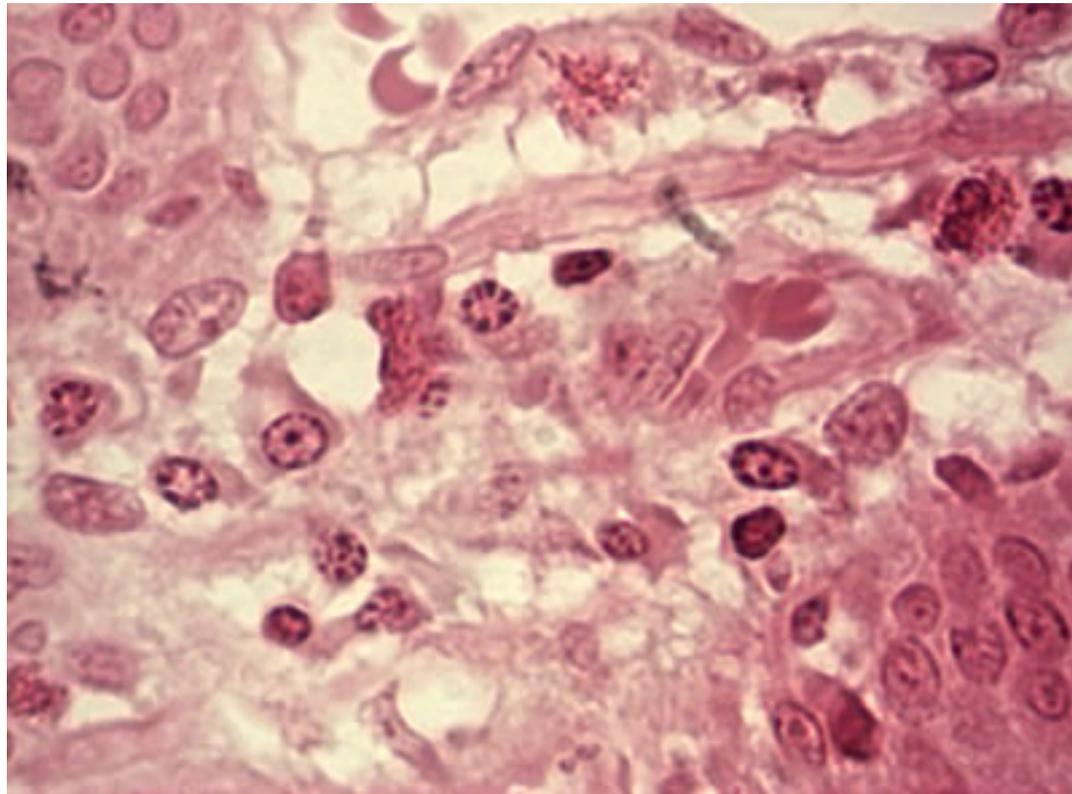


plasma cells are identified by the low-staining region next to the nucleus (LM), which is occupied by the Golgi apparatus

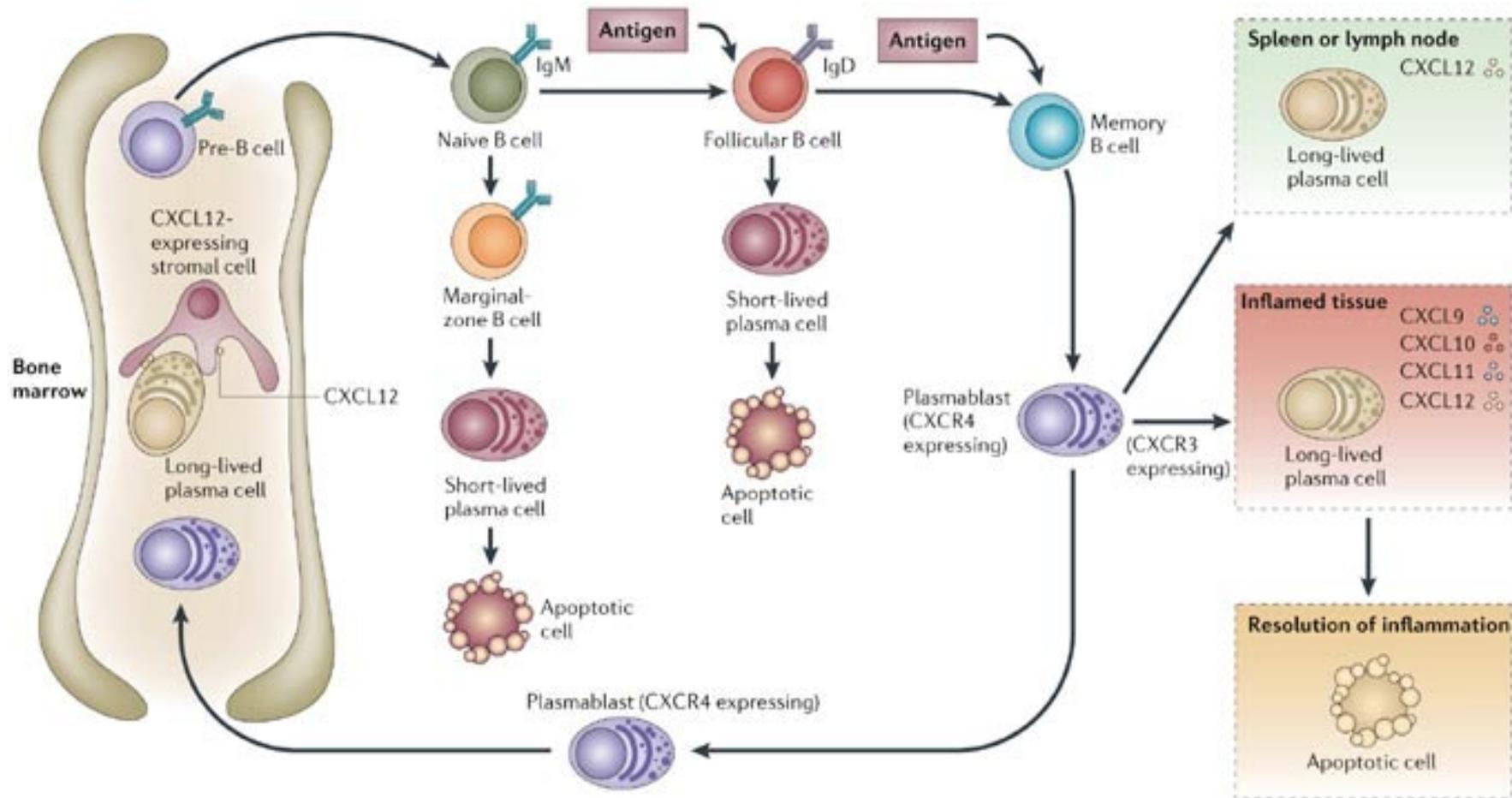
Stained plasma cells in bone marrow tissue



The bone-marrow plasma cells secrete antibodies to circulate throughout the system



Plasma cells in villus stained dark pink



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Nature Reviews | Immunology

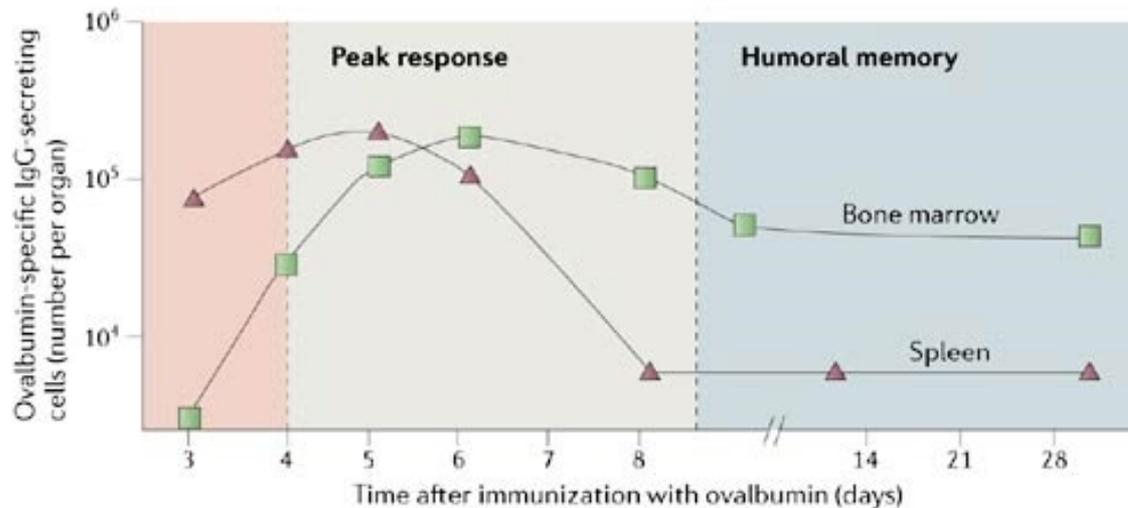
**Plasma cells migrate to bone marrow, spleen or nodes.
They may be attracted to and sequestered in any area of inflammation**

Peak response — inflamed tissue

- Plasmablasts migrate to inflamed tissue
- Plasma cells survive in niches in inflamed tissue and in the spleen
- Successful immune reaction terminates survival niches in inflamed tissue
- Dislocated plasma cells cannot relocate and therefore die

Humoral memory — bone marrow

- Plasmablasts invade the bone marrow and compete with resident plasma cells for occupancy of survival niches
- Plasmablasts become long-lived plasma cells
- Dislocated plasma cells cannot relocate and therefore die
- Memory slowly fades owing to competition



Molecular mimicry

Cross reactivity between food and self peptides

Food Antigens and Molecular Mimicry

- Peptide fragments of proteins, released on partial digestion in the stomach, are the most common antigenic substances in food
- Some food peptides are identical to peptides in the connective and other tissues of the human body
- Antibodies to the food peptides can initiate inflammation in distant areas of the body
- Cross-reactive peptides have been identified in glutenous grains, milk, corn, soy, egg and many nuts
- Reactivity to peptides is genetically determined, and cannot be “outgrown.”

Toxic gliadin peptides

Amino acid sequences	Position on gliadin protein
VPVPQLQPQNPSQQQPQEQ	α -03–21
PGQQQPFPPQQPY	α -31–43
PGQQQPFPPQQPYQPQPQPF	α -31–49
PGQQQPFPPQQPYQPQPQPFPSQQPY	α -31–55
PQPQPFPSQQPY	α -44–55
SQQPYLQLQPFPPQPQLPY	α -51–70
LQLQPFPPQPQLPYQPQLPY	α -56–75
QQYPLGQGSFRPSQQNPQA	α -202–220
LGQGSFRPSQQN	α -206–217

These peptides initiate inflammation in the intestinal mucosa via non-specific mechanisms

R. Cicocioppo et al. The immune recognition of gluten in coeliac disease.
Clinical and Experimental Immunology 140:408–416

Immunogenic gliadin and glutenin peptides

Amino acid sequences

VRVPVPLQLPQNPSQQQPQ
 QNPSQQQPQEQVPLVQQQ
 QVPLVQQQFPGQQPFPPQ
 PGQQQFPFPQQYPQPQPF
 FPGQQQFPFPQQYPQPQPF
 QPYPQPQFPFSQQPYLQL
 PQQPFSQQPYLQLQPFQ
 PQQQLPYPQPQLPY
 QLQPFQQLPY
 QLQPFQ
 LQLQPFQQLPYQPQLPYQPQLPYQPQPF
 FQPFQQLPY
 PQQQLPYPQPQLPY
 PFRPQQYPQPQPF
 LIFCMDVWLQ
 QQPLQQYPLGQGSFRPSQQNPQAQ
 QYPLGQGSFRPSQQNPQA
 PSGQGSFQPS
 PSGQGSFQPSQQ
 SGQGSFQPSQQN
 QGSFQPSQQN
 LQPQQPFPQQPQQYPQQPQ
 FPQQPQQPYPQQPQ
 FSQPQQQFPQPQ
 OQPQQSFPEQQ
 VQGGQIIPQQPAQL
 QQQQPFPFSQQQSPFSQQQQ
 QQPFPFSQQQQLPQ
 SGQQQRPGQWLQPGQQQGGYYPTSPQQSG
 PGQQQQGGYYPTSPQQSGQ
 GYYPTSPQQSGGQQQLGQ
 GYYPTSPQQSG
 QGGYYPTSPQQS
 QGGYYPTSPQQSG
 GQQGGYYPTSPQQSG
 GQQGGYYPTSPQQS

Position

a-gliadin: 1–19
 a-gliadin: 11–28
 a-gliadin: 21–40
 a-gliadin: 31–49
 a-gliadin: 30–49
 a-gliadin: 41–58
 a-gliadin: 46–63
 a-gliadin: 62–75
 a-gliadin: 57–68
 a-gliadin: 57–63
 a-gliadin: 57–89
 a-gliadin: 58–69
 a-gliadin: 63–76
 a-gliadin: 93–106
 a-gliadin: 123–132
 a-gliadin: 198–222
 a-gliadin: 203–220
 a-gliadin: 205–214
 a-gliadin: 205–216
 a-gliadin: 206–217
 a-gliadin: 208–217
 a-gliadin: 60–79
 a-gliadin: 66–78
 a-gliadin: 102–113
 a-gliadin: 134–153
 a-gliadin: 222–236
 glutenin: 40–59
 glutenin: 46–60
 glutenin: 707–742
 glutenin: 719–736
 glutenin: 725–742
 glutenin: 725–735
 glutenin: 724–734
 glutenin: 723–735
 glutenin: 722–735
 glutenin: 722–734

Immunogenic peptides on the A-gliadin portion of the alpha-gliadin molecule or the glutenin molecule

Does not include possible peptides on the other 2 gliadin chains. The authors estimate that at least 50 immunogenic peptides can be found throughout the gluten molecule

The QLQPFQ peptide is immunoreactive in all celiac patients tested. Nine other peptides were reactive in most patients, and the rest only in some patients and not in others.

Implications for food allergy testing

- Some responses may be via the innate immune system rather than the specific
- Innate responses in the gut may induce Leaky Gut Syndrome
- Because multiple antigens and antigen-classes are involved, lab testing for antibodies may produce a high rate of false negative results

Autoimmune conditions in celiac disease

- Autoimmune nephropathy
 - Sategna-Guidetti C et al. Do IgA antigliadin and IgA antiendomysium antibodies show there is latent coeliac disease in primary IgA nephropathy? *Gut*. 1992 Apr;33(4):476-8.
- Autoimmune thyroid disease
 - Sategna-Guidetti C et al. Autoimmune thyroid diseases and coeliac disease. *Eur J Gastroenterol Hepatol*. 1998 Nov;10(11):927-31.
- Type I diabetes (autoimmune)
 - Sategna-Guidetti C et al. Celiac disease and insulin-dependent diabetes mellitus. Screening in an adult population. *Dig Dis Sci*. 1994 Aug;39(8):1633-7.
- Systemic lupus
 - Hadjivassiliou M, et al. Gluten sensitivity masquerading as systemic lupus erythematosus. *Ann Rheum Dis*. 2004 Nov;63(11):1501-3.

Gluten ataxia

Ataxia	% with anti-gliadin antibodies
Idiopathic	32
Sporadic, familial	14
Sporadic, systemic disease	13
Sporadic, not as above	41
Control	12

Hadjivassiliou M, et al. Gluten ataxia in perspective: epidemiology, genetic susceptibility and clinical characteristics. Brain. 2003 Mar;126(Pt 3):685-91.

Molecular mimicry and wheat

- A specific protein in wheat has been found to be a molecular mimic of a similar protein in the pancreas
 - MacFarlane AJ et al. A type 1 diabetes-related protein from wheat (*Triticum aestivum*). cDNA clone of a wheat storage globulin, Glb1, linked to islet damage. *J Biol Chem*. 2003 Jan 3;278(1):54-63. Epub 2002 Oct 29.
- Antibodies in the serum of celiac patients can also attack protein in the cardiac muscle of primates.
 - Sategna-Guidetti C et al. Binding by serum IgA antibodies from patients with coeliac disease to monkey heart tissue. *Scand J Gastroenterol*. 2004 Jun;39(6):540-3.

- Gluten peptides have bio-identical sequences to the protein *calreticulin*, which is present in the gut wall, and also throughout the cells of the body and their nuclei.
 - Karská K, et al. Calreticulin--the potential autoantigen in celiac disease. *Biochem Biophys Res Commun.* 1995 Apr 17;209(2):597-605.
- Antibodies to calreticulin are elevated in systemic lupus.

Antigenic peptides in cow's milk

At least 20 peptide epitopes have been indentified in various milk proteins including various fragments of:

- Alpha lactalbumin: 4 IgE binding and 3 IgG binding regions identified
- Beta (β)-lactoglobulin (BLG): 7 IgE and 6 IgG binding epitopes detected
- Other: Bovine insulin (BI), Bovine serum albumin (BSA), Peptide beta (β)-casomorphin 7 (BCM-7)

Järvinen KM, Chatchatee P, Bardina L, Beyer K, Sampson HA. IgE and IgG binding epitopes on alpha-lactalbumin and beta-lactoglobulin in cow's milk allergy. *Int Arch Allergy Immunol.* 2001 Oct;126(2):111-8.

Milk protein and autoimmunity

- Casein protein is associated in systemic lupus
 - Riemekasten G et al. Casein is an essential cofactor in autoantibody reactivity directed against the C-terminal SmD1 peptide AA 83-119 in systemic lupus erythematosus. *Immunobiology*. 2002 Dec;206(5):537-45.
- Multiple sclerosis.
 - Winer S et al. T cells of multiple sclerosis patients target a common environmental peptide that causes encephalitis in mice. *J Immunol*. 2001 Apr 1;166(7):4751-6.
- Type I diabetes.
 - Cavallo MG et al. Cell-mediated immune response to beta casein in recent-onset insulin-dependent diabetes: implications for disease pathogenesis. [Lancet](#). 1996 Oct 5;348(9032):926-8.
- Atherosclerosis
 - Muscari A Association of serum IgA antibodies to milk antigens with severe atherosclerosis. *Atherosclerosis*. 1989 Jun;77(2-3):251-6

Milk protein mimicry and IDDM

- A 8-amino-acid peptide on bovine serum albumen, present in cow's milk, has been found to be bio-identical to the same peptide in pancreatic islet cells.
- T-cells sensitized to that peptide were found in 28 of 31 children with recent onset of IDDM (Type I diabetes).
- None were found in non-diabetic controls, or in matched children with systemic lupus or juvenile rheumatoid arthritis.
 - Cheung R et al. T cells from children with IDDM are sensitized to bovine serum albumin. *Scand J Immunol.* 1994 Dec;40(6):623-8.
- 24 of 57 patients with IDDM were found to have anti-casein antibodies, vs 0/10 patients with thyroid disease or 1/36 healthy controls.
 - Cavallo MG et al. Cell-mediated immune response to beta casein in recent-onset insulin-dependent diabetes: implications for disease pathogenesis. [*Lancet.*](#) 1996 Oct 5;348(9032):926-8

Milk and atherosclerosis

Percent of patients with high titers of IgA antibodies to milk proteins

	Severe atherosclerosis n=23	Control n-20	P score
beta-lactoglobulin	70%	25%	< .002
xanthine oxidase	39%	5%	<.01
bovine IgG	74%	35%	<.02
casein	61%	25%	<.02

Muscari A Association of serum IgA antibodies to milk antigens with severe atherosclerosis. *Atherosclerosis*. 1989 Jun;77(2-3):251-6

Milk protein mimicry and atherosclerosis

- Cross reactive antibodies to milk proteins and oxidized LDL are present in a high percentage of patients with atherosclerosis.
 - Steinerová A et al. Significant increase in antibodies against oxidized LDL particles (IgoxLDL) in three-month old infants who received milk formula. *Atherosclerosis*. 2004 Mar;173(1):147-8
- Antibodies to milk protein may also cross react with apolipoproteins
 - Muscari A et al. Serum IgA antibodies to apoproteins and milk-proteins in severe atherosclerosis. *Ann Ital Med Int*. 1992 Jan-Mar;7(1):7-12.
- Denatured bovine immunoglobulin may be cross reactive with arterial tissues
 - Annand JC et al. Denatured bovine immunoglobulin pathogenic in atherosclerosis. *Atherosclerosis*. 1986 Mar;59(3):347-51.

Milk protein, insulin resistance

- IgG Antibodies to various foods were elevated in a group of obese teenage boys compared to controls.
- Scans of their carotid arteries showed the early stages of atherosclerosis.
- CRP was significantly elevated in the boys, and both the CRP levels and the levels of atherosclerosis were tightly correlated with the levels of anti-food antibodies.
- The authors conclude: **“We hypothesize that the gut might represent one of the key organs to induce and to perpetuate low grade chronic inflammation.”**
 - Wilders-Truschnig M et al. IgG antibodies against food antigens are correlated with inflammation and intima media thickness in obese juveniles. *Exp Clin Endocrinol Diabetes*. 2008 Apr;116(4):241-5. Epub 2007 Dec 10.

Process:

Food intolerance and systemic inflammation

- The “lymphatic triad” of B-lymphocytes, T-lymphocytes, and antigen-presenting cells is present in the outermost surface area of the gut wall.
- Persistent exposure to food antigens promotes cloning and specialization of the enteric surface lymphocytes, and a flow of cytokines and potential autoantibody-producing migratory plasma cells to the peripheral tissues.
- May occur *in the absence of* leaky gut syndrome; chronic inflammation may **promote** leaky gut syndrome.

Chronic inflammatory conditions routinely cured with screening and removal of food intolerances.

- ▶ Connective tissue autoimmunity. (100%). Multiple lupus cases
- ▶ Fibromyalgia
- ▶ Chronic upper GI (GERD) 100%
- ▶ Chronic bowel (UC, Crohn's, IBS) (100%)
- ▶ Chronic UTI/IC:
- ▶ Cervical dysplasia
- ▶ Chronic musculoskeletal pain.
- ▶ Vague neurological complaints.

(From more than 3000 patient cases in a general practice.)

Disk 5 Medications and Herbs

Medications

Herbs for pain

Herbs and Leaky gut

Insulin resistance

Alterative herbs

Steroids and NSAID

Anti-inflammatory drugs

Steroids

- Unselective inhibition of all prostaglandin-mediated activities
- Inhibition of immunity
- Inhibition of tissue healing and regeneration
- Atrophy of adrenal glands

NSAID

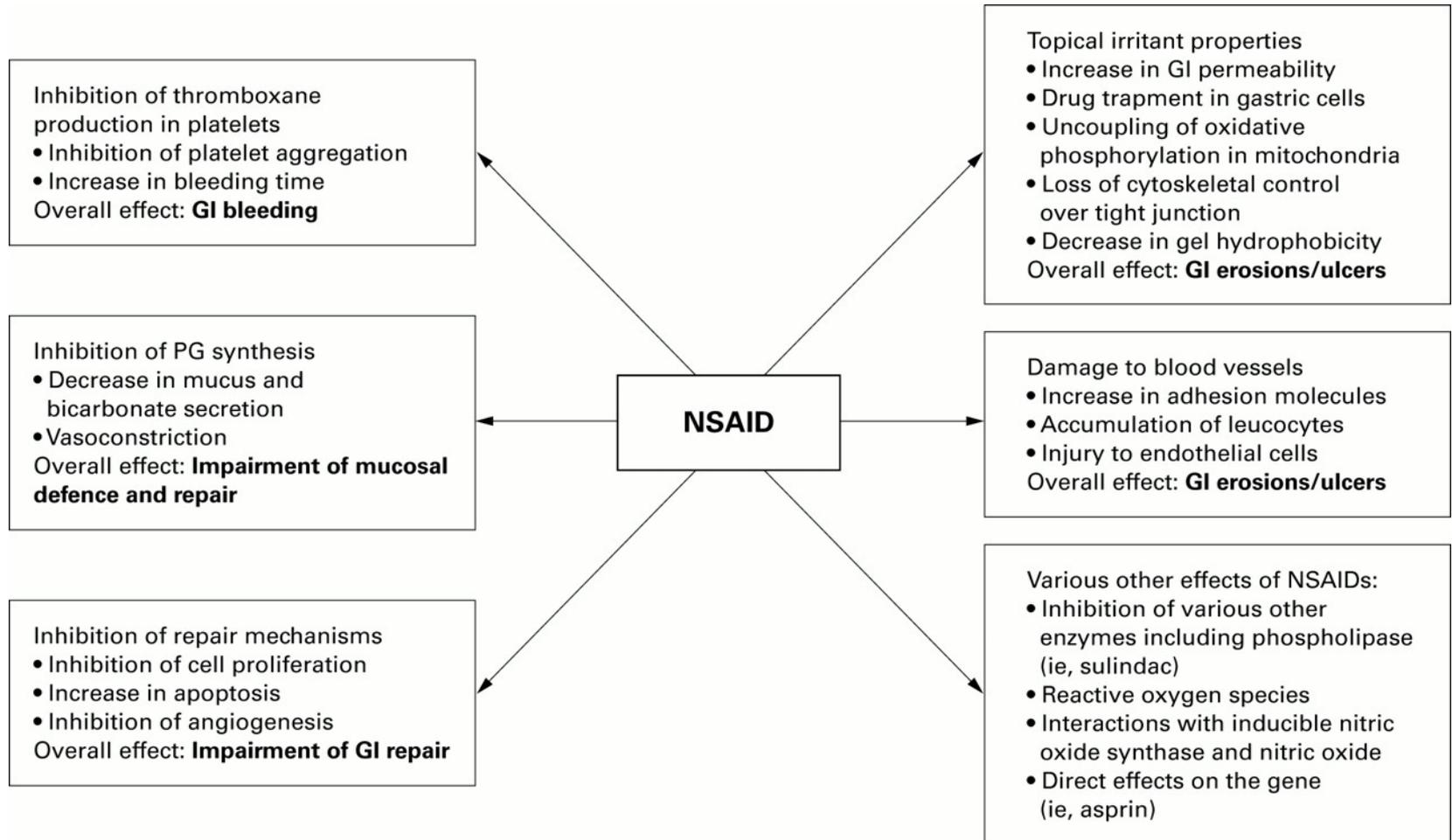
- Inhibition of gut lining regeneration via COX inhibition
- Inhibition of healing time
- Inhibition of host antiviral defences
- Increase in viral shedding in influenza

Process

NSAID and vicious cycle

- NSAID promotes leaky gut syndrome
- Weaning from NSAID should be a fundamental skill of all medical herbalists.
- Withdrawal bring about rapid inflammatory rebound
- Acute formula for pain, especially as it affects sleep.
- Chronic formula for inflammation. May base on Curcuma, in combination with Glycyrrhiza and Zingiber and modifying herbs.

Diagrammatic presentation of the mechanisms of non-steroidal anti-inflammatory drug (NSAID) injury to the gastrointestinal tract.



HALTER F et al. Gut 2001;49:443-453

Acute formula for pain

- Anodyne portion: Piscidia, Corydalis, Eschscholtzia, Lactuca
- Antispasmodic Portion: Viburnum opulus, Dioscorea, Paeonia, Pedicularis
- Sedative portion: Humulus, Passiflora, Scutellaria tea, Paeonia, Pedicularis (smoke), Piscidia
- Hypnotic herbs: Humulus, Sculellaria, Passiflora, Valeriana
- “Blood moving” herbs.
- When formula is effective for pain, it will make the individual dopey. Don’t drive. Prefer at bedtime.

“Blood moving” herbs

- Angelica *Angelica archangelica* combines well with *Apium seed*
- Dang gui *Angelica sinensis* combines well with *Ligusticums*
- *Ligusticum* (Chinese or Western) combines well with *Commiphora*
- Turmeric *Curcuma longa* combines well with *Glycyrrhiza*
- Myrrh *Commiphora myrrha* combine with small amount of *Capsicum*
- Rosemary *Rosmarinus officinalis* combines well with *Salvia off*

Herbs and the Leaky Gut Syndrome

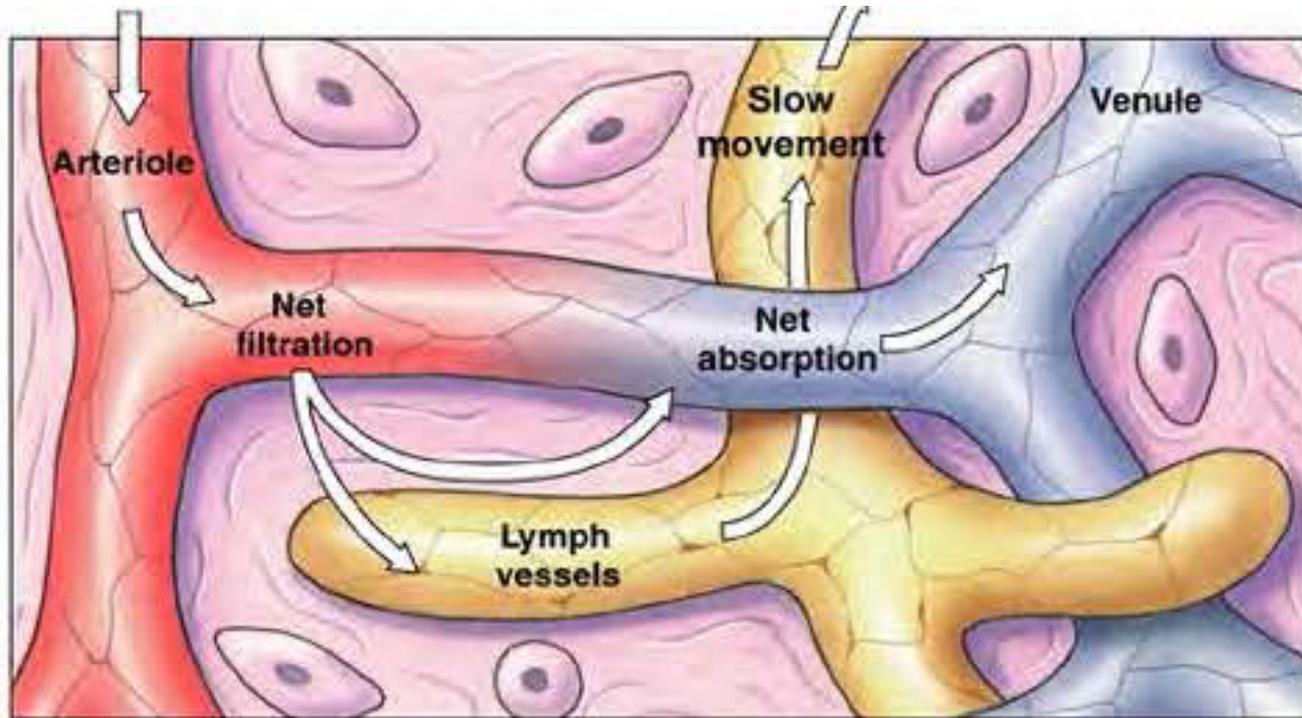
- Anti-inflammatories with benefits to digestion: *Matricaria*, *Mentha*
- Anti-inflammatories with benefits on the wound healing and immune processes: *Plantago* and *Calendula*.
- Demulcent anti-inflammatories: *Glycyrrhiza*, *Althea*, *Aloe juice*, *Oenothera*.
- Prefer powders or decoctions between meals or during intermittent fasting

Process: Insulin resistance

- Insulin resistance with compensatory hyperinsulinemia promotes oxidation and inflammation.
- The anabolic effects of insulin and its IGF-1 counterpart overstimulation growth, division, metabolism and oxidative damage in non-insulin-resistant epithelial and endocrine tissues.
- Insulin resistance promotes the production of CRP
- Botanical medicines may support efforts to modify insulin resistance/sensitivity but must be part of a larger program that includes cross-training of the muscles, low carbohydrate diet, and supplementation with insulin-sensitizing nutrients.

Process:

Poor detoxification of extracellular spaces



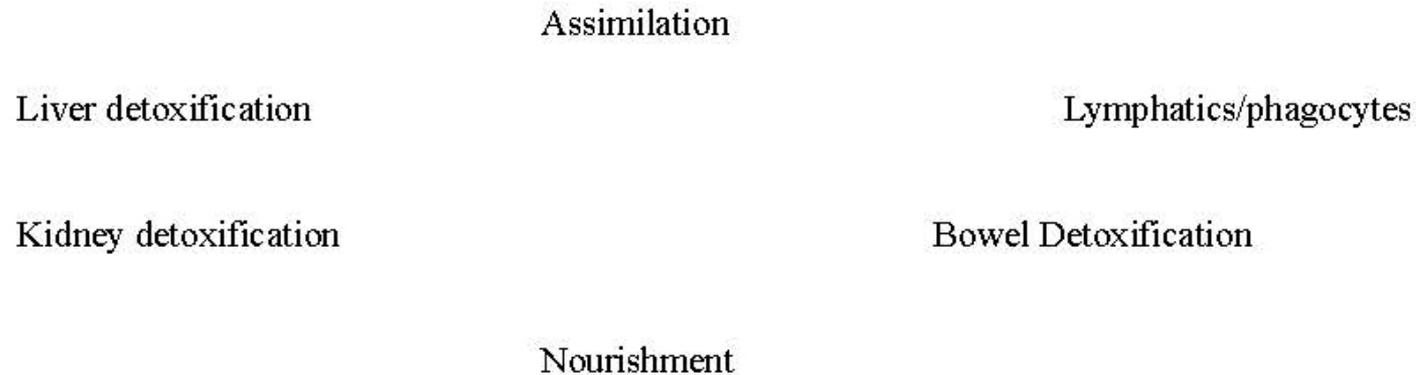
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Autophagy

- Programmed non-inflammatory removal of cells and subcellular particles.
- Makes amino acids available locally in abundance.
- Promoted by exercise
- Promoted by fasting
- May be promoted by traditional alterative and lymphatic herbs.
- Alternative is inflammatory removal of debris. May be correlated with “damp heat” in traditional systems

		hot	cold	moist	dry	skin	liver	lymph	bowel	kidney	immune	nutritive	tumors
<i>Allium sativum</i>	garlic	x			x			x			x		
<i>Anemopsis californicum</i>	yerba mansa	x			x	x		x			x		
<i>Arctium lappa</i>	burdock		x		x	x	x	x	x	x	x	x	x
<i>Baptisia tinctoria</i>	wild indigo		x		x			x			x		
<i>Calendula officinalis</i>	pot marigold	x			x	x	x	x	x		x		
<i>Ceanothus americanum</i>	red root		x		x		x	x			x		
<i>Echinacea spp.</i>	coneflower		x		x	x		x			x		
<i>Eupatorium perfoliatum</i>	boneset		x		x	x	x	x	x	x	x		
<i>Fucus vesiculosus</i>	kelp		x		x							x	
<i>Galium aparine</i>	cleavers		x		x			x		x	x		
<i>Iris versicolor</i>	Iris		x		x	x	x	x	x		x		
<i>Mahonia spp.</i>	Oregon grape		x		x	x	x	x			x		
<i>Medicago sativum</i>	alfalfa											x	
<i>Rumex crispus</i>	yellow dock		x		x	x	x	x	x		x		
<i>Sambucus nigra</i>	elderberry		x		x	x		x		x	x	x	
<i>Solanum dulcamara</i>	woody nightshade	x			x	x							
<i>Stillingia sylvaticum</i>	Queens root				x	x		x			x		
<i>Taraxacum officinale</i>	dandelion		x		x	x	x		x	x		x	
<i>Trifolium pratense</i>	red clover		x			x		x				x	x
<i>Urtica dioica</i>	stinging nettle				x	x				x	x	x	

A Model of alterative therapy



Alterative -therapy- is anything that improves the nutrition and increases the wastes gently and gradually. This is an approach to healing, not just a category of herbs. Lifestyle factors such as exercise and rest, fasting, dietary factors, and alterative herbs of various sorts may all constitute an alterative approach.

Alterative formulas

More herbs rather than less

- 1 or more liver alteratives
- 1 or more digestive alteratives
- 1 or more kidney alteratives
- 1 or more lymphatic alteratives
- 1 or more bowel alteratives
- 1 or more immune alteratives

Disk 6 Natural therapeutics/herbs

Fasting

Intermittent fasting

Breakfast

Coffea

Salicylate containing herbs

Curcuma

Ginger

More antiinflammatory herbs

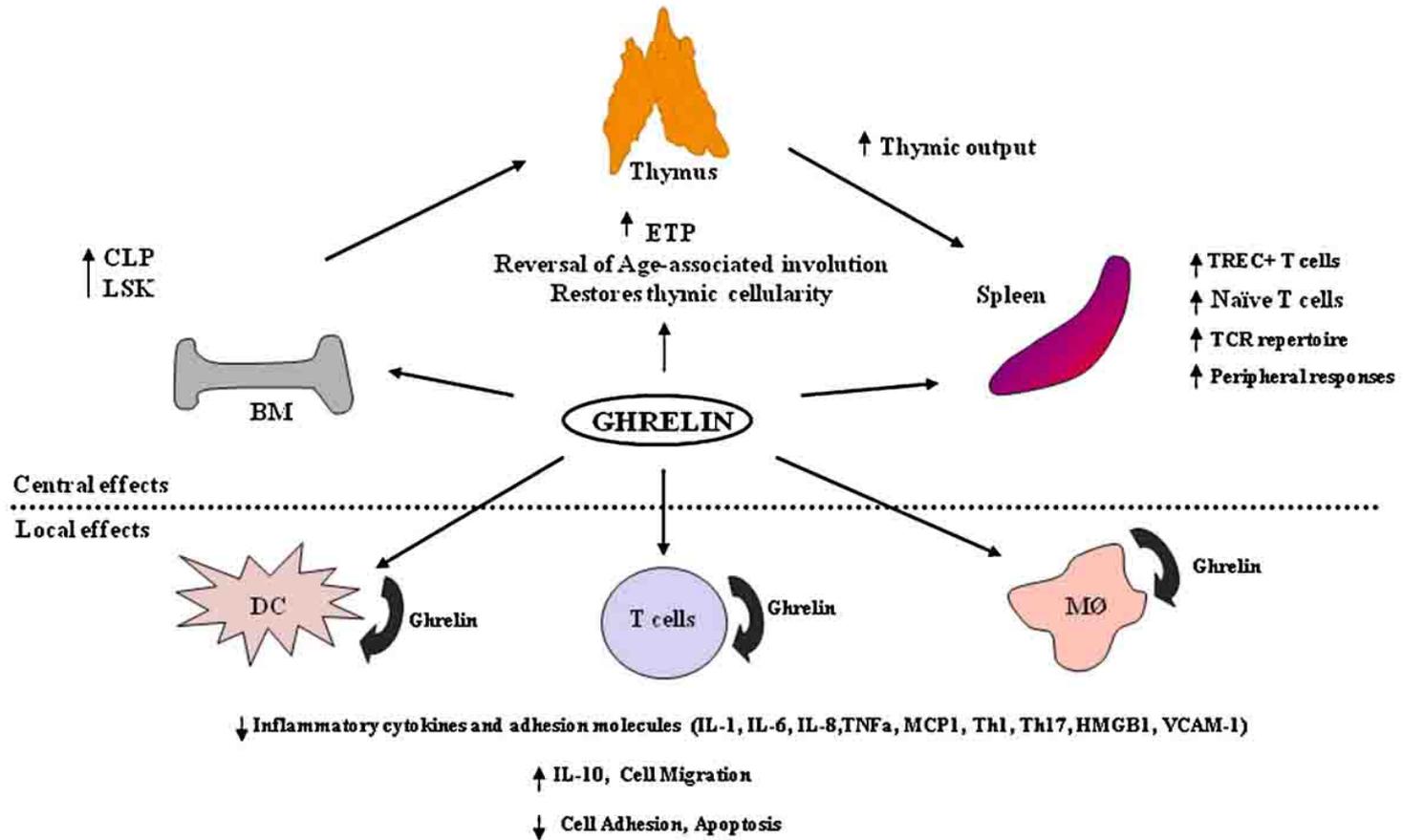
Hydrastis and myrrh

Fasting and inflammation

Fasting and Ghrelin

- Secreted by the gut wall of the stomach, small intestine, and large intestine when empty
- Stimulates hunger centers in hypothalamus
- Promotes growth hormone
- Has systemic anti-inflammatory effects
- May act as selective Cox-2 inhibitor
- Has febrifuge effects
- Promotes autophagy in the system and locally in the gut
- Promotes gut remodeling.

Fasting, ghrelin and inflammation



Possible therapeutic effects on:

- Endotoxemia and Sepsis
- Colitis and Inflammatory Bowel Syndrome
- Cardiovascular, Hepatic, Respiratory and Renal Inflammation/Injury/Fibrosis
- Traumatic Brain Injury/Pain/Parkinson's disease
- Cachexia/Anorexia
- Ischemia/Reperfusion Injury
- Arthritis and Multiple Sclerosis
- Burn Injury
- Age-Associated Inflammation
- Thymic and bone marrow development Development and Involution

Fasting

- Fasting during acute inflammatory attacks
- Fasting during fever
- Emptying the stomach and bowels at onset of febrile illness or inflammatory attack.
- Intermittent, partial: eating:fasting on 8hr:16hr schedule
- Intermittent, short: dinnertime to dinnertime 1-2 non-sequential days/wk.
- Caution with any longer fast unless the individual is robust, damp, warm, and excess in constitution or condition.
- Henry Lindlahr: “May cause serious and permanent harm.”

The effects of alterative herbs and gut-healing formulas are greatly enhanced during the fasting/ghrelin state. The cue is the hungry growling stomach.

Anti-inflammatory herbs

- *Coffea arabica* consumption is associated with lower hsCRP in all recent trials.

Yamashita et al. Association of coffee consumption with serum adiponectin, leptin, inflammation and metabolic markers in Japanese workers: a cross-sectional study. *Nutr Diabetes*. 2012 Apr 2;2:e33.

Pham et al. Combined effects of coffee consumption and serum γ -glutamyltransferase on serum C-reactive protein in middle-aged and elderly Japanese men and women. *Clin Chem Lab Med*. 2011 Oct;49(10):1661-7.

Bjerkeset et al. C-reactive protein with depression and myocardial infarction in 9258 women and men from the HUNT population study. *Psychol Med*. 2011 Feb;41(2):345-52.

Maki et al. The relationship of coffee and green tea consumption with high-sensitivity C-reactive protein in Japanese men and women. *Clin Chem Lab Med*. 2010 Jun;48(6):849-54.

Arsenault et al. Obesity, coffee consumption and CRP levels in postmenopausal overweight/obese women: importance of hormone replacement therapy use. *Eur J Clin Nutr*. 2009 Dec;63(12):1419-24.

Kotani et al. The relationship between usual coffee consumption and serum C-reactive protein level in a Japanese female population. *Clin Chem Lab Med*. 2008;46(10):1434-7.

Anti-inflammatory materia medica

- Most salicylate-containing herbs probably act through other constituents or through humoral effects. An exception is probably *Filipendula*, which has the strong aroma of methyl salicylate.
- Oils of wintergreen and sweet birch (methyl salicylate) are potent and potentially toxic.

Matricaria, Achillea

- Azulenes, chamazulenes, in both, other constituents specific to each
- Topical, intestinal, hepatic inflammation
- Substantial research in vitro, in vivo, and clinical research

Althea, calendula, plantago

- **Althea as topical and GI antiinflammatory**

Hage-Sleiman R, Mroueh M, Daher CF. Pharmacological evaluation of aqueous extract of *Althaea officinalis* flower grown in Lebanon. *Pharm Biol.* 2011 Mar;49(3):327-33. Epub 2011 Feb 1.

- **Calendula**

Parente LM, Lino Junior Rde S, Tresvenzol LM, Vinaud MC, de Paula JR, Paulo NM. Wound Healing and Anti-Inflammatory Effect in Animal Models of *Calendula officinalis* L. Growing in Brazil. *Evid Based Complement Alternat Med.* 2012;2012:375671. Epub 2012 Jan 24.

- **Plantain**

Turel I, Ozbek H, Erten R, Oner AC, Cengiz N, Yilmaz O. Hepatoprotective and anti-inflammatory activities of *Plantago major* L. *Indian JPharmacol.* 2009 Jun;41(3):120-4.

Urtica

- Traditional use in Europe for arthritis, internally, and externally via its sting.
- Substantial in vitro and in vivo research on mechanisms.
- Some clinical trials of generally poor quality
Chrubasik JE, Roufogalis BD, Wagner H, Chrubasik SA. A comprehensive review on nettle effect and efficacy profiles, Part I: herba urticae. *Phytomedicine*. 2007 Jun;14(6):423-35. Epub 2007 May 10. Review.
- Substantial empirical success, one of the best herbs to give with first onset of arthritis, as tea. Combines well with *Filipendula* for this purpose.
- Use of a combination product of fish oil, vitamin E and Urtica extract reduced the need for pain medications by 60% compared to placebo in arthritis patients.
Jacquet A, Girodet PO, Pariente A, Forest K, Mallet L, Moore N. Phytalgic, a food supplement, vs placebo in patients with osteoarthritis of the knee or hip: a randomised double-blind placebo-controlled clinical trial. *Arthritis Res Ther*. 2009;11(6):R192. Epub 2009 Dec 16.

Turmeric and Glycyrrhiza

- In animal trials, turmeric has efficacy in various panels comparable to steroids. There is no evidence of suppressive side effect in humans in doses that significantly decrease inflammation.
- Licorice may support anti-inflammatory strategies by extending the half-life of cortisol, an endogenous anti-inflammatory steroid
- In empirical usage, the combination can help wean patients off NSAID, and in some cases is more effective than NSAID for chronic inflammatory pain.
- Licorice may also offer potent topical anti-inflammatory effect on skin or the upper GI gut lining.

Zingiber

- Eight published trials demonstrating effectiveness (481 participants), were included in a systematic review.

Terry R, Posadzki P, Watson LK, Ernst E. The use of ginger (*Zingiber officinale*) for the treatment of pain: a systematic review of clinical trials. *Pain Med.* 2011 Dec;12(12):1808-18. doi: 10.1111/j.1526-4637.2011.01261.x. Epub 2011 Nov 4.

- Example trial with effective dose (2 grams per day)

Black CD, Herring MP, Hurley DJ, O'Connor PJ. Ginger (*Zingiber officinale*) reduces muscle pain caused by eccentric exercise. *J Pain.* 2010 Sep;11(9):894-903. Epub 2010 Apr 24.

- Combines well with turmeric and licorice. Modify curcumin:zingiber:glycyrrhiza proportions for patient depending on presenting pattern. Corrigent is honey or almond oil.

Angelica archangelica and Apium

- Traditional pairing in European herbal rheumatology

Sarker SD, Nahar L. Natural medicine: the genus *Angelica*. *Curr Med Chem*. 2004 Jun;11(11):1479-500.

- Articles on *Apium* leaf and seed

Mencherini T, Cau A, Bianco G, Della Loggia R, Aquino RP, Autore G. An extract of *Apium graveolens* var. *dulce* leaves: structure of the major constituent, apiin, and its anti-inflammatory properties. *J Pharm Pharmacol*. 2007 Jun;59(6):891-7.

Powanda MC, Rainsford KD. A toxicological investigation of a celery seed extract having anti-inflammatory activity. *Inflammopharmacology*. 2011 Aug;19(4):227-33. Epub 2010 Jun 22.

Rosmarinus and Salvia

- Rosmarinic acid is anti-inflammatory

al-Sereiti MR, Abu-Amer KM, Sen P. Pharmacology of rosemary (*Rosmarinus officinalis* Linn.) and its therapeutic potentials. *Indian J Exp Biol.* 1999 Feb;37(2):124-30.

- Salvia review

Kamatou GP, Makunga NP, Ramogola WP, Viljoen AM. South African *Salvia* species: a review of biological activities and phytochemistry. *J Ethnopharmacol.* 2008 Oct 28;119(3):664-72. Epub 2008 Jul 2.

Berberine-containing herbs

- Berberis, Mahonia, Coptis, Hydrastis, and related plant contain berberine and related proto-berberine alkaloids.
- Substantial research into anti-inflammatory and antidiabetic actions of berberine.
- In three trials of berberine in diabetes. 1000-1500 mg of berberine. If berberine content of Mahonia is 2%, that means the minimum dose would be 50 grams. Impossible to attain this with reasonable doses of crude herb.

Meng S, Wang LS, Huang ZQ, Zhou Q, Sun YG, Cao JT, Li YG, Wang CQ. Berberine ameliorates inflammation in patients with acute coronary syndrome following percutaneous coronary intervention. Clin Exp Pharmacol Physiol. 2012 Jan 3.

Commiphora gum

- Alone or in combination with Boswellia, in vitro trials
- Traditional Thomsonian combination: Myrrh and capsicum, 16 parts myrrh tincture to one part capsicum tincture.
- Used internally to enhance host resistance and stimulate vitality, and also as topical stimulant and antimicrobial.
- Unani corrigent is honey, corrigent for capsicum is milk or ghee.
- Myrrh also combines well with bitter berberine containing herbs

Disk 7 Pathophysiology of food intolerance

Food Intolerance Overview

Digestive pathologies

Therapeutics Overview

Gut ecology and evolution

Nutrition for enterocytes

Food Intolerance and the gut barrier

Lectins

Gluten and oats

Outline of second half of course

- Overview of digestive pathologies and therapeutics.
- Gut ecologies and the evolution of enterocytes
- Conditions routinely cured with removal of food intolerance.
- Elimination diets in history
- Clinical Observations
- Assessment
- Withdrawal and rechallenge protocol
- Modified fasting and dietary therapeutics
- Herbal therapeutics

Digestion is the trunk of the Tree of Life

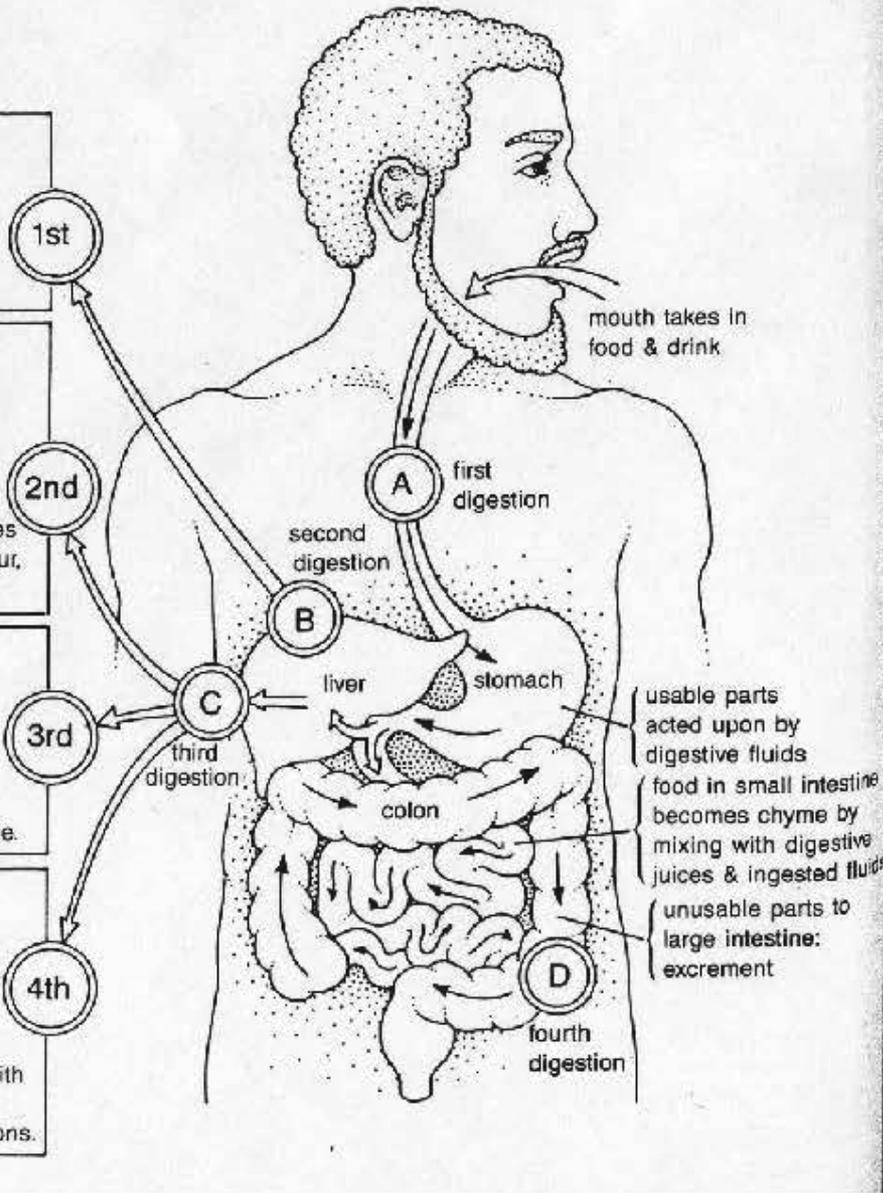
A primary target of therapeutics for chronic or acute disease in all systems of traditional medicine

Blood Humor
(hot & moist)
superior nutrients
are taken via blood-
stream to heart &
general bloodstream

Phlegm Humor
(cold & moist)
normal digestion
converts into mucus,
saliva, gastric &
intestinal mucus
abnormal digestion causes
excess mucus (sweet, sour,
thick, thin, etc.)

Bilious Humor
(hot & dry)
normal bile formed in
liver, affects blood &
acts in small intestine.
abnormal humor causes
destructive changes in bile.

Atrabilious Humor
(cold & dry)
normal humor goes to
spleen & blood, & mixes
with phlegm essence.
abnormal humor passed
out as ash, or admixes with
blood & other humors
producing morbid conditions.



Greek Medicine

All humors arise during the stages of digestion.

The primary therapeutics are diet and herbal formulas which promote healthy digestion and elimination.

Identical concepts in Ayurvedic and Chinese medicine.

Essential digestive pathologies

- Under- or over eating, generally and specific
- *Individual incompatible foods*
- *Immunologically incompatible foods*
- Chronic dysbiosis
- *Failure to maintain healthy gut barrier*
- Iatrogenic injury to gut wall or microbiome
- Acute bacterial or viral infection
- Parasitic infection
- *Stress / sleep debt*

Therapeutic interventions

- Nutritional support for digestive processes
- *Dietary selection / screening for offending foods*
- Withdrawal from drugs which damage the gut ecosystem.
- Intermittent fasting
- Probiotics/prebiotics
- Herbal therapeutics

Gut ecology and co-evolution

- The gut surface from the *muscularis mucosa* out into the microbiome may be viewed as a unified semi-independent ecology.
- This ecological system may be viewed as a functional organ with profound effects throughout the body through:
 - Signaling from bacterial metabolites (SCFA etc)
 - Immune signaling via lymphocytes

Nutrition for the enterocytes

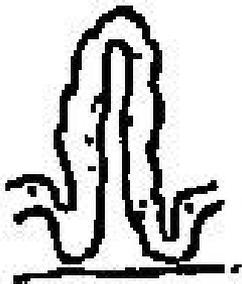
- The enterocyte layer regenerates completely in 3-6 days. The blood supply cannot supply sufficient nutrients to support this regeneration.
- The enterocytes have co-evolved with the microbiome, and depend on short chain fatty acids for fuel and metabolic signaling.
- 10-15% of average human nutrition, both local in the gut and systemic, may come from SCFA metabolized in the colon.
- They also require amino acids and nucleotides from the lumen (from diet or from recycled cell material)

*Consider implications for archetypal paleodiet rich in **protein, vegetables, roots.***

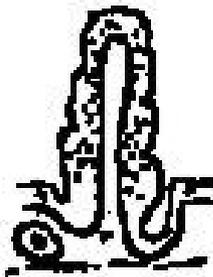
Food intolerance and the gut barrier

- Foods may injure in a non-specific manner via non-specific immune responses.
- Activation of the lymphocytes in the gut lining may cause systemic inflammation, allergy, or autoimmunity through immune cytokine secretion, antibody production, or migratory immune cells throughout the system.
- Chronic activation through repeated and heavy exposure to food antigens is one of the pillars of contemporary chronic disease

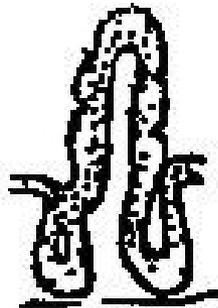
Stages of celiac disease



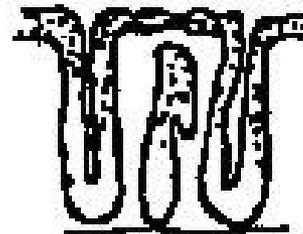
"Pre-infiltrative"
(Type 0)



"Infiltrative"
(Type 1)



"Hyperplastic"
(Type 2)



"Destructive"
(Type 3)



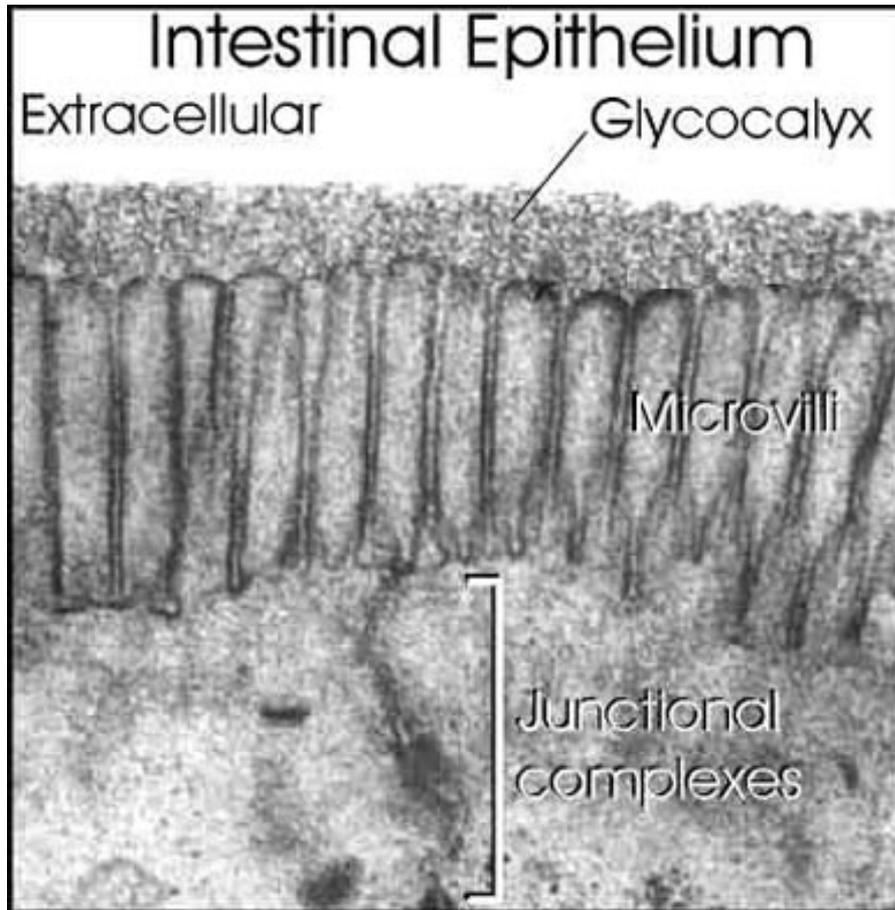
"Hypoplastic"
(Type 4)

All-cause Mortality in the stages of Celiac disease

	Hazard Ratio	Mortality Rate #/(1000 person yrs.)
Latent	1.35	6.7
Inflammation of bowel	1.72	25.9
Villous atrophy	1.39	10.4

Ludvigsson JF, et al. Small-intestinal histopathology and mortality risk in celiac disease. JAMA. 2009 Sep 16;302(11):1171-8.

Food Lectins



- May damage gut by injuring the glycocalyx in a non-immunological manner.
- May also injure endothelial glycocalyx
- Lectins common in grains, beans, and nightshades

Lectin avoidance trial

- 200 patients with risks for heart disease, 72% with endothelial dysfunction
- Avoided grains, beans, and nightshades
- Replaced with green vegetables, meats, fish, and olive oil, also took fish oil and vitamins.
- After six months, only 20% had endothelial dysfunction.
- Not strong science, but unusual intervention.

Gundry SR. Lectin Linked with endothelial dysfunction. American Heart Association's Arteriosclerosis, Thrombosis and Vascular Biology 2013 Scientific Sessions

Leaky gut syndrome

- Failure of gut regeneration and tight junctions due to malnutrition
- Failure of regeneration and junctions due to disturbed microbiome composition or function
- Drug injury from antibiotics or anti-inflammatory drugs
- Injury due to non-specific inflammation or lectin damage
- Chronic immunological reaction to foods.

“Unless you are willing to screen all your patients for incompatible foods, coach them through an elimination, and counsel them to avoid those foods strictly and permanently, you may as well find another profession.”

Dr Harold Dick to Paul Bergner, NCNM, 1986.

Some digestive disorders routinely cured with food elimination

- ▶ Chronic upper GI (GERD) 100%
- ▶ Poor appetite, chronic nausea 100%
- ▶ Chronic digestive bloating 100%
- ▶ Chronic constipation
- ▶ Chronic diarrhea
- ▶ Chronic lower bowel (ulcerative colitis, Crohn's disease, Irritable bowel syndrome. (100%)

Based on review of 3000+ cases

Some systemic conditions routinely cured with elimination of food intolerances

- ▶ Connective tissue autoimmunity. (100%). Multiple lupus cases
- ▶ Fibromyalgia
- ▶ Chronic lymphadenopathy
- ▶ Chronic URI (sinus, sore throat, bronchitis). (100%)
- ▶ Chronic inhalant allergies/asthma (100%)
- ▶ Chronic UTI: (secondary to dysbiosis)
- ▶ Cervical dysplasia
- ▶ Chronic musculoskeletal pain:
- ▶ Vague neurological complaints.
- ▶ Chronic insomnia. Recovery may be complicated by sleep med addiction
- ▶ Chronic anxiety/panic disorder (100%) 6 cases.
- ▶ Chronic depression. Many cases.

Based on review of 3000+ cases

Disk 8 Food Intolerance I

Case studies detail

Elimination diets in history

Salisbury diet

Homeopaths

NAIMH Experience

Cases from Day 1

- Cases 1 and 2. CHF. Both patients removed milk products and strictly adhered to the diet.
- Cases 3 and 4. SLE. Both patients removed all milk and glutenous grains, took anti-inflammatory fish and oils, and treated leaky gut with herbs.
- Cases 5 and 6. Nephritis and ITP. Pt 5 removed gluten, Pt 6 removed gluten and dairy. Both now regress if they eat small amounts of the food.

- Case 7. RA and IDDM. Removed dairy, took omega-3 rich fish and oils, herbs for leaky gut syndrome and followed whole food diet.
- Case 8. Severe migraines. Removed milk, took leaky gut herbal formula. Migraines recurred with exposure to “non-dairy” creamer containing casein protein
- Case 9. Severe eczema. Buttermilk solids in gluten free flour mix.
- Case 10. Fibromyalgia and mental illness. Removed dairy and glutenous grains. Herbs for leaky gut syndrome. Omega-3 rich fish and oils. Whole foods diet.

- Cases 11 and 12. Ulcerative colitis. Both patients removed milk. Patient 11 had comprehensive natural therapy with oils, probiotics, and herbs. Patient 12 improved diet but did little other than remove the dairy.
- Case 13. Lymphadenopathy. Removed gluten.
- Case 14. Panic and anxiety. All 6 removed either dairy or glutenous grains or both. All were anxiety free within 3 weeks of withdrawal.
- Case 15. Bipolar. Patient eliminated soy protein and dairy. Began to eat a whole foods diet.
- Case 16. Patient eliminated dairy and glutenous grains. Takes vitamin D. eats a vegetable rich whole foods diet. Takes herbs for leaky gut.
- Case 17. Fish and non-starchy vegetables for 21 days.
- Case 18. Powders of Calendula, Plantago, and Althaea in applesauce

Food elimination traditions in history

- Hippocratic Corpus recognized milk allergy as potential cause of serious disease, and noted a dose/threshold effect.
- Alexandrian medicine, to the present: fasting during inflammation or fever.
- Alexandrian/Roman medicine. Meat and vegetable diet as prevention and intervention in chronic disease (Celsus, *De Medicina*).
- Henry Lindlahr, ND (1913) noted that some patients could not digest milk or bread, and prescribed the meat and vegetables diet for some. Said to prefer potato to wheat for starch.
- Contemporary movement = Paleolithic/Primal Diet

“One should ascertain that food which first causes heartburn, followed by bloating, and ultimately by constipation or copious gas, and avoid it.”

From the label of an alterative formula from the Napiers
Clinic, Edinburgh, Scotland 1947

James Salisbury, MD

- Army doctor during the war, experimented with dietetics for tuberculosis, recovery from typhoid, and chronic diarrheal diseases.
- Did experiments with subjects eating single foods for 3-30 days. Found meat to be the only food that could be eaten without ill effects.
- Developed a high meat (2/3 of intake) diet with hot water, and limited grain.
- An intervention diet for 4-12 weeks.
- Note importance for *gut healing*

- U.S. Homeopaths ca. 1890s. “Of all the schools of medicine practicing today, the Homeopaths are strictest in their insistence that the patient avoid those foods which oppress the stomach or burden the system.”

The Eclectic John Scudder, MD commenting on the success of Homeopathic medicine.

Experience at NAIMH, Boulder, CO

- Between 1996 and 2013, 236 students completed 2 years of more culminating in clinical training
- Students were encouraged to perform a well-managed elimination and rechallenge of suspected food intolerances as part of their training.
- By the time of graduation 235 of 236 students had found an intolerance to either dairy or gluten. About 1/3 were intolerant of both.
- Many also had a 3rd or 4th intolerance

Most common intolerances seen

- Milk products
- Glutenous grains
- Soy
- Egg
- Nuts
- Occasionally seen: Nightshades, pork, beef, misc.

Disk 9 Food Intolerance II

Clinical Observations

Addictive relationship with foods

Common erroneous beliefs

Allergy vs intolerance

Complete elimination

Clinical observations

- Everyone seen with chronic disease had a food intolerance
- 3-6 weeks elimination is necessary to assess effects. Much longer for full recovery of some chronic symptoms
- Withdrawal must be *complete*. Small or covert exposure may negate test.
- Withdrawal must be *permanent*.
- Most patients have an addictive relationship with their allergen, characterized by denial and minimization.

Common erroneous beliefs

- People outgrow their allergies.
- After a withdrawal, it is OK to have a little bit without consequences.
- Because my former chief complaint is gone, or lessened, then the small amounts I eat are not causing me any problems
- A lifestyle of food elimination is miserable and impossible to sustain.

Practitioner skills: treat or cure?

- “Will you explore cooperatively with your patient the roots of their chronic illness and invite them to a *higher level of self-mastery*, or will your practice burn itself out in the endless pursuit of the next shiny bauble or magic bullet”
- For the practitioner: “You can’t push spaghetti uphill (G. Patton)”

Withdrawal must be complete

- 32 y.o female with eczema (archetypal case)
- Withdrew all dairy and milk except cream in coffee
- Eczema improved, but lingered
- Patient removed cream from coffee reluctantly
- 3 weeks later, eczema disappeared completely
- 6 months later she reintroduced the cream in the coffee
- 3 weeks later, eczema returned
- Resolution on re-withdrawal



Severe eczema caused by covert milk-solids in gluten-free pancake mix.
Completely resolved with elimination of milk

Archetypal case

- A patient with long standing systemic lymphadenopathy and severe inhalant allergies was certain that she had done a gluten elimination for more than one year, with no improvement
- After a well-coached true elimination and rechallenge, her symptoms were almost entirely due to gluten.
- She had been drinking beer (contains gluten) several days a week during the original elimination trial.

Case

“I knew there was something going on when I found myself dancing to Marvin Gaye while I fixed breakfast for my teenage sons”

Many patients find a new level of health they did not know was possible after elimination. They had previously become habituated to the food intolerance symptoms and thought they were normal.

Disk 10 Assessment I

Assessment

Digestive symptoms

Abdominal bloating

Constipation

Chinese liver patterns

Diet assessment

Symptomology: The food allergy triangle

Gastrointestinal

Connective Tissue

Mood/Energy

Signs of a poorly functioning digestion

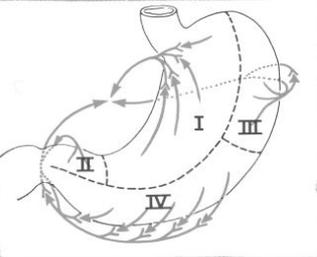
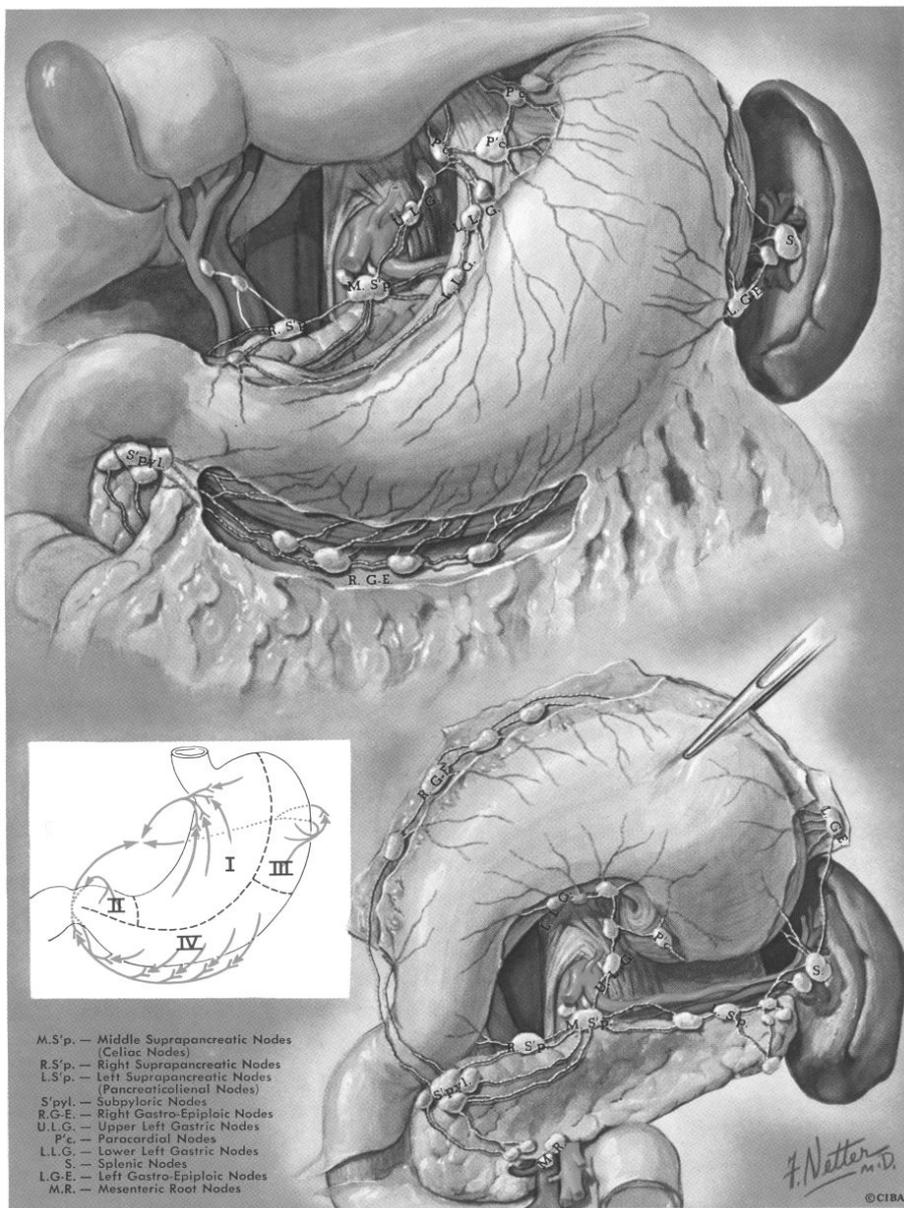
- Flatulence or belching
- Nausea
- Pain anywhere in the digestive tract
- Undigested food in the stool
- Offensive breath
- Constipation (less than one bowel movement per day)
- Lethargy or depression after meals
- Food cravings other than normal hunger
- Lack of satisfaction after meals
- Lack of hunger for breakfast

*The patient habituated to any of these symptoms may consider them normal. Exploration during **interview** may be essential to discover imbalances*

Food Intake List all foods & drinks consumed		Fine Tune Your Diet			
Today's Date:		Place a check to the left of all descriptions that describe your experience 1-2 hours after each meal			
Meal: Breakfast Lunch Dinner (circle one)	Appetite Satiety Cravings	<input type="checkbox"/>	Feel full, satisfied	<input type="checkbox"/>	Feel physically full, but still hungry
		<input type="checkbox"/>	Do NOT have sweet cravings	<input type="checkbox"/>	Have desire for something sweet
		<input type="checkbox"/>	Do NOT desire more food	<input type="checkbox"/>	Not satisfied, felt like something was missing
		<input type="checkbox"/>	Do NOT feel hungry	<input type="checkbox"/>	Already hungry
		<input type="checkbox"/>	Do NOT need to snack before next meal	<input type="checkbox"/>	Feel the need for a snack
Foods Consumed:	Energy Levels	<input type="checkbox"/>	Energy feels renewed	<input type="checkbox"/>	Meal gave too much or too little energy
		<input type="checkbox"/>	Have good lasting "normal" sense of energy	<input type="checkbox"/>	Became hyper, jittery, shaky, nervous or speedy
		<input type="checkbox"/>	Energy tanked from meal-exhaustion, sleepiness, drowsiness, listlessness or lethargy	<input type="checkbox"/>	Felt hyper but exhausted underneath
	Mind Emotions Well-Being	<input type="checkbox"/>	Improved well-being	<input type="checkbox"/>	Mentally slow
		<input type="checkbox"/>	Sense of feeling refueled, renewed and restored	<input type="checkbox"/>	Inability to think quickly or clearly
		<input type="checkbox"/>	Some emotional upliftment	<input type="checkbox"/>	Hyper, overly rapid thoughts
		<input type="checkbox"/>	Improved mental clarity and sharpness	<input type="checkbox"/>	Inability to focus or concentrate
		<input type="checkbox"/>	Normalization of thought process	<input type="checkbox"/>	Apathy, depression, withdrawal or sadness
		<input type="checkbox"/>		<input type="checkbox"/>	Anxious, obsessive, fearful angry or irritable

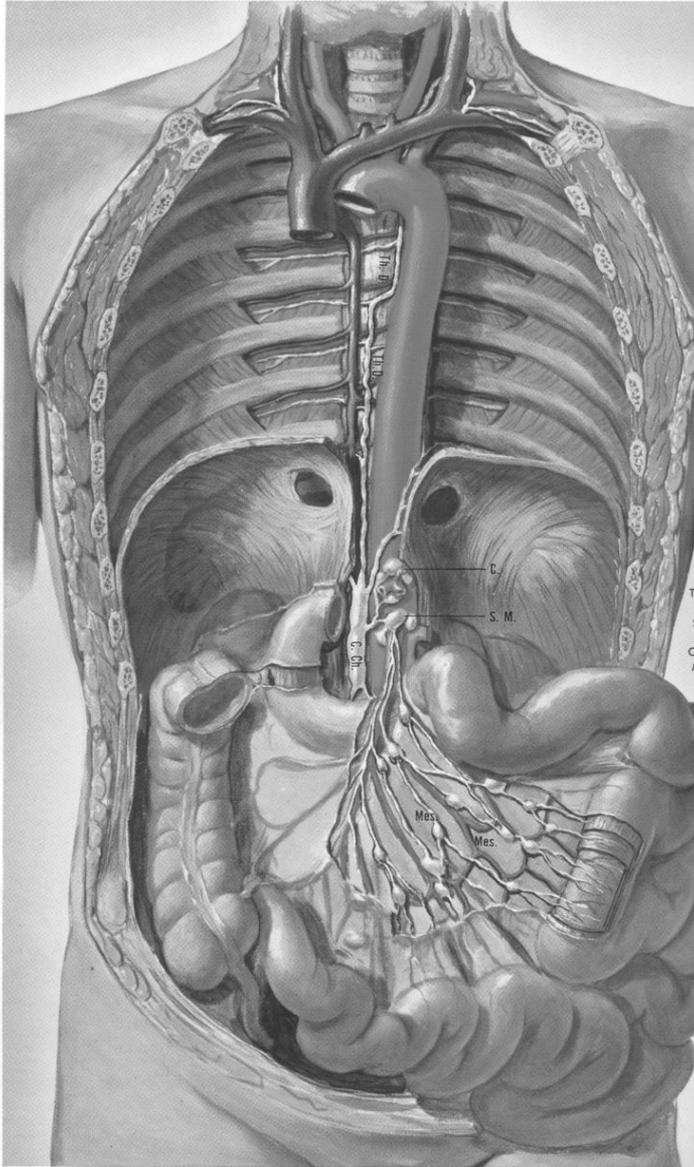
Metabolic and psychological symptoms of poor digestion at 2 hours post-meal.

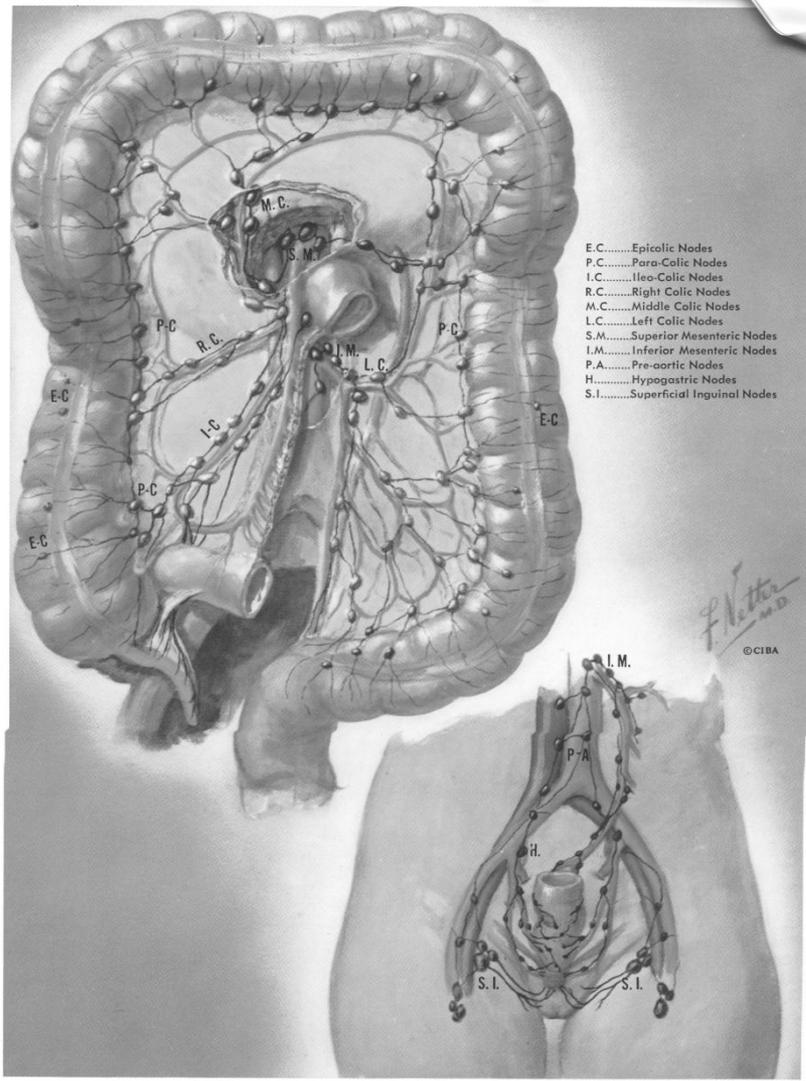
The patient may have to experiment with food eliminations, macronutrient balance, etc in order to find their specific 'best diet.'



- M.S'p. — Middle Suprapancreatic Nodes (Celiac Nodes)
- R.S'p. — Right Suprapancreatic Nodes
- L.S'p. — Left Suprapancreatic Nodes (Pancreaticocolleal Nodes)
- S'pyl. — Subpyloric Nodes
- R.G.E. — Right Gastro-Epiploic Nodes
- U.L.G. — Upper Left Gastric Nodes
- P'c. — Paracardial Nodes
- L.L.G. — Lower Left Gastric Nodes
- S. — Splenic Nodes
- L.G.E. — Left Gastro-Epiploic Nodes
- M.R. — Mesenteric Root Nodes

F. Netter M.D.
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- E.C.....Epiploic Nodes
- P.C.....Pari-Colic Nodes
- I.C.....Ileo-Colic Nodes
- R.C.....Right Colic Nodes
- M.C.....Middle Colic Nodes
- L.C.....Left Colic Nodes
- S.M.....Superior Mesenteric Nodes
- I.M.....Inferior Mesenteric Nodes
- P.A.....Pre-aortic Nodes
- H.....Hypogastric Nodes
- S.I.....Superficial Inguinal Nodes

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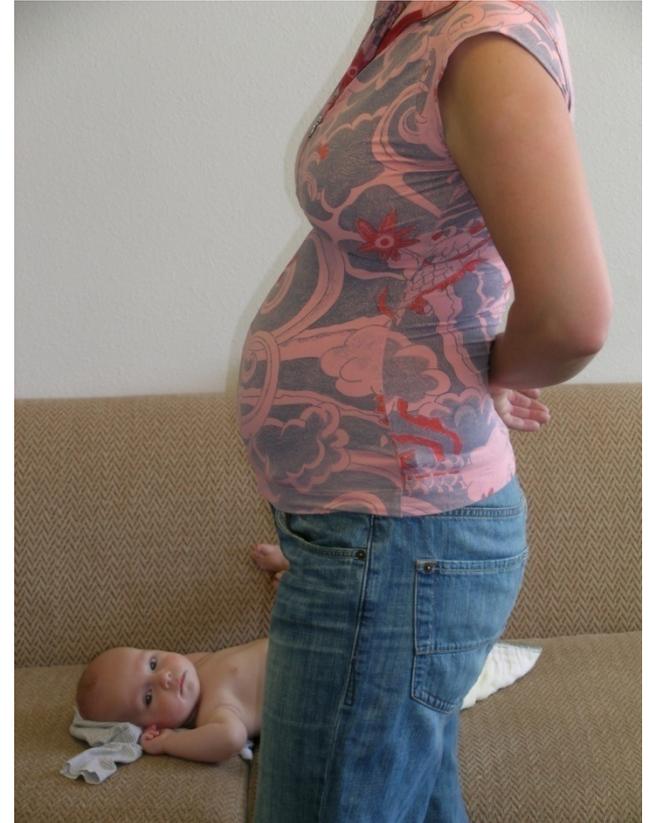
Evening-to-morning bloating pattern before dairy removal



Resolved chronic headaches, chronic yeast infections, constant nausea, and chronic fatigue



Abdominal lymphadenopathy after re-exposure to chicken-egg antigens



Bloating resolved within a week of return to avoidance of eggs. Patient eventually was cured of long-standing MRSA infection

Abdominal swelling before and after elimination of dairy and gluten



Migraine headaches completely absent after withdrawal

Constipation

Milk allergy may be the cause of 60-80% of cases of chronic constipation in children.

Gluten and other food intolerances may cause constipation

Magazzi and Scoglio. Gastrointestinal manifestations of cow's milk allergy. *Ann Allergy Asthma Immunol.* 2002 Dec;89(6 Suppl 1):65-8.

Pattern from Chinese medicine

- Stuck Liver Chi; Liver Fire Rising; False cold
- Patient has heat signs at the core. May also manifest in the head and/or the pelvis, but along vertical axis.
- Hands and feet always cold.
- Irritable, depressed.
- Affects about 1 / 3 of general student/patient community.
- Most common causes: food intolerance; exogenous hormones
- Usually resolves completely with removal of foods.

Quick diet assessment

- Quick query on typical, best, and worst meals
- Ask about breakfast, lunch, dinner, and snacks.
- Ask about exceptions, like when traveling, under stress, unable to prepare or obtain preferred food, binges, etc. Be sure to get the *frequency* that such meals or snacks are consumed. This is often where people “cheat” on their known allergens and this is frequently how the inflammation/autoimmunity is kept at a rolling boil.
- Look for patterns of common allergens.

Disk 11 Assessment II

Diet diary

Interview process

Intuitive eating exercise

Lab Testing

Lab test studies

Diet diary

- First discuss if the patient has issues or resistance to doing a diet diary, and explore interest/willingness.
- Offer that the patient may keep the diary to themselves if they don't want to show it to you. Simply going through the process will often improve the patient's insights and diet.
- Emphasize the need to eat typically, including binge foods, and to record honestly. (diet diaries typically underreport soft drink consumption by about 50% according to industry statistics)
- Have columns for time, food or drink, activity, and mood/energy for 3-4 days.
- Look for patterns of common allergens, or mood/energy crashes after meals or after specific foods.

Interview Process

- If digestive symptoms are present on intake, inquire into the other two legs of the FI Triangle.
- “Do you have any food which causes heartburn, bloating, constipation, and/or gas or other symptoms?” (May
- supplement with diet/mood/energy diary)
- Ask if the person has a known intolerance
- Ask if the person suspects an intolerance
- Ask if patient was allergic to anything in childhood
- Ask if patient has an addictive relationship with common allergen.

Intuitive eating exercise

“Just before shopping, before selecting food in your kitchen, before selecting a restaurant to eat at, and before selecting food from a menu, perform the following exercise:

- 1) Take a few breaths, and then make the affirmation that you intend to set aside all your preconceptions about what foods are good or bad for you today.
- 2) Take a few more breaths, and make the affirmation that you intend to consult your highest and most accurate intuition about what foods are good or bad for you today.
- 3) Be open to the many ways that intuition can give you a response.
- 4) When you get a response, pose the question to your intuition whether the response is a true intuition or a craving.

See Hunter-gatherer Hardwiring article in resource directory.

Lab testing for food intolerances

- Not all food intolerances are mediated by specific immunity and measurable by antibodies.
- Antibody or cytotoxic testing have well documented rates of false positives and false negatives.
- Immunological tests are not validated according to contemporary lab standards.
- Many labs fail “split sample” testing standards. 2 of 3 labs in Bastyr study; 1 of 2 labs in NCNM study.

Lab testing study #1

- 65 patients with either irritable bowel syndrome or functional dyspepsia, plus 20 controls.
- Patients were evaluated for serum IgG and IgE antibodies to 14 common food allergens. Total serum IgE to all foods was also assessed. Symptoms severity scores were obtained for their conditions.
- Patients with IBS had higher titres of IgG antibody to egg, shrimp, crab, soy, and wheat. FD patients had higher IgG antibodies to egg and soy. There was no difference in IgE antibodies between the three groups.
- **No correlation** was found between IgG antibody titres and symptoms scores in IBS and FD patients.
 - Zuo XL et al. Alterations of food antigen-specific serum immunoglobulins G and E antibodies in patients with irritable bowel syndrome and functional dyspepsia. Clin Exp Allergy. 2007 Jun;37(6):823-30

Lab testing study #2

- In a review letter, one expert in IBS and IgG testing provides comprehensive references showing that antibody levels show poor correlation to results of rigorous elimination diets in IBS
- In responding to a study that found elevated IgG antibodies to food antigens in 100% of patients with IBS, he states that one-third of IBS patients fail to respond to rigorous elimination of any specific food, and that elimination based on IgG antibodies would be wasted in that percentage of patients, and ineffective in many of the others.
 - Hunter JO. Food elimination in IBS: the case for IgG testing remains doubtful. *Gut*. 2005 August; 54(8): 1203

Lab testing study #3

- The study design modeled real-life office-based conditions where lab reports are assessed, and diet changes to an extensive list of foods is recommended. In addition, dieticians provided six-week detailed meal plans. The average number of foods eliminated was 24, with a range of 13 to 35.
- After establishing the baseline parameters with a normal diet, in a cross over design, each patient spent six weeks each on the elimination diet and six more on an allergen-rich provocation diet.
- Days with a migraine decreased 30% during the elimination, and number of attacks decreased 32%. There was no change during the provocation period. Baseline headaches ranged from 4.5 to 13.5; during elimination the range was from 2.5 to 10.0.
 - Alpay, K et al. Diet restriction in migraine, based on IgG against foods: A clinical double-blind, randomised, cross-over trial . Cephalalgia. 2010 July; 30(7): 829–837.

Complete resolution of migraines is common with the methods taught in this course

Disk 12 Elimination and rechallenge

Why withdrawals fail

Elimination protocol

Two dietary approaches

Flower essences

Follow up

Rechallenge

GAPS diet

Blood type diet

Why withdrawals fail

- Withdrawal was not complete due to poor instructions
- Withdrawal was not complete due to covert foods
- Withdrawal did not last long enough
- *Withdrawal succeeded but progress was not accurately assessed*
- There is a second and/or third allergen involved
- Persistent intestinal dysbiosis
- Persistent leaky gut from nutrient deficiencies/under-eating
- Persistent leaky gut from vitamin D deficiency

When the patient agrees to an elimination

1. Explain the need for complete withdrawal
2. Explain covert sources. See many internet resources.
3. Explain possible benefits
4. Spend 30 minutes discussing favorite foods that are *not* the allergen. Provide recipes, cookbook ideas.
5. Do a complete listing of all symptoms on the triangle with severity scores
6. Do a complete evaluation of objective signs, abdominal sx; range of motion, etc.
7. Initiate comprehensive GI therapeutics protocol

Two approaches to hypoallergenic diet

- Negative approach:
Elimination of suspected allergens.
- Start with suspected major allergen
- Then eliminate further suspects if symptoms persist
- Positive approach: List of ad-libitum foods
- Select according to tastes and likes of the patient
- Counseling, meal planning for breakfast, lunch, dinner, and snacks
- Planning for restaurant meals
- Planning for times of anticipated “cheats”

Framing the diet

- Specific Allergen-free
- Grain-free
- Meat, fish, vegetables
- Paleo
- Primal
- etc.

Follow up and flower essences

- Withdrawal triggers strong emotional responses and negative mental/emotional states
- Follow with counseling, encouragement, and if possible, flower essence therapy at least weekly.
- At 3 weeks, *without rechallenge*, do a complete listing of all symptoms on the triangle with severity scores, plus a complete evaluation of objective signs, abdominal sx, range of motion, etc. Compare to original symptoms.
- Reevaluate GI therapeutic protocol

Patient 1 had “no improvement”

Joints and Muscles

	Week 1	Week 6
pains or aches in joints	5	2
stiffness	4	2
pains or aches in muscles	5	2
weakness	4	2
numbness	4	1
Score	22	9

Patient 2 had “a little bit” of improvement

Joints and Muscles

	Week 1	Week 3
pains or aches in joints	5	3
Stiffness	2	0
pains or aches in muscles	3	0
Numbness	2	0
swelling in hands or feet	2	0
Total	14	3

Patients reported little or no improvement

After:

- Disappearance of chief complaint, hip pain disturbing sleep,
 - after 3 weeks
- Disappearance of panic attacks after 3 weeks
- Disappearance of deep depression after 3 weeks (patient
 - was enraged)

Rechallenge

The patient will frequently do an unintentional rechallenge before the six weeks is up. Encourage them to do a full rechallenge at six weeks.

At six weeks, the patient consumes the food daily for at least 4 days, 7 days is better, noting and journaling any symptoms that appear

After the 4th day of rechallenge, perform again a global assessment of symptoms, and compare to the original and 3rd week assessments.

Continue symptoms journal for 2-3 weeks after second elimination

Disk 13 Therapeutics

Overview

Nutrition

Probiotics

Bitters

Candidiasis

Parasites

Herbal therapeutics

Therapeutics Overview

- Complete and permanent elimination of antigen
- Removal of injurious drugs/herbal substitutions
- Optimize vitamin 25(OH) D3 to >60 ng/mL
- Optimize protein, glutamine nutrition
- Optimize nucleotide nutrition
- Optimize wound-healing nutrients (Zn, C, Vitamin A)
- Optimize anti-inflammatory nutrition.
- Intermittent fasting
- Probiotic therapy
- Foods and herbs for the microbiome
- Support normal digestion with herbs
- Wound healing herbs in gut
- Consider lymphatic and immunomodulating herbs
- Psychospiritual: Flower essences, Homeopathy

Macronutrient considerations

- High protein diet. Nutrient rich, protein rich meat soups and stews
- Enrich with trace elements and mineral nutrition with wild foods, herbs, ocean fish, seaweeds, etc.
- High soluble fiber low glycemic carbohydrates, specifically vegetables, fruits, roots. Aim for 10 half-cup servings of fruits and vegetables per day, emphasizing greens and vegetables. Prefer cooked vegetables.

Glutamine supplementation in clinical trials

- 18–30 g per day, orally
- 10 g three times per day, orally
- 0.57 g per kg of body weight per day
- 14 g of glutamine per day in combination with arginine and HMB for up to 24 weeks

Acute or chronic glutamine use as isolated amino acid may cause excitotoxicity in some patients

Ranges of glutamine and zinc in a Paleolithic human diet

	Zn	Glutamine
30 oz buffalo	50mg	38g
30 oz venison	42mg	31g
30 oz beef 95% lean	62mg	39g

Implications for Paleodiet, Salisbury diet, etc.

Fasting and Ghrelin

- Secreted by the gut wall of the stomach, small intestine, and large intestine when empty
- Stimulates hunger centers in hypothalamus
- Promotes growth hormone
- Has local and systemic anti-inflammatory effects
- May act as selective Cox-2 inhibitor
- Has febrifuge effects
- *Promotes autophagy in the system and locally in the gut, releasing amino acids and nucleotides locally*
- *Promotes gut remodeling.*

Fasting

- Fasting during acute inflammatory attacks
- Fasting during fever
- Emptying the stomach and bowels at onset of febrile illness or inflammatory attack.
- Intermittent, partial: eating:fasting on 8hr:16hr schedule
- Intermittent, short: dinnertime to dinnertime 1-2 non-sequential days/wk.
- Caution with any longer fast unless the individual is robust, damp, warm, and excess in constitution or condition. Never in the hypersensitive patient.
- Henry Lindlahr: “May cause *serious* and *permanent* harm.”

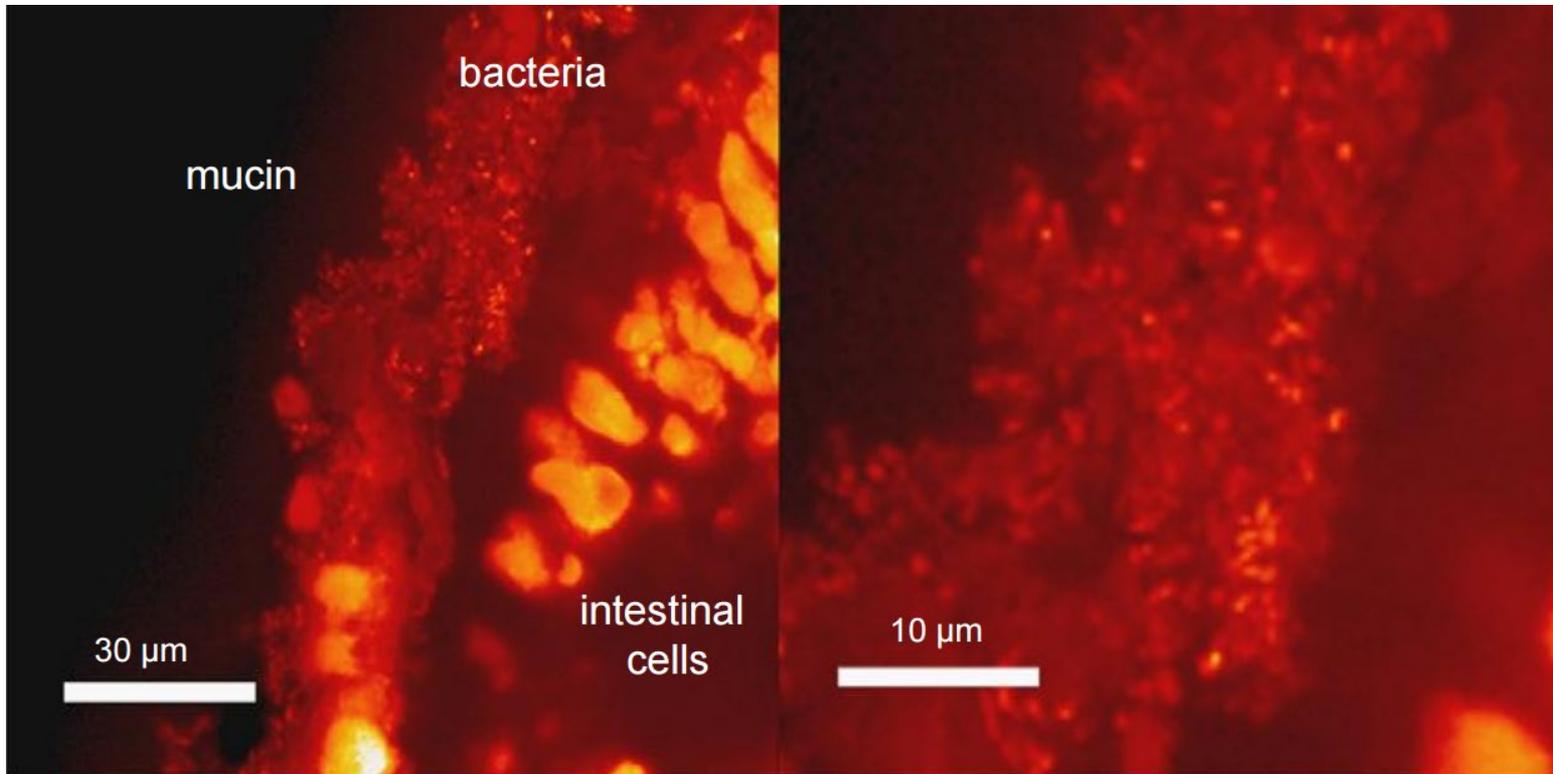
*The effects of some herbs are **greatly magnified** during the fasting state*

- Detoxifying alteratives
- GI antiinflammatories
- Gut-Healing vulneraries

Probiotics

Probiotics

- *Acidophilus* and *Bifidobacter* genera are most important.
- Adherent, lactic acid producing, also produce SCFA
- SCFA signals trigger tight junctions in the gut
- Probiotics “train” t-regulatory cells in the gut, reducing inflammation and autoimmunity.
- Probiotics reduce pathological strains in the tract.
- Live in the mucosal layer of the intestine. Can metabolize mucin.
- Absolute numbers are important
- Biodiversity of species is important



Bacterial biofilm in gut mucosal layer. Site not specified.

Lactobacillus in distal small intestine

Table 1
Rod-shaped bacteria tightly associated with ileal epithelial cells.

Biopsy n°	Strain name	Species ^a	Gene bank accession number
1	SF1031	<i>Lactobacillus mucosae</i>	FN400925
1	SF1036	<i>Bifidobacterium breve</i>	FN400926
2	SF1087	<i>Lactobacillus mucosae</i>	FN400927
2	SF1091	<i>Lactobacillus mucosae</i>	FN400928
2	SF1108	<i>Lactobacillus mucosae</i>	FN400929
2	SF1109	<i>Lactobacillus gasseri</i>	FN400930
3	SF1111	<i>Lactobacillus mucosae</i>	FN400931
4	SF1146	<i>Lactobacillus mucosae</i>	FN400932
5	SF1183	<i>Lactobacillus gasseri</i>	FN400933
6	SF1232	<i>Lactobacillus mucosae</i>	FN400934
7	SF1233	<i>Lactobacillus mucosae</i>	FN400935

^a Assessed on the basis of the nucleotide sequence of the gene coding for 16S RNA and of biochemical (API) tests.

On recovery, most species

- Produced antimicrobial substances
- Formed biofilms
- Degraded mucin
- Survived simulated gastric environment

Fakhry S, Manzo N, D'Apuzzo E, Pietrini L, Sorrentini I, Ricca E, De Felice M, Baccigalupi L. Characterization of intestinal bacteria tightly bound to the human ileal epithelium. Res Microbiol. 2009 Dec;160(10):817-23.

Commercial product from Klaire Labs

Lactobacillus acidophilus

Lactobacillus rhamnosus

Lactobacillus casei

Lactobacillus plantarum

Lactobacillus salivarius

Lactobacillus bulgaricus

Lactobacillus paracasei

Bifidobacterium bifidum

Bifidobacterium breve

Bifidobacterium longum

Bifidobacterium lactis

Streptococcus thermophilus

25 billion organisms per capsule

Lactobacillus in stomach and duodenum

- Patients with bacterial overgrowth in stomach and duodenum (SIBO) after long-term PPI use.
- 10 billion mixed *Lactobacillus* organisms
- 30 mg of N-acetyl-cysteine (anti-biofilm)
- 2.34 g potato maltodextrin (prebiotic)
- QD with main meal for 10 days.

Del Piano M, Anderloni A, Balzarini M, Ballarè M, Carmagnola S, Montino F, Orsello M, Pagliarulo M, Tari R, Soattini L, Sforza F, Mogna L, Mogna G. The innovative potential of *Lactobacillus rhamnosus* LR06, *Lactobacillus pentosus* LPS01, *Lactobacillus plantarum* LP01, and *Lactobacillus delbrueckii* Subsp. *delbrueckii* LDD01 to restore the "gastric barrier effect" in patients chronically treated with PPI: a pilot study. *J Clin Gastroenterol.* 2012 Oct;46 Suppl:S18-26.

- Strong bacterial overgrowth in the stomach and duodenum of people treated with PPIs
- “Marked antagonistic activity” of *Lactobacillus* towards 5 strains of *E. coli*
- Significantly reduced bacterial overgrowth.
- *Lactobacilli* dominated bacterial counts (gastric/duodenal) post-treatment.
- Demonstrated ability to colonize/recolonize the stomach and duodenum.
- A significant decrease in fecal enterococci, total coliforms, *E. coli*, molds, and yeasts in subjects treated was recorded at the end probiotic supplementation compared with baseline.

TABLE 3. Quantification of Total Bacterial Cells and Total Lactobacillus (Mean \pm SEM, log₁₀ CFU/mL of Gastric Juice or Gram of Duodenal Brushing) at d₀ (all Groups) and d₁₀ (Group B): Comparison Between Time 0 (d₀) and d₁₀ in Group B

Time	Group B		P†
	log CFU/mL or log CFU/g	% of Total <i>Lactobacillus</i>	
d ₀			
Gastric juice			
Total bacteria	8.60 \pm 0.17		*
Total Lactobacillus	7.15 \pm 0.25	3.51	*
Duodenal brushing			
Total bacteria	8.32 \pm 0.33		*
Total Lactobacillus	6.76 \pm 0.33	2.74	*
d ₁₀			
Gastric juice			
Total bacteria	7.71 \pm 0.27		0.0023
Total Lactobacillus	7.70 \pm 0.27	98.03	0.0742
Duodenal brushing			
Total bacteria	7.47 \pm 0.32		0.0256
Total Lactobacillus	7.44 \pm 0.32	93.50	0.0355

*Comparison reference time (d₀).

†Comparison between baseline (d₀) and d₁₀.

	Day 0	Day 10
Gastric juice		
Total bacteria	600,000,000	71,000,000
Lactobacillus	11,500,000	70,000,000

Duodenal brushing		
Total bacteria	320,000,000	47,000,000
Lactobacillus	7,600,000	44,000,000

TABLE 8. Quantification of Specific Microbial Groups in Fecal Samples at d₀ (all Groups) and d₁₀ (Group B): Comparison Between Baseline (d₀) and d₁₀ in Group B

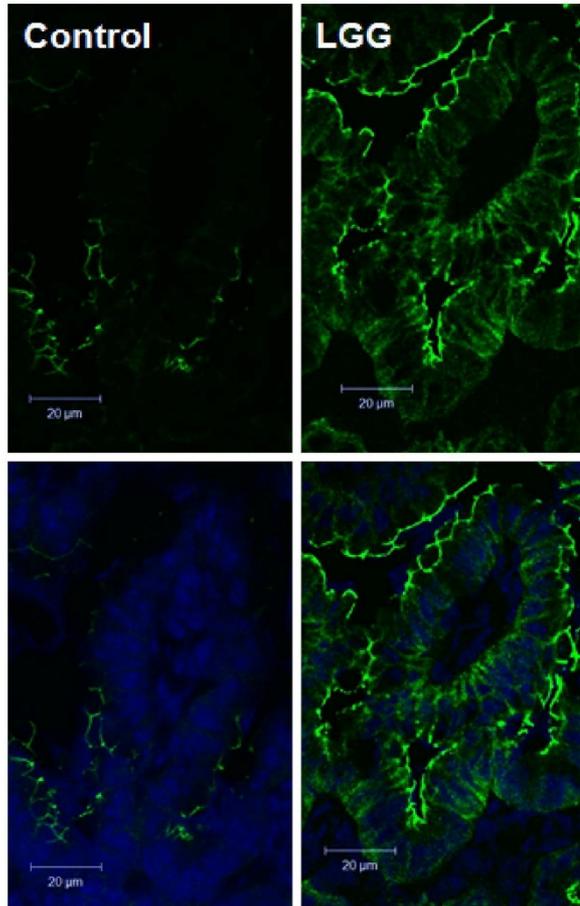
Time	Group B	
	log ₁₀ CFU/g	P [†]
d ₀		
<i>Enterococcus spp.</i>	7.80 ± 0.25	*
Total coliforms	9.55 ± 0.16	*
<i>Escherichia coli</i>	9.44 ± 0.18	*
Yeasts	5.95 ± 0.14	*
Molds	5.64 ± 0.14	*
d ₁₀		
<i>Enterococcus spp.</i>	6.99 ± 0.23	0.0155
Total coliforms	8.01 ± 0.24	0.0064
<i>Escherichia coli</i>	7.97 ± 0.23	0.0105
Yeasts	3.56 ± 0.18	0.0066
Molds	4.30 ± 0.15	0.0053

Results are expressed as log₁₀ CFU/g of feces (mean ± SEM).

*Comparison reference time (d₀).

†Comparison between baseline (d₀) and d₁₀ in group B.

Stool bacterial counts of the measured species declined on the order of 10-100 times.



Images of intestinal *Lactobacillus* biofilms in humans are difficult to find. More common are images in mice and birds.

In this scan of a mouse intestine, before and after treatment with a *Lactobacillus* species (LGG), the effects of the LGG mucosal colonization on the expression of junction protein claudin-3 is shown with the luminescent dye.

Patel RM, Myers LS, Kurundkar AR, Maheshwari A, Nusrat A, Lin PW. Probiotic bacteria induce maturation of intestinal claudin 3 expression and barrier function. *Am J Pathol.* 2012 Feb;180(2):626-35.

Prebiotics

- Inulin, a fructo-oligosaccharide, is a common storage starch in sunflower family plants. An indigestible starch but metabolized to SCFA by many bacteria.
- 50% of *Arctium* root by weight; 40% of *Inula helenium*; 25% of *Taraxacum*
- Of the 3 herbs, only *Arctium* can be taken in regular food-like quantities.
- Inulin is highly soluble in hot water
- Recipe from Wm Cook: 2 ounces burdock root in quart of water, simmer to 1 pint. Taken in 2-4 ounce doses TID

Probiotic/prebiotic strategy

- Flooding strategy: 150 billion organisms per day for 4-7 days.
Mixed species of *Acidophilus*, *Bifidobacter*, etc
- Follow with 10 billion organisms per main meal for 10 days.
- Maintain with 10 billion organisms per main intermittently with breaks in therapy.
- With each dose, take 1-2 tsp of *Arctium* powder in water.
- Keep an influx of the probiotic and the prebiotic present in the ecology at all times during supplementation
- *Arctium* powder is inexpensive, about \$8 per pound at wholesale, and has a mildly sweet taste.

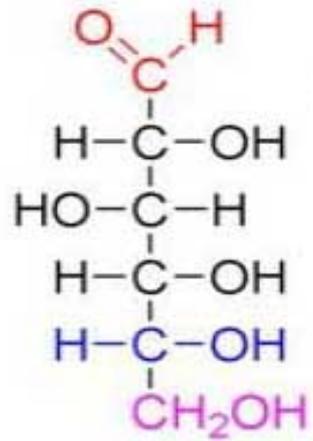
Cultured foods

- Consider renewable yoghurts, kefir, coconut kefir, etc fortified with a variety of superstrain capsules.
 - GEM cultures for kefir starters.
- Mature sauerkraut is dominated by mixed strains of acidophilus.
- Consider fortifying homemade soured vegetables with superstrains from commercial products.
- Consider specialty starter cultures.

- Deliver probiotic/prebiotic treatment after an initial course of therapy for bloated patient.
- During removal of food intolerance
- After reduction of inflammation and bloating with a course of herbal treatments.

Food for the microbiome

- Starches
- Polysaccharides
- Pectins
- Inulin
- Insoluble fiber



Carbohydrates: Not all created equal





Herbal Therapeutics for Leaky Gut Syndrome

Caution with bitters

- Acute or short term use of bitters may help the secretions of the upper GI tract.
- Used longer term, bitters, especially strong ones, may cause *cold injury* to the upper and middle GI. Bitters by nature are cooling, drying, and draining, and persistent use is warned against in traditional four humors medicine and also Chinese medicine.

Case

- A college-aged woman with warm constitution all her life took a tincture of Dandelion root and Oregon Grape root daily for about 8 weeks.
- Dose was 1-2 droppers 3 times per day.
- At the end of this time, her entire constitution had become cold, and her digestion impaired.
- After several months of follow up treatment, the injury was enduring.

The candida myth and antifungal herbs

- Many individuals and practitioners will encounter the individual with their gut ecology in disarray, and reflexively diagnose a “candida” infection. The condition is an Herban Legend.
- Intestinal candidiasis, an infection of the gut wall with candida yeast, or systemic candidiasis, in which the yeast is in the blood, exist as rare medical conditions and constitute grave and often fatal conditions.
- See the directory handout [Candidiasis Notes and Links](#).

- Herbs, supplements or drugs used to “kill candida” never resolve the root problems of the intestinal dysfunction.
- “Anti-candida” diets are sometimes beneficial because they omit grains and sugar, which have benefits unrelated to yeast.
- Cold, harsh, or bitter *antifungal herbs* can cause further injury to a system that is already fragile and dysfunctional.

Parasites and gut health

- Parasitosis is very real, the chief culprits being *Giardia lamblia* and *Entamoeba histolytica*. The latter is a serious disease that can have systemic consequences.
- Herbal or pharmaceutical treatments for these will work better in the context of an ecological approach to gut dysfunction.
- Many people are misdiagnosed with parasites by alternative practitioners, when parasites are not present, or are not the root cause of gut dysfunction.
- Some “parasites” reported by alternative labs are probably commensal, and harmless organisms
- Very hot or cold harsh bitter herbs (such as black walnut or clove) typically given for parasites can cause substantial injury to an already fragile ecosystem.

Herbal categories

Standard

- Mild bitters
- Carminatives
- Demulcents
- Alteratives

Special

- Topical antiinflammatories:
- Wound healing
- Lymphatic
- Immunomodulating

Prefer milder herbs

Important wound-healing herbs for restoring gut integrity

- Plantain
- Calendula
- Althaea

Deliver as powder in Aloe juice or applesauce.

All three plants are anti-inflammatory

All three plants promote wound healing

Topical anti-inflammatories for gut healing

- Matricaria
- Achillea
- Mentha
- Calendula
- Plantago
- Althea
- Aloe vera juice

Use decoctions or powders in demulcent media

Immunomodulating herbs

Astragalus

Use tea (soup) or prepared extract, not tincture. Caution on overheating or overstimulating the immune system

Lentinus (Shiitake)

- Add mushrooms to soup or stir fry.
- Reconstitute dried mushrooms in water for stir fry.

Reishi

- Use long decoction or prepared extract
- Must include water-extracted portion
- Decoction tastes really bad, compliance poor
- Brand: JHS (Mushroom Science) products include water-extraction

Basic formula for herbal decoction or powder

- Mentha – carminative, antiinflammatory
- Matricaria – bitter, carminative, antiinflammatory
- Foeniculum – Carminative, antispasmodic
- Glycyrrhiza – Demulcent, antiinflammatory
- Plantain -- mild bitter, vulnerary, anti-inflammatory
- Screen with patient for preferences or aversions to mint, licorice

Formulation modification 1

- Mentha 1
- Matricaria 1
- Foeniculum 1
- Glycyrrhiza 1
- Plantain 1

- If bloating and/or nausea and/or loose stool
 Add Zingiber, Calendula, Yarrow, and/or Agrimonia;
 Decrease glycyrrhiza

Formula modification 2

- Mentha 1
- Matricaria 1
- Foeniculum 1
- Glycyrrhiza 1
- Plantain 1

- If cold and/or dry presentation
 Add Althea, Ulmus, Aloe juice, increase fennel
 and Glycyrrhiza, add Cinnamomum

Formula modifications 3

- Mentha 1
- Matricaria 1
- Foeniculum 1
- Glycyrrhiza 1
- Plantain 1
- Modifications for constitution or presentation

- If taking probiotics
 - Add Arctium, Taraxacum as decoction or powder for inulin content

- If liver involvement with dampness and heat
 - Add Taraxacum, Mahonia. alteratives

Reevaluate formulas every 1-3 weeks

- Disappearance of damp symptoms
Reduce or remove drying herbs
- Disappearance of heat or cold symptoms
Modify appropriately for warming or cooling herbs

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See Supplemental materials at: <http://naimh.com/csch>

North American Institute of Medical Herbalism

<http://naimh.com>

Medical Herbalism journal

<http://medherb.com>