

Gluten Intolerance and Rheumatic Diseases

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INSTITUTE *for* SPECIALIZED MEDICINE

State-of-the-Art Integrative Care for Arthritis and Autoimmune Diseases

Case Study

- 42 y.o. woman presumable fibromyalgia diagnosis
- Seeking second opinion regarding the nature and management of her pain
- Developed pain in her muscles and joints over 20 years ago that coincided with initial onset of endometriosis
- Seen by a local pain management physician
- Diagnosed with fibromyalgia and started on anti-depressants
- Developed severe eye, mouth and vaginal dryness
- Stopped the drugs
- Consulted by a rheumatologist and diagnosed with ankylosing spondylitis
- Started anti-inflammatory drugs and then intravenous infusions of Remicade
- Therapy did not affect her pain level, but resulted in recurrent sinus infections
- Drugs discontinued after 6 months



Case Study

Main complaints during initial consultation included:

- Generalized muscle pain
- Fatigue
- Morning stiffness
- Eye, mouth and vaginal dryness
- Osteoporosis
- Frequent migraine headaches
- Irregular bowel movements with a predominant constipation
- Bloating



Case Study

Her family history was pertinent for:

- Osteoporosis
- Irritable bowel syndrome
- Sjogren's syndrome
- Hypothyroidism

Physical examination was pertinent for:

- Skin rash over shoulders
- Eye and mouth dryness
- Mild abdominal tenderness
- Generalized muscle tenderness

Lab test results:

- Mild anemia due to iron deficiency
- Low level of vitamin D
- Positive genetics for celiac disease associated genes

Her **endoscopy** was requested and small intestinal biopsy was negative for celiac disease



Case Study

- Patient went on gluten-free diet
- Started oral iron and vitamin D supplementations
- **One month** after initiation of the gluten-free diet, her pain subsided by 40-50%
- In **three months** she became pain-free
- Accidental consumptions of gluten resulted in a transient near complete reproduction of her pain
- **Six months** after initiation of the gluten free diet, she started noticing improvement of the mucosal dryness
- Currently, **two years** after initiation of the diet, the patient is still symptom free



Gut and Rheumatic Disease

The gastrointestinal system is the main entry for foreign materials (foods) into the human body and the main transitory route for an enormous mass of microorganisms and products of their activity in the form of feces.

- In an average person, the absorptive surface area of the **small intestine** is roughly **2700 square feet** - the size of a tennis court
- The total alveolar area of the **lungs** is equal to **1700 square feet**
- In comparison, the average **skin** surface area is only **17 square feet**



Gut and Rheumatic Disease

- Food and microbial products are the main stimulants of the immune system and the main external regulator of various metabolic pathways.
- Accordingly, composition of the consumed food can influence immune responses and inflammatory processes leading to the development of distinct forms of rheumatic diseases.



Focus on Gluten Intolerance

- Most common food-driven autoimmune disease affecting humans
- 10 to 35% of general population are genetically predisposed
- The mortality rate in patients with gluten intolerance exceeds that in the general population by a factor of 1.9–3.8, mainly due to malignant diseases
- After 1–5 years on a gluten-free diet, the reduction in excess mortality suggests that this diet is protective against malignant diseases in patients with gluten intolerance



Dietary Grains and Proteins that Trigger Gluten Intolerance

| GRAIN | PATHOGENIC PROTEINS |
|------------------|------------------------------|
| WHEAT | GLIADINS |
| RYE | SEKALINS |
| BARLEY | HORDEINS |
| DURUM | GLIADIN-LIKE PROTEINS |
| SPELT | |
| TRITICALE | |
| KAMUT | |
| EINCORN | |



Gluten Intolerance—a disease that goes against the grain

Gluten intolerance is a permanent, genetically based intolerance to ingested gluten that results in chronic inflammation and systemic autoimmune responses



Why Gluten?

- Human digestive enzymes cannot completely digest gluten in the gastrointestinal tract
- Consumption results in formation of large protein fragments stimulating inflammatory reaction within the intestinal wall
- Gluten peptides can penetrate in systemic circulation and trigger immune responses in internal organs distant from the intestine (thyroid gland, salivary glands, brain etc)
- Gluten peptides can be detected in breast milk and can trigger various undesirable reaction in breast-fed infants



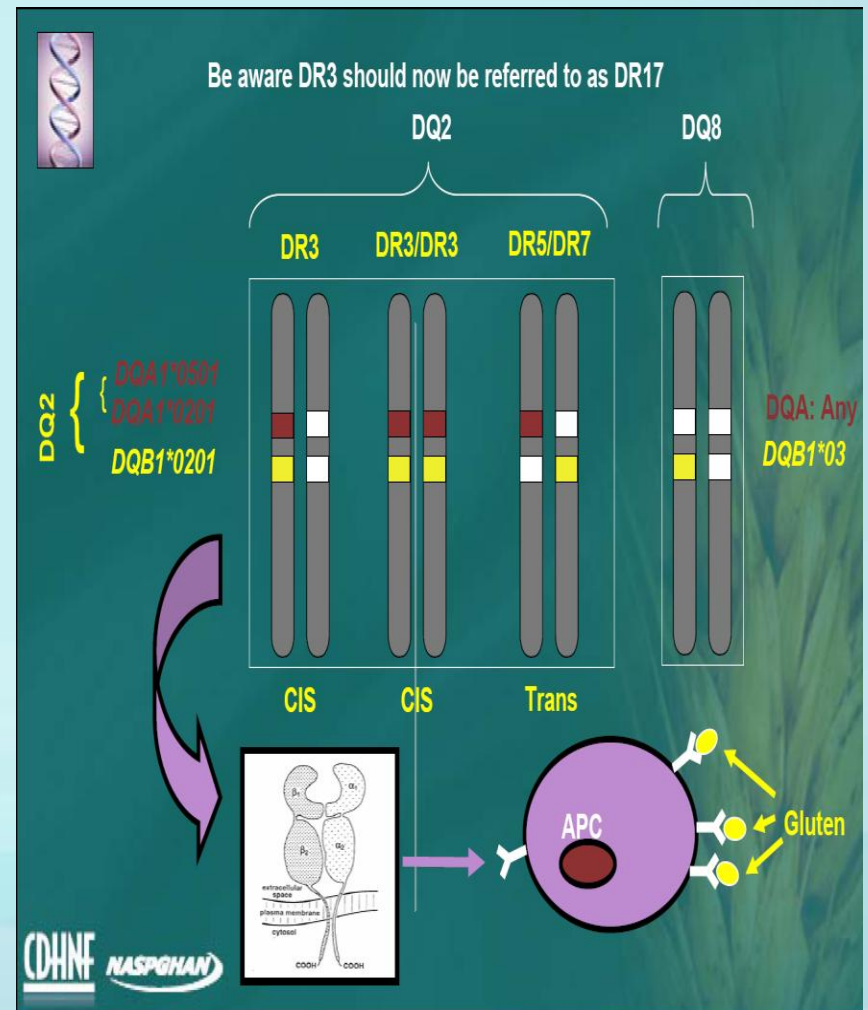
Genetics of Gluten Intolerance

- Patients with gluten intolerance demonstrate a strong association with specific HLA class II genotypes
- If people genetically predisposed to gluten intolerance do not ingest gluten, the illness will not manifest



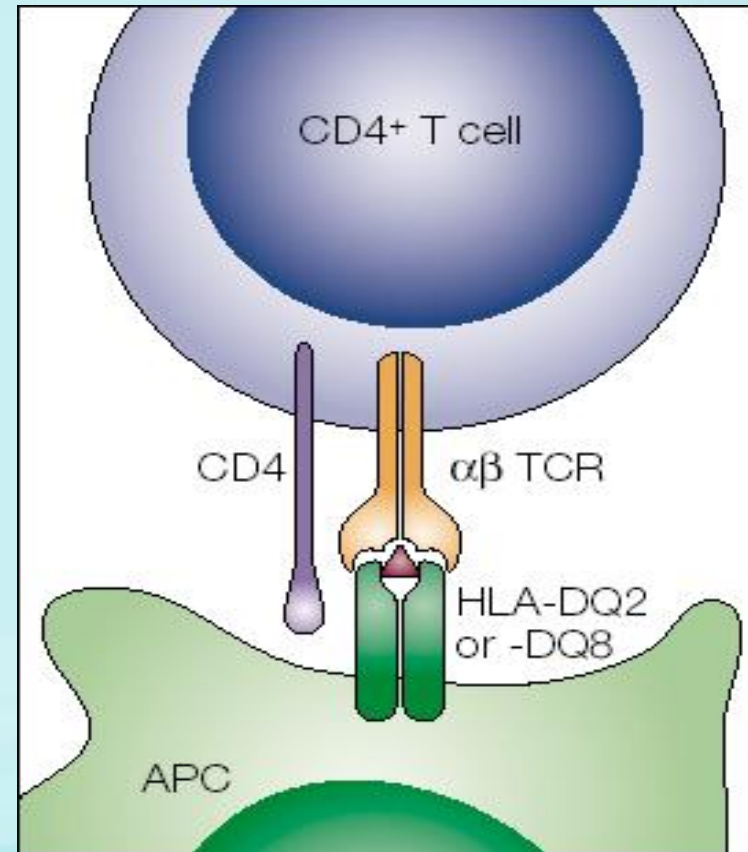
Genetics of Gluten Intolerance

Approximately 95% of patients with gluten intolerance have a particular type of HLA DQ alpha and beta chain encoded by two genes, HLA-DQ2 (85-90%), and HLA-DQ8 (5-10%)



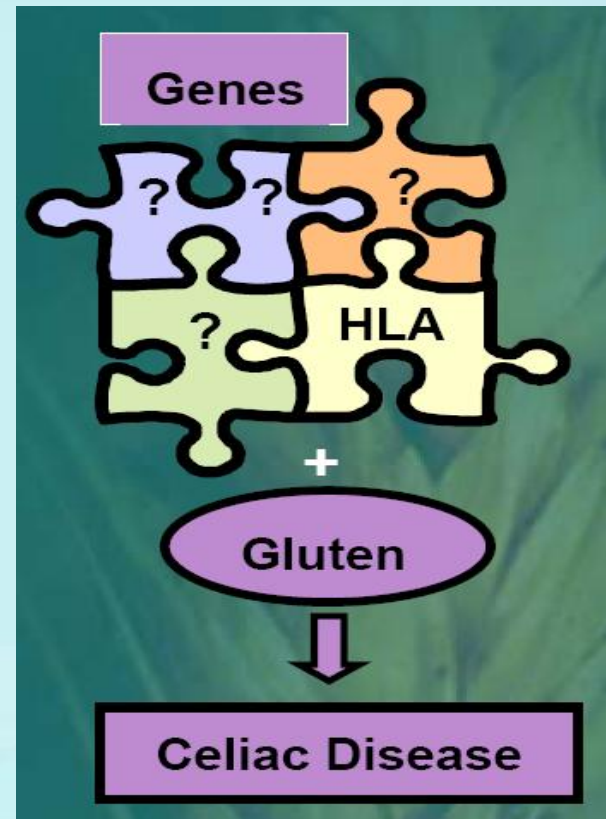
Immunology of Gluten Intolerance

- T lymphocytes invariably recognize gluten peptides that are presented by HLA-DQ2 or DQ8 molecules.
- This results in the lymphocyte activation and initiation of the inflammatory reaction and autoimmune responses.

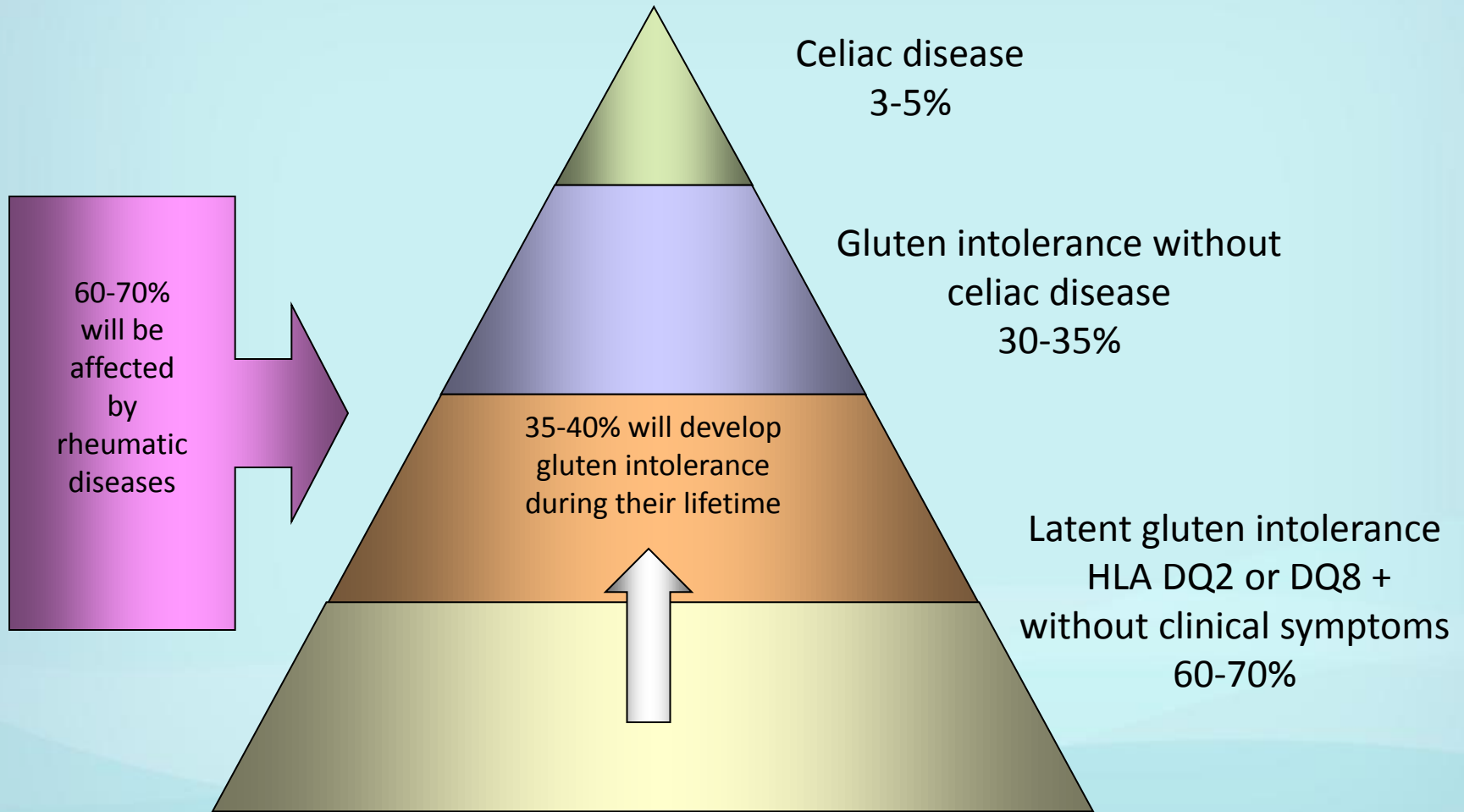


Genetics of Gluten Intolerance

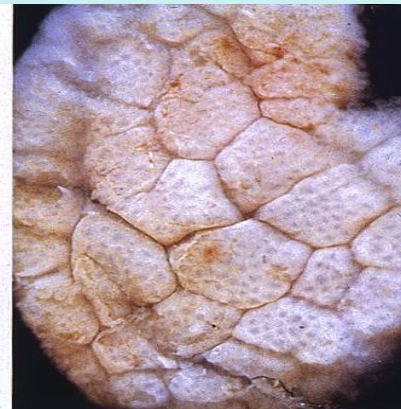
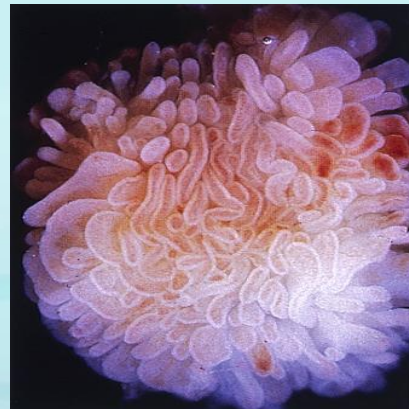
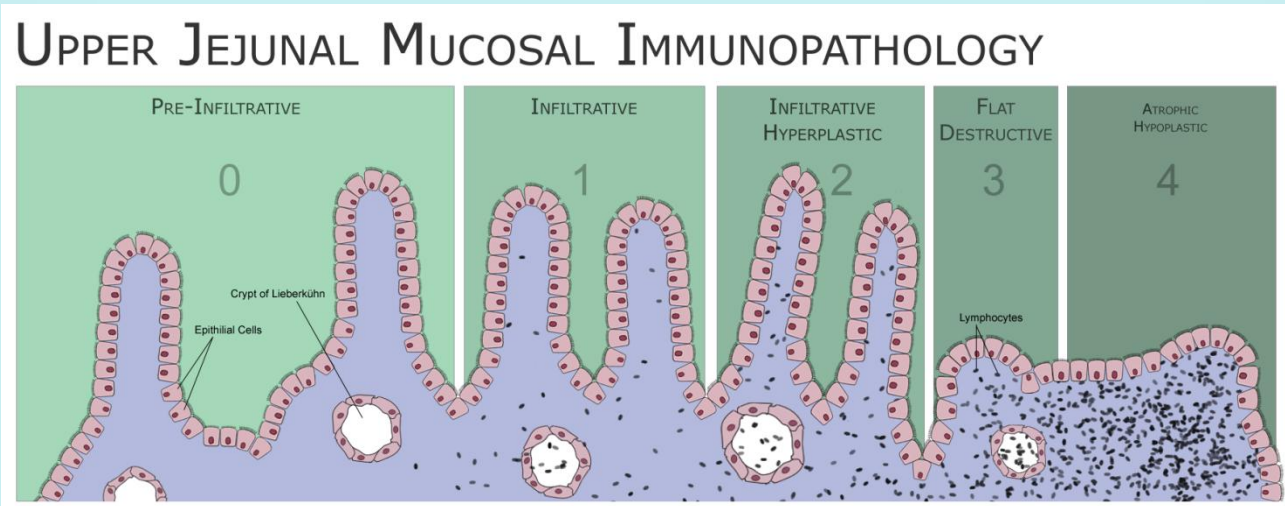
MYO9B (myosin IXB) gene polymorphisms is associated with celiac disease, ulcerative colitis, SLE and RA susceptibility, presumably through alteration of the intestinal permeability



Spectrum of Gluten Intolerance



Gastrointestinal Involvement in Gluten Intolerance

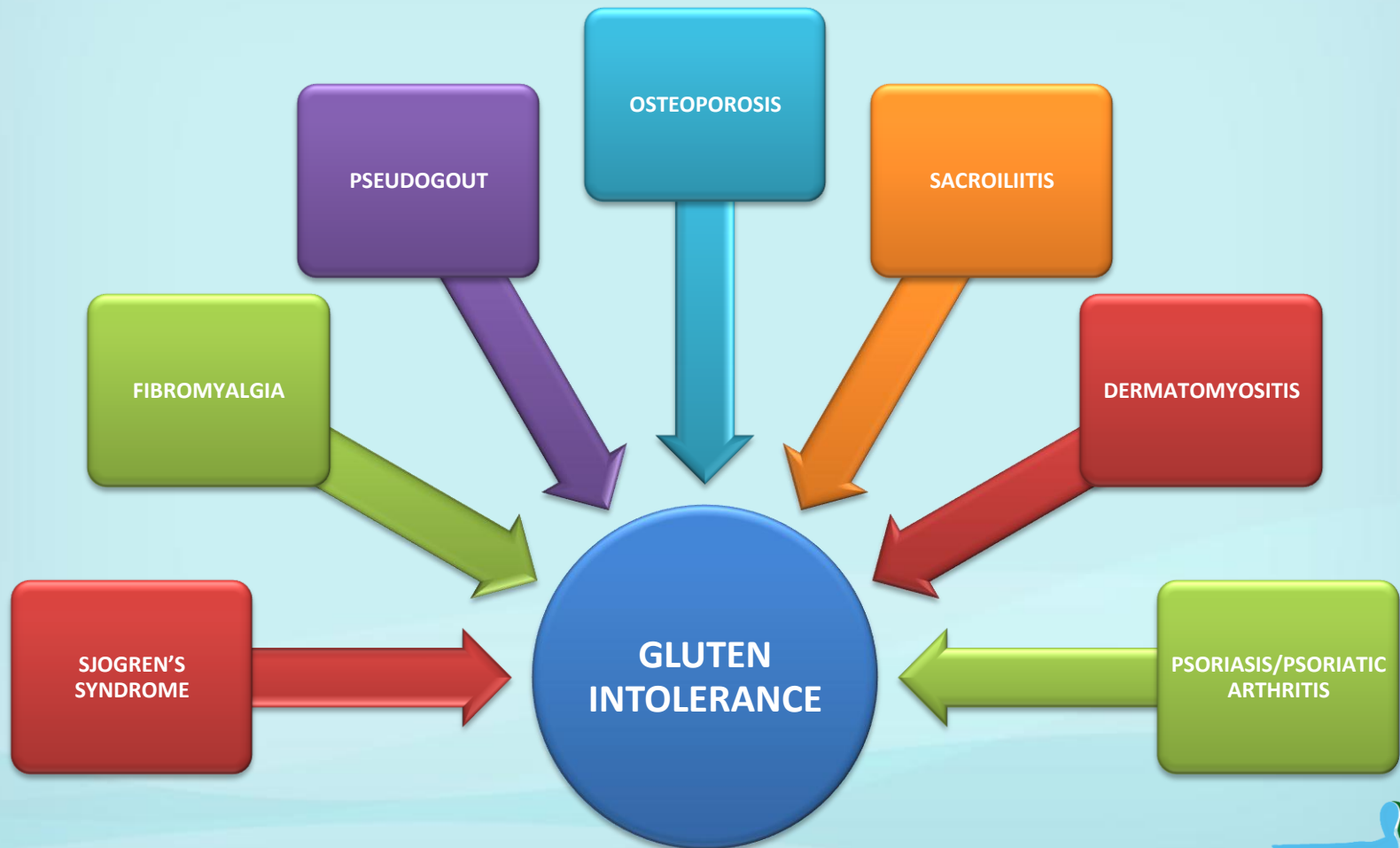


Metabolic Problems Associated with Gluten Intolerance

- Malabsorption of vitamins (vitamin D, A, E, K, B1, B6), macroelements (iron, calcium, magnesium) and microelements (zinc, copper selenium)
- Leaky gut syndrome
- Pernicious anemia (vitamin B12 deficiency due to autoimmune damage of gastric parietal cells)
- Osteoporosis
- Disbacteriosis



Rheumatic Diseases Commonly Associated with Gluten Intolerance



Sjogren's Syndrome

Sjogren's syndrome is an autoimmune disease affecting glands that produce tears and saliva (the lacrimal and salivary glands). Damage to these glands causes a reduction in both the quantity and quality of their secretions.



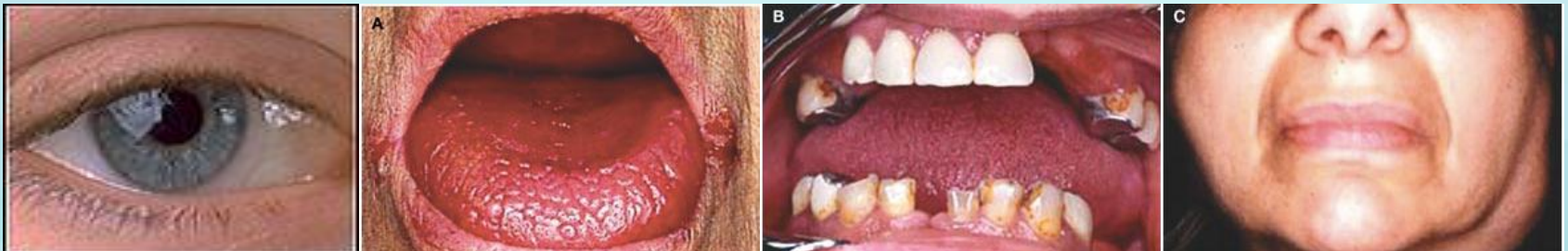
ADAM



Sjogren's Syndrome

Main symptoms are:

- **Dry eyes** –burning or itching, sandy feeling, blurry vision, light sensitivity
- **Dry mouth** –chalky or cotton like, difficulty swallowing, speaking, or tasting, dental decay (cavities) and mouth infections.



Sjogren's Syndrome

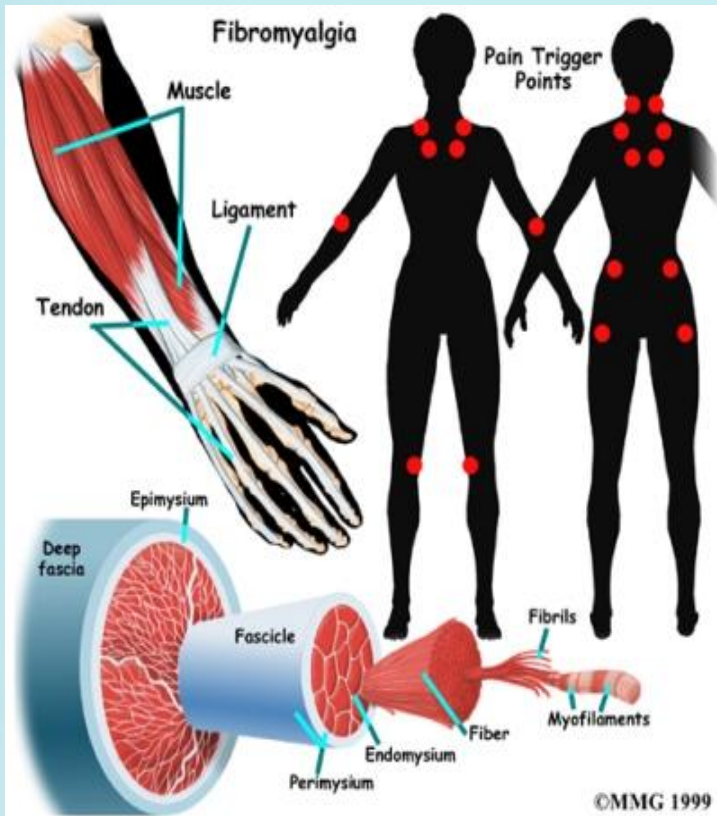


Effects on other parts of the body:

- multiple sites of joint and muscle pain
- prolonged dry skin
- skin rashes on the extremities
- chronic dry cough
- vaginal dryness
- numbness or tingling in the extremities
- prolonged fatigue that interferes with daily life



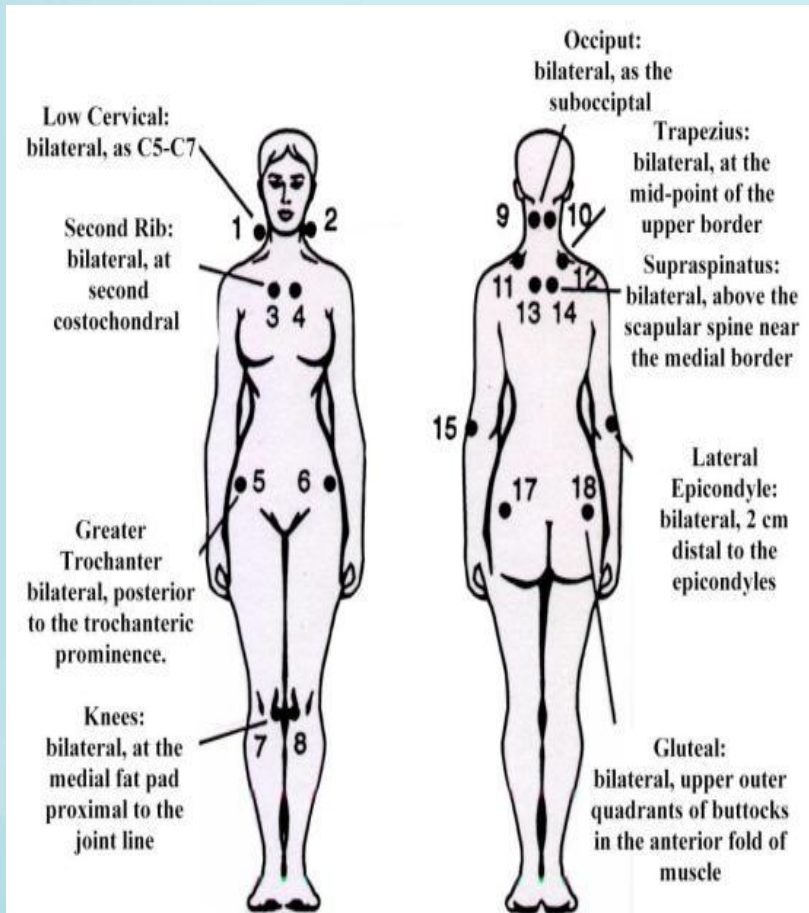
Fibromyalgia



Fibromyalgia meaning muscle and connective tissue pain. Is a disorder classified by the presence of chronic widespread pain and a heightened and painful response to gentle touch.



Fybromyalgia

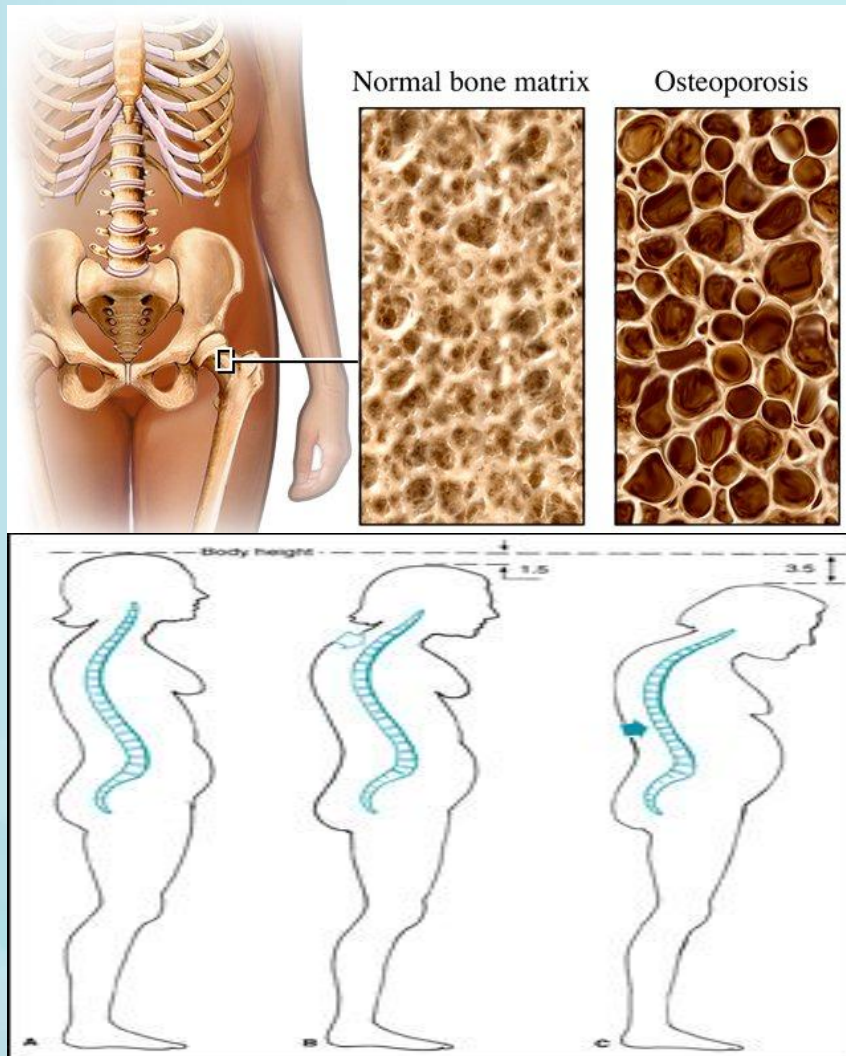


Other core features of the disorder include:

- debilitating fatigue
- sleep disturbance
- joint stiffness
- difficulty with swallowing
- functional bowel and bladder abnormalities
- difficulty breathing
- diffuse sensations of numbness and tingling (non-dermatomal paresthesia)
- abnormal motor activity (i.e. nocturnal myoclonus, sleep bruxism)
- cognitive dysfunction



Osteoporosis



- Bone disease that leads to an increased risk of fracture
- Bone mineral density is reduced
- Bone microarchitecture is disrupted
- Amount and variety of non-collagenous proteins in bone is altered
- No specific symptoms
- Increased risk of bone fractures.
 - Osteoporotic fractures are known as *fragility or stress fractures*. Typically, these fractures occur in the vertebral column, rib, hip and wrist
- Gluten intolerance increases risk of osteoporosis due to malabsorption of vitamins (vitamin D in particular), minerals and microelements



Pseudogout

Calcium Pyrophosphate Deposition Disease



- Type of arthritis that can mimic gout, and represents an inflammatory body reaction to the crystal deposits of calcium pyrophosphate
- Can cause severe episodes of localized pain and swelling resulting in incapacitation
- Can cause more chronic arthritis that mimics osteoarthritis or rheumatoid arthritis
- Knees are most often involved but wrists, shoulders, ankles, elbows or hands can be affected
- The most common cause of pseudogout in patients with gluten intolerance is vitamin D deficiency causing secondary hyperparathyroidism



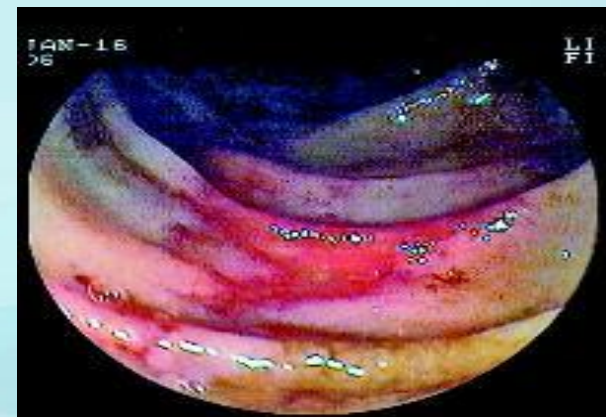
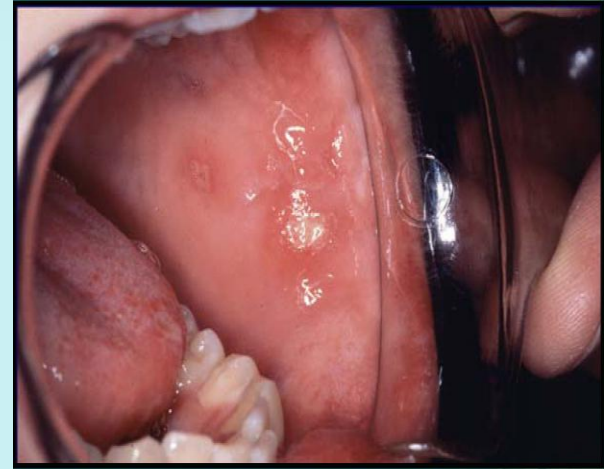
Rheumatic Diseases Less Commonly Associated with Gluten Intolerance

- Scleroderma
- Rheumatoid Arthritis
- SLE
- JRA



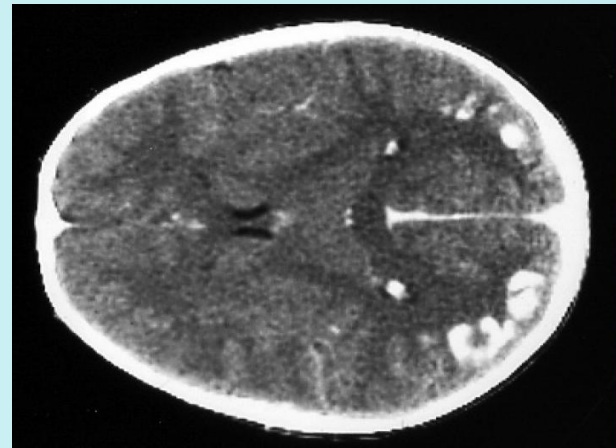
SLE Symptoms with Potential Gluten-Driven Mechanism

- Aphthous stomatitis
- Intestinal vasculitis
- Mucosal dryness / Sjogren's syndrome
- Methotrexate intolerance
- Thyroiditis



SLE Symptoms with Potential Gluten-Driven Mechanism

- CNS lupus: seizures, “brain fog”, vasculitis, encephalopathy
- Peripheral neuropathy
- Anti-phospholipid antibody syndrome
- Osteoporosis
- Malar rash
- Persistent lymphadenopathy



Nonrheumatic Diseases Commonly Associated with Gluten Intolerance

IRRITABLE
BOWEL
SYNDROME

DERMATITIS
HERPETIFORMIS

CELIAC
DISEASE

AUTISM

BIPOLAR
DISORDER

SECONDARY
HYPERPARATHYROIDISM

ADDH

PERIPHERAL
NEUROPATHY

SEIZURE DISORDER

SCHIZOPHRENIA

CHRONIC FATIGUE
SYNDROME

Indicators of Gluten Intolerance

Medical History

- Thyroid disorders
- Irritable bowel syndrome
- Iron deficiency
- Osteoporosis
- Sjogren's syndrome
- Asthma



Indicators of Gluten Intolerance

Skin Conditions

**KERATOSIS
PILARIS**



**PERIUNGUAL
ERYTHEMA**



**DERMATITIS
HERPETIFORMIS**



Laboratory Findings Suspicious for Gluten-Driven Autoimmune Process

- Low levels of vitamin D1 or D3
- Elevated PTH
- Positive anti-neuronal antibodies
- Positive anti-SSA/SSB antibodies
- Positive anti-cardiolipin antibodies
- Hyperprolactinemia
- Persistently elevated β 2-microglobulin
- Positive anti-TPO antibodies
- Low level of vitamin A or retinol

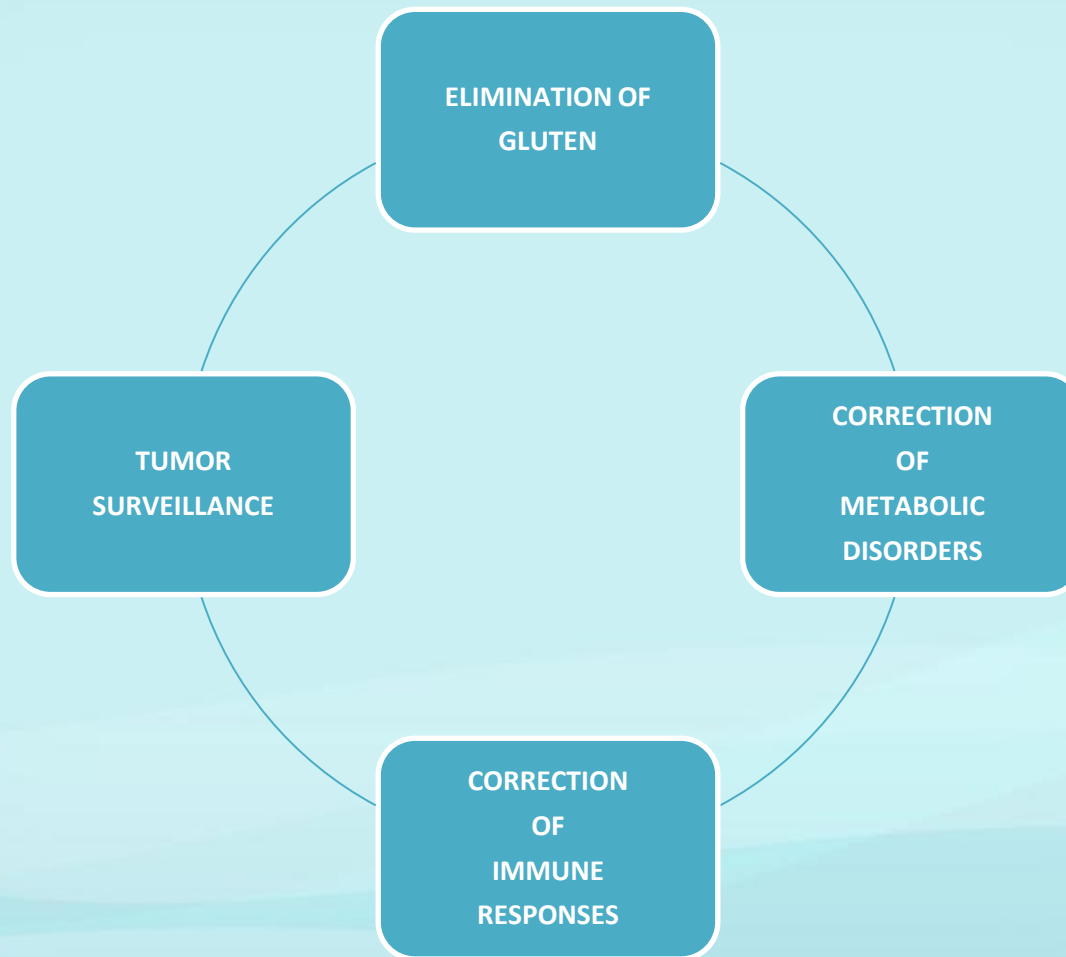


How to Diagnose Gluten Intolerance

- Genetic testing
- Immunologic testing
 - blood
 - Feces
- Intestinal / colon biopsy
- Elimination diet with subsequent gluten challenge



Treatment of Gluten Intolerance



Elimination of Gluten



Elimination of Gluten

Gluten-containing grains to avoid

| | | |
|--------------|----------|---------------------|
| Wheat | Bulgar | Filler |
| Wheat Bran | Couscous | Triticale |
| Wheat Starch | Durum | Kamut |
| Wheat Germ | Einkorn | Matzo |
| Flour/Meal | Emmer | Barley |
| Semolina | Faro | Barley Malt/Extract |
| Spelt | Rye | Graham Flour |



Elimination of Gluten

Obvious Sources

- Bread
- Bagels
- Cakes
- Cookies
- Pasta/noodles
- Cereal
- Pastries/pies
- Rolls

Potential Sources

- Candy
- Communion wafers
- Cured pork products
- Drink mixes
- Gravy
- Imitation meat/seafood
- Sauce
- Self-basting turkeys
- Soy sauce



Elimination of Gluten

- Lipstick/gloss/balms
- Mouthwash/toothpaste
- Play dough
- Stamp and envelope glues
- Prescription or OTC medications
- Vitamin, herbal and mineral preparations



Elimination of Gluten

- Only 50% of Americans with a chronic illness adhere to their treatment including:
 - Diet
 - Exercise
 - Medication
- Dietary compliance can be the most difficult aspect of treatment



Correction of Metabolic Disorders

- Management of malabsorption and leaky gut syndrome
- Therapy of hormonal imbalance
- Management of osteopenia and osteoporosis



Correction of Metabolic Disorders

- Low Iron
- Low Folate
- Low Vitamin B12
- Low Vitamins ADEK
- Low Thiamine
- Low B6 (rare)
- Low Beta-carotene
- Low Zinc
- Essential fatty acid deficiency
- Low Niacine



Correction of Immune Responses

- Therapy of autoimmune disorders
- Normalization of gastrointestinal ecology



Tumor Surveillance

- Biochemical markers
- Physical surveillance





INSTITUTE *for* SPECIALIZED MEDICINE

State-of-the-Art Integrative Care for Arthritis and Autoimmune Diseases

- Institute for Specialized Medicine (www.ifsmed.com) was founded in San Diego in 2008
- The mission of the institute is to provide comprehensive medical care for chronic inflammatory, autoimmune and metabolic diseases
- Our philosophy is based on an integrative approach of patient care, which includes the most advanced technologies in traditional medicine in combination with the best of complementary therapies



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