



Celiac Disease

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Questions?





What We'll Talk About

- ▶ Definition of celiac disease (CD)
- ▶ Other wheat-related conditions
- ▶ How common CD is in the US and around the world
- ▶ What factors increase risk of developing CD
- ▶ How CD is diagnosed
- ▶ Treatment of CD
- ▶ Potential treatments of CD (research)



Celiac Disease

- ▶ Celiac disease is a disease of the small intestine triggered by the protein gluten (in wheat) and related proteins in barley and rye
- ▶ CD damages the small intestine, leading to malabsorption and to related conditions
- ▶ CD is an autoimmune disease; certain genes increase risk
- ▶ Variable symptoms (intestinal and non-intestinal)
- ▶ Only treatment is the consistent and permanent removal of gluten from the diet, the gluten-free diet (GFD)



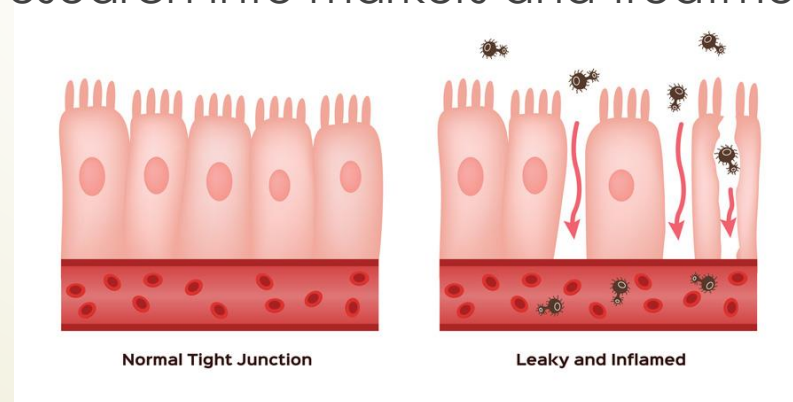
Celiac Disease



- ▶ Gluten proteins are naturally found in wheat
- ▶ Make bread products chewy and gives them an elastic quality
- ▶ Vital wheat gluten and seitan are concentrated sources of gluten
 - ▶ Vital wheat gluten is made by combining flour with water to make dough and knead it to develop the gluten network; the dough is then rinsed in water until all starch is removed and only the rubbery gluten remains, which is then dried and ground before packaging
 - ▶ Seitan is a vegan meat substitute made by rinsing wheat dough to remove the starch (produced by kneading wheat flour with water to develop sticky strands of gluten protein, the dough is then rinsed to wash away the starch)
- ▶ Gluten can be added to whole grain flours to strengthen dough, to retain more gas, resulting in greater volume and lighter crumb
- ▶ Extra gluten is beneficial in “gluten-challenged” dough containing lower gluten flours (like whole wheat or rye) or sharp or bulky components (nuts, seeds, or bran) that can sever gluten strands; can also enhance the chewiness of breads like bagels

Gluten-related Disorders

- Celiac Disease (CD)
- Wheat Allergy (WA)
- Non-Celiac Gluten/Wheat Sensitivity (NCGS/WS)
 - Functional symptoms related to gluten/wheat ingestion without positive tests for CD or WA (a diagnosis of exclusion)
 - Leaky gut leading to activation of all-body immune response?
 - Ongoing research into markers and treatment





FODMAPs

- ▶ The symptoms of IBS and NCGS may not be caused by the protein gluten, but rather carbohydrates in foods
 - ▶ Fermentable
 - ▶ Oligosaccharides – fructans (inulin) and galactans
 - ▶ Disaccharides – lactose
 - ▶ Monosaccharides – fructose in excess of glucose
 - ▶ Polyols – sugar alcohols
- ▶ A diet low in FODMAPs relieves symptoms in some patients with IBS and NCGS

Eliminate foods containing fodmaps

excess fructose

fruit

apple, mango, nashi, pear, tinned fruit in natural juice, watermelon

sweeteners

fructose, high fructose corn syrup

large total fructose dose

concentrated fruit sources, large serves of fruit, dried fruit, fruit juice

honey

corn syrup, fruisana



lactose

milk

milk from cows, goats or sheep, custard, ice cream, yoghurt

cheeses

soft unripened cheeses eg. cottage, cream, mascarpone, ricotta



fructans

vegetables

artichoke, asparagus, beetroot, broccoli, brussels sprouts, cabbage, eggplant, fennel, garlic, leek, okra, onion (all), shallots, spring onion

cereals

wheat and rye, in large amounts eg. bread, crackers, cookies, couscous, pasta

fruit

custard apple, persimmon, watermelon

miscellaneous

chicory, dandelion, inulin, pistachio

galactans

legumes

baked beans, chickpeas, kidney beans, lentils, soy beans



polyols

fruit

apple, apricot, avocado, blackberry, cherry, longon, lychee, nashi, nectarine, peach, pear, plum, prune, watermelon

vegetables




cauliflower, green capsicum (bell pepper), mushroom, sweet corn

sweeteners

sorbitol (420)
mannitol (421)
isomalt (953)
maltitol (965)
xylitol (967)



Foods suitable on a low-fodmap diet

fruit	vegetables	grain foods	milk products	other
<p>fruit banana, blueberry, boysenberry, canteloupe, cranberry, durian, grape, grapefruit, honeydew melon, kiwifruit, lemon, lime, mandarin, orange, passionfruit, pawpaw, raspberry, rhubarb, rockmelon, star anise, strawberry, tangelo</p> <p>Note: if fruit is dried, eat in small quantities</p> 	<p>vegetables alfalfa, bamboo shoots, bean shoots, bok choy, carrot, celery, choko, choy sum, endive, ginger, green beans, lettuce, olives, parsnip, potato, pumpkin, red capsicum (bell pepper), silver beet, spinach, squash, swede, sweet potato, taro, tomato, turnip, yam, zucchini</p> <p>herbs basil, chili, coriander, ginger, lemongrass, marjoram, mint, oregano, parsley, rosemary, thyme</p>	<p>cereals gluten-free bread or cereal products</p> <p>bread 100% spelt bread</p> <p>rice</p> <p>oats</p> <p>polenta</p> <p>other arrowroot, millet, psyllium, quinoa, sorgum, tapioca</p> 	<p>milk lactose-free milk*, oat milk*, rice milk*, soy milk*</p> <p>*check for additives</p> <p>cheeses hard cheeses, and brie and camembert</p> <p>yoghurt lactose-free varieties</p> <p>ice-cream substitutes gelati, sorbet</p> <p>butter substitutes olive oil</p>	<p>tofu</p> <p>sweeteners sugar* (sucrose), glucose, artificial sweeteners not ending in '-ol'</p> <p>honey substitutes golden syrup*, maple syrup*, molasses, treacle</p> <p>*small quantities</p> 

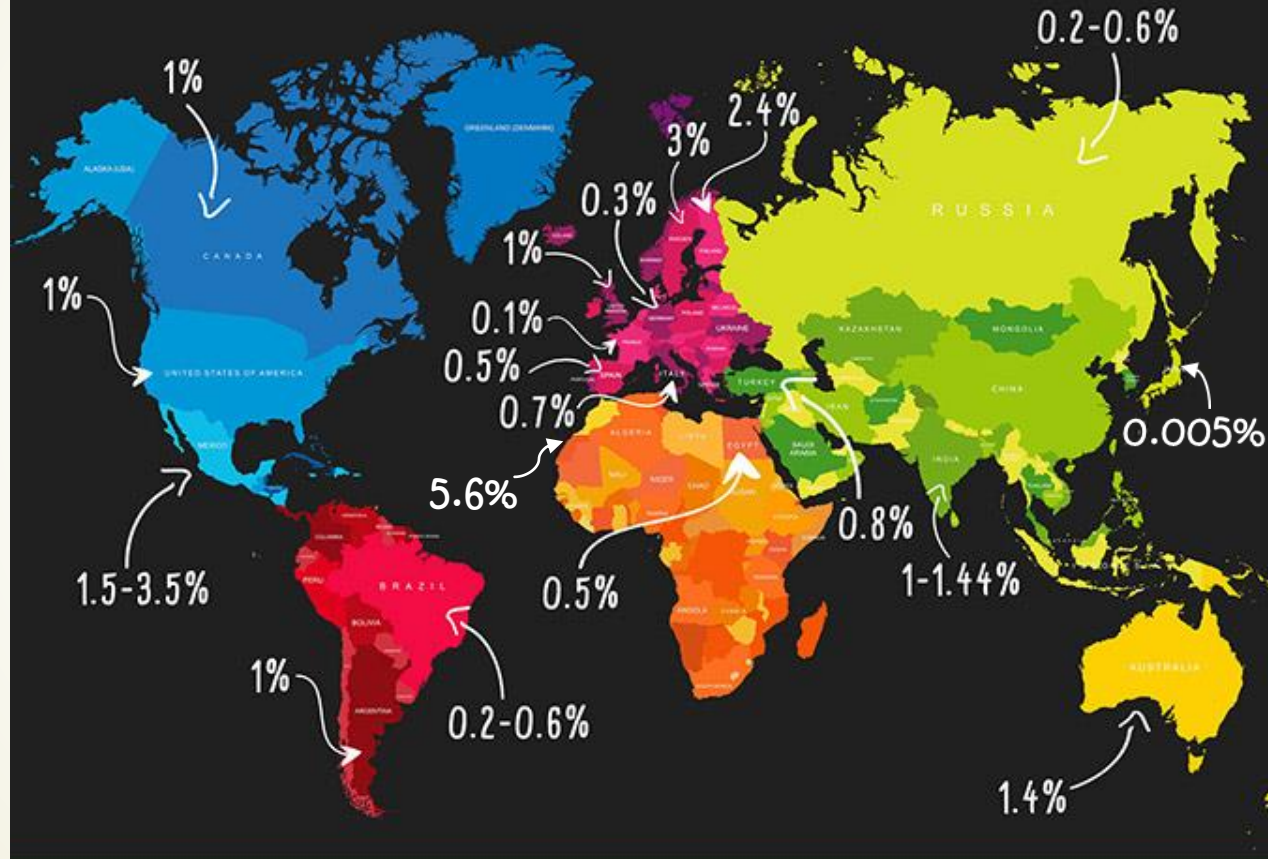


Celiac Disease

- ▶ Occurs worldwide, prevalence varies
- ▶ Affects ~ 1% of US and European populations
- ▶ Onset at any age
- ▶ Impacts almost every body system
- ▶ Non-intestinal symptoms > 50% of new diagnoses
- ▶ In the US ~ 50% with CD have been diagnosed

CELIAC DISEASE

PERCENTAGE OF POPULATION WITH CELIAC DISEASE IN VARIOUS COUNTRIES:



AROUND THE WORLD



Celiac Disease

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CD Prevalence

US population	1%	Autoimmune		Genetic	
1st deg. relative	10%	Type 1 DM	8%	Turner's	4-8%
Sibling	15%	Thyroiditis	15%	Down's	5-12%
Parents	9%	Arthritis (RA)	1-8%	William's	8%
Children	8%	Sjögren's	2-15%	IgA Deficiency	7%

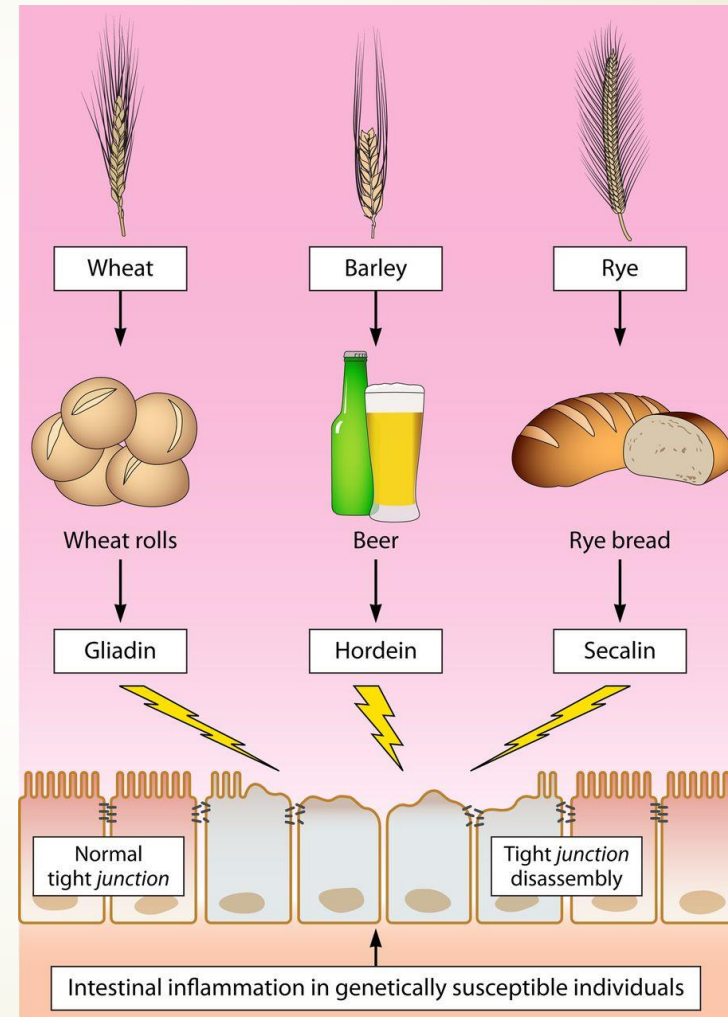


CD Prevalence

- ▶ Mayo Clinic study (9/2019) found that 44% of screened first-degree relatives had celiac disease; 94% had non-classic symptoms or no symptoms
- ▶ Sample of 104 patients diagnosed with CD 1983 – 2017; identified 477 first-degree relatives, 360 were screened for CD
- ▶ Of those, 160 were diagnosed with CD; median period between diagnosis of the initial patient and the relative was just under six months
- ▶ More screening for CD among family members could prevent long-term complications, such as nutritional deficiencies, development of new autoimmune conditions, and small bowel malignancy
- ▶ Most CD physicians suggest relatives get tested at the same time their family member is diagnosed, then every 2 to 3 years or anytime potential symptoms emerge (because celiac disease can develop at any age, it's possible for a relative to have an initial negative test result, but then test positive 12 years later)

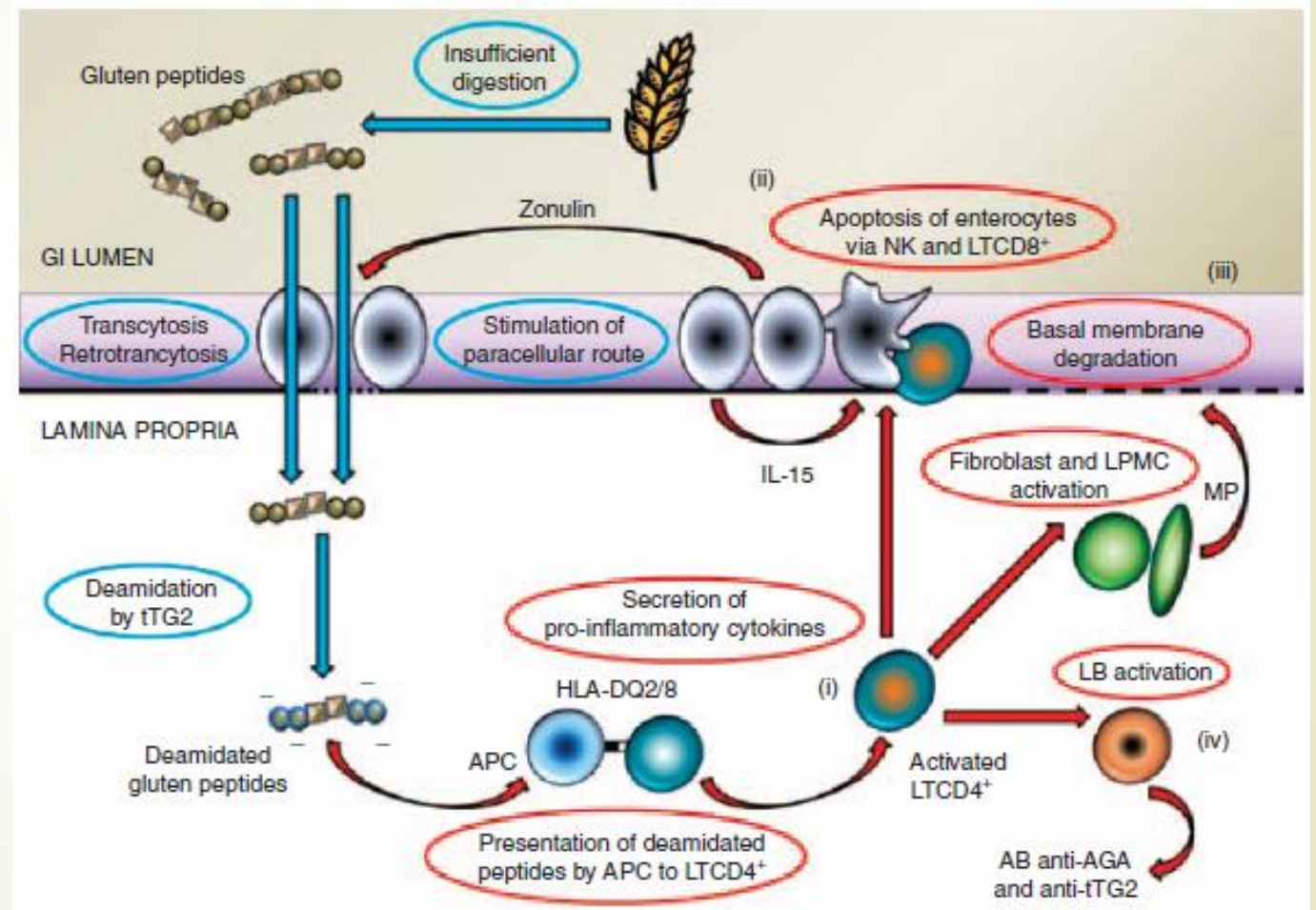
CD Disease Process

1. Gluten entry into submucosa
2. Chemical change of gluten by tissue transglutaminase
3. Immune activation

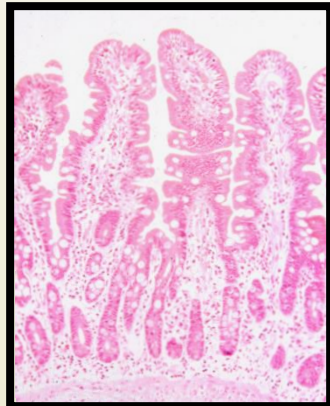
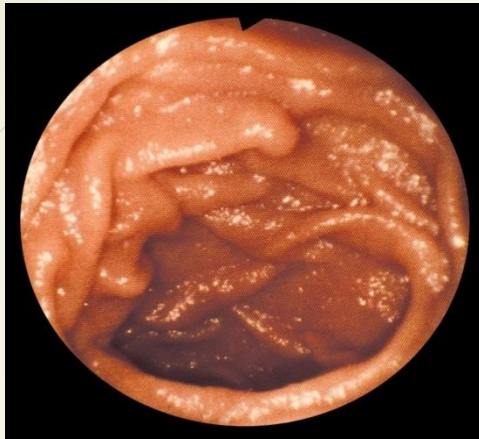


CD Disease Process

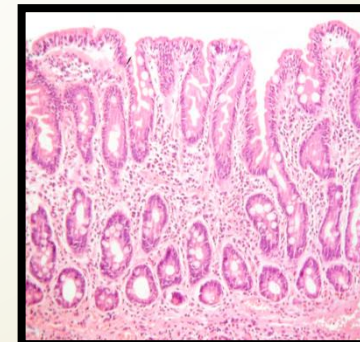
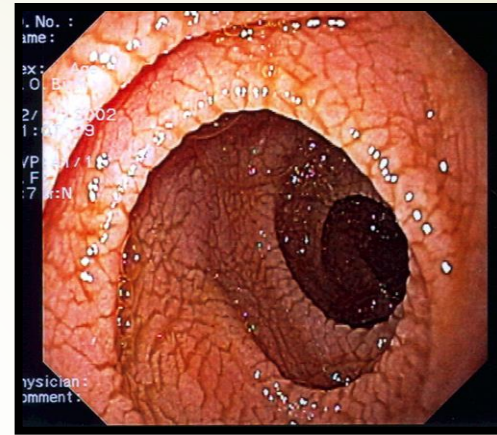
1. Gluten entry into submucosa
2. Deamidation of gluten by tissue transglutaminase
3. Immune activation



Normal small bowel

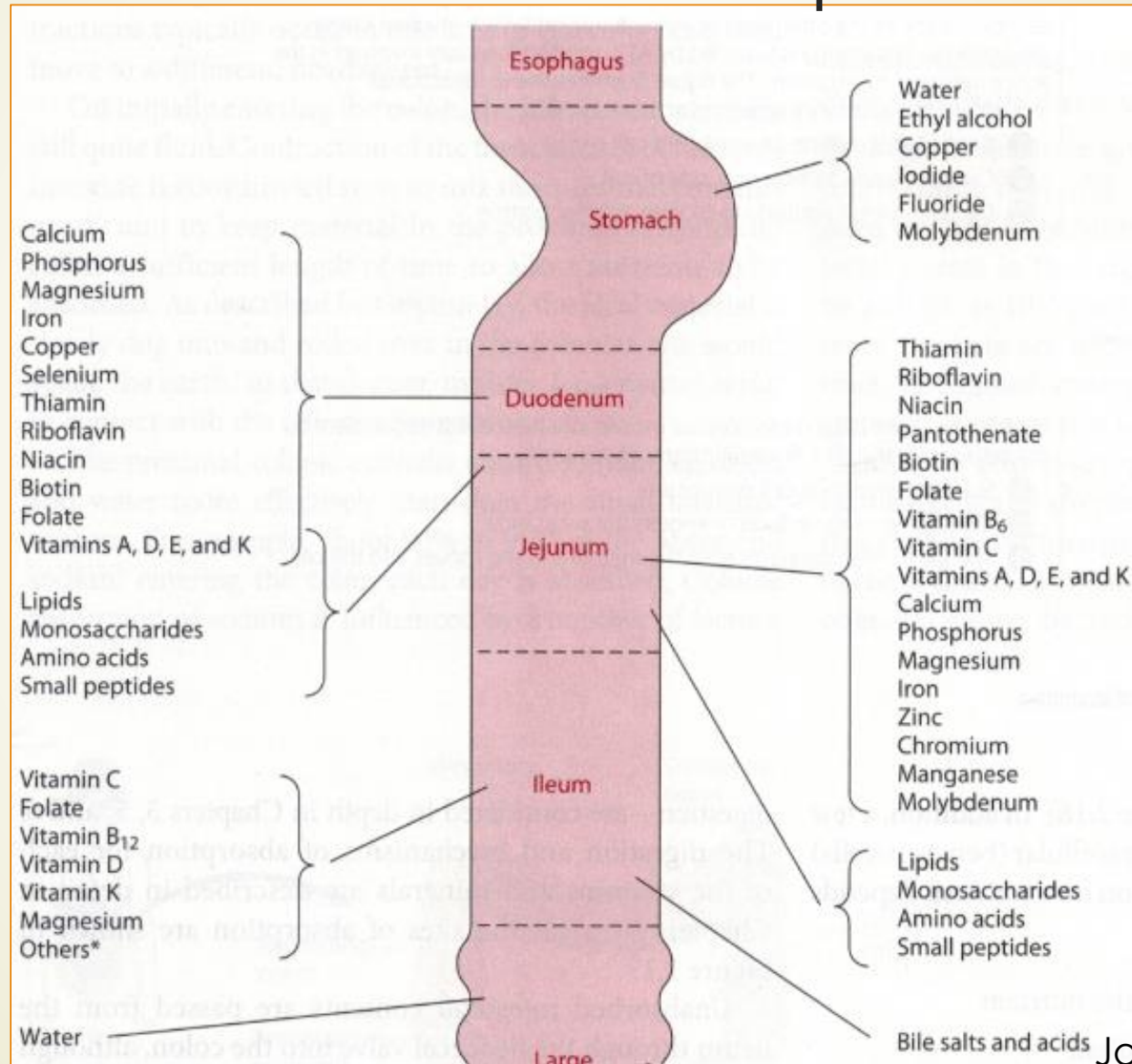


Celiac disease



Gluten (> 4hr)
→
←
Gluten-free diet

Sites of Nutrient Absorption





Risk Factors - Genetic

- ▶ Human leukocyte antigen (HLA) genes regulate the immune system
- ▶ HLA-DQ2 (DQ2.2 or DQ2.5) and/or HLA-DQ8 genes are believed to be *required* for CD (also called “permissive genes”) – so if not present have a good negative predictive value
 - ▶ > 95% of those with CD have DQ2 or DQ8
 - ▶ > 90% of people with CD have DQ2
 - ▶ Having double HLA-DQ2 (1 from mom and 1 from dad) increases risk/severity of CD; DQ2.5 has highest risk



Risk Factors - Genetic

- ▶ 30-40% of the US population has DQ2 and/or DQ8; only 2-3% of those will develop CD; accounts for 30-40% of genetic risk
- ▶ Researchers have identified 39 other, non-HLA genes associated with increased risk for CD
- ▶ These genes might help researchers identify what “goes wrong” and so discover treatment options



Environmental Triggers - Gluten

- ▶ Gluten is required
- ▶ Studies in people at risk for CD are inconsistent regarding:
 - ▶ The timing of gluten introduction
 - ▶ Duration of breastfeeding or maintenance during gluten introduction
- ▶ How much gluten we eat does seem to matter
- ▶ Protein content of wheat (and so gluten content) has not changed significantly over the years; but the amount of wheat and vital gluten intake has increased



Environmental Triggers - Gluten

- ▶ The Environmental Determinants of Diabetes in the Young (TEDDY)
 - ▶ Gluten intake > 2 gm/day at age 2 years increased risk of CDA and CD
- ▶ Diabetes Autoimmunity Study in the Young (DAISY)
 - ▶ Children in the highest third of gluten intake between the ages of 1 and 2 years had a 2-fold greater risk of CDA and CD than those in the lowest third
 - ▶ The risk of developing CDA increased by 5% per daily gram increase in gluten intake in 1-year-olds

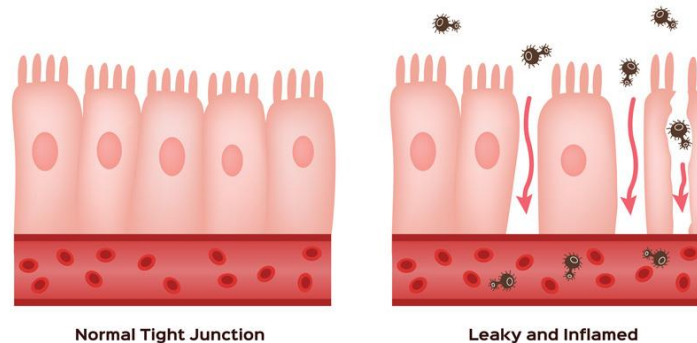
Environmental Triggers - Hygiene Hypothesis



- ▶ People are exposed to less germs early in childhood due to cleaner living conditions
- ▶ Decreased exposure to microbes and infectious agents does not allow immune system to mature normally
- ▶ Supported by a study that found dramatically different prevalence of celiac disease antibodies in Finland (1.4%) and Russian Karelia (0.6%)
 - ▶ Despite geographical proximity
 - ▶ Similar prevalence HLA-DQ2/DQ8
 - ▶ But, major differences in economic development

Environmental Triggers - Infectious Agents

- ▶ Rotavirus (causes vomiting and watery diarrhea):
 - ▶ Almost all children have had rotaviral infection by age 5
 - ▶ ≥ 2 infections in children increased risk of CD
- ▶ Significantly higher risk of CD in children with high infection frequency in first 18 months of life (any infection)
- ▶ Reovirus (causes colds) also implicated in CD
- ▶ Alteration in gut permeability or activate the autoimmune system



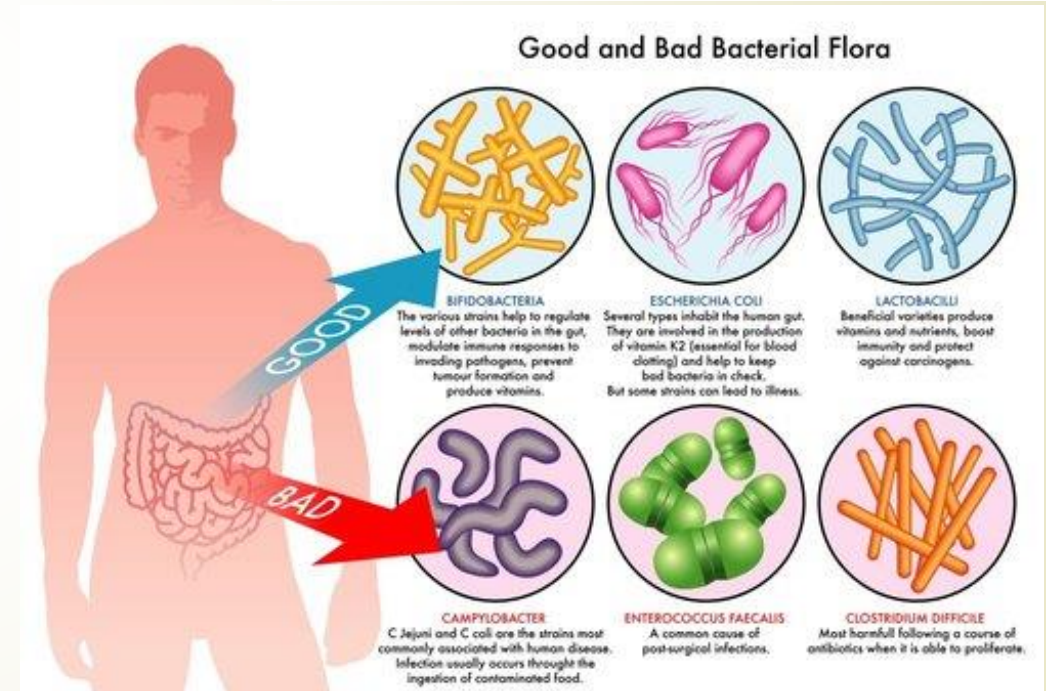
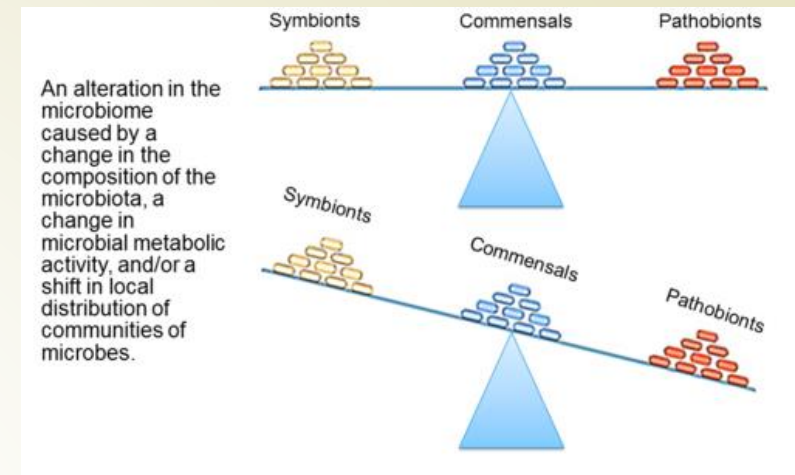
Environmental Triggers - Microbiome

- ▶ Microbiome has key beneficial health functions:
 - ▶ Affect food digestion
 - ▶ Healthy bacteria help prevent pathogens from entering the body by reinforcing the epithelial barrier (mucus and short chain fatty acids)
 - ▶ Exerts great effect on immune system development; human immune system and gut microbiota interact in a way that each shapes the other

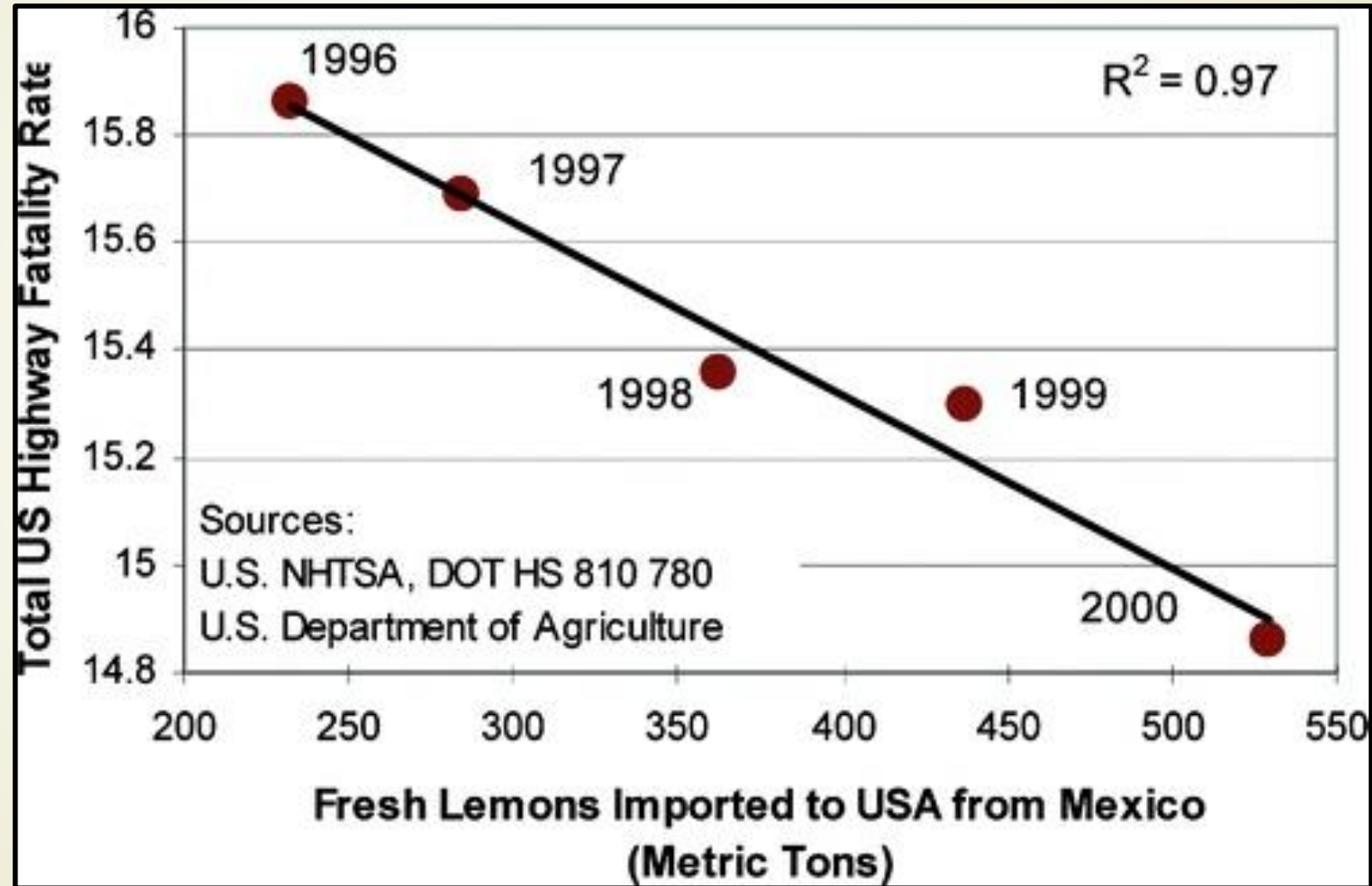


Environmental Triggers - Microbiome

- Dysbiosis may cause autoimmunity by altering good/bad microbiotic balance and so our immune responses
- Research indicates that the microbiome is different between groups of people with CD (untreated CD, treated CD, treated but symptomatic CD)
- Unclear whether changes in types of gut bacteria are a cause or a result of intestinal inflammation



Correlation is Not the Same as Causation





Signs and Symptoms: Malabsorptive

Gastrointestinal

Near/total malabsorption

- ▶ Diarrhea
- ▶ Abdominal distension
- ▶ Anorexia
- ▶ Failure to thrive/wt loss
- ▶ Abdominal pain
- ▶ Vomiting
- ▶ Constipation

Extraintestinal

Some malabsorption

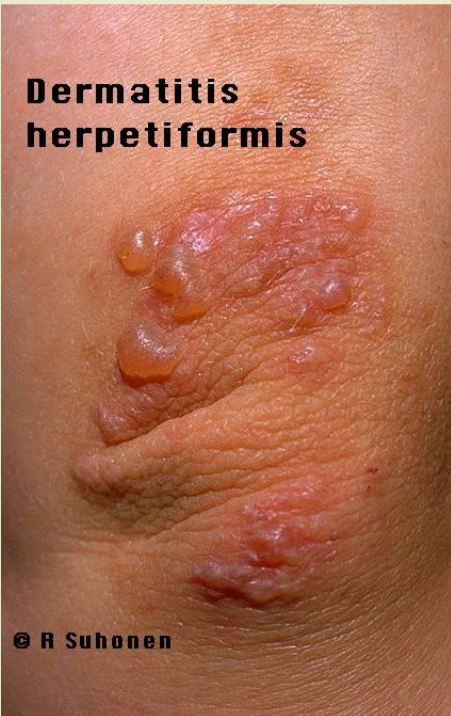
- ▶ Anemia
- ▶ Short stature
- ▶ Osteopenia, osteoporosis, bone fracture
- ▶ Recurrent abortions
- ▶ Hepatic steatosis
- ▶ Abdominal pain

Signs and Symptoms: Absorption Independent/Extraintestinal

- ▶ Dermatitis herpetiformis
- ▶ Dental enamel hypoplasia
- ▶ Ataxia
- ▶ Alopecia
- ▶ Primary biliary cirrhosis
- ▶ Isolated hypertransaminasemia
- ▶ Non-alcoholic fatty liver
- ▶ Recurrent aphthous stomatitis
- ▶ Fertility problems
- ▶ Myasthenia gravis
- ▶ Recurrent pericarditis
- ▶ Psoriasis
- ▶ Polyneuropathy
- ▶ Epilepsy
- ▶ Vasculitis
- ▶ Dilative cardiomyopathy
- ▶ Hypo/hyperthyroidism
- ▶ Intestinal lymphoma

May be related to autoimmune inflammation or other tTG targets - nine human transglutaminase enzymes identified *TG2* → CD, *TG3* → DH, *TG6* → *gluten ataxia*

Associated Conditions: Dermatitis Herpetiformis and Dental Enamel Defects



Screening for CD

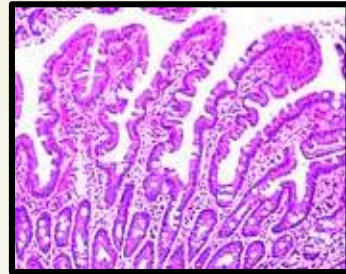
Blood Test	Sensitivity	Specificity	Comments
TTG-IgA* Tissue transglutaminase	90-100%	95-100%	Lower cost, ease of test, reliable, standardized - for initial screening
DGP-IgA*/DGP-IgG* Deamidated gliadin peptide	80-95%	86-98%	Very good in children < 2 yr; can identify CD in pts with IgA deficiency
EMA-IgA Endomysial	93-100%	98-100%	Operator dependent, prone to subjective error, expensive
HLA typing	98%		Good negative predictive value
IgA*			If IgA antibodies negative, test IgG-TTG/DPG
Biopsy (Gold standard for dx)	Poor	High	<u>Damage can be patchy</u> ; depends on grade cut-off point, biopsy orientation, pathologist
AGA-IgA Gliadin	Significantly lower sensitivity and specificity; false positive: true positive 10:1 May be a biomarker for NCGS		

Celiac Panel

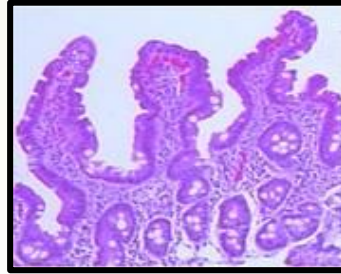
Celiac Panel	Normal	Weak +	Positive
IgA	34-305 mg/dL	NA	NA
TTG-IgA	< 20 CU	20 - 30 CU	> 30 CU
DPG-IgA	< 20 CU	20 - 30 CU	> 30 CU
DPG-IgG	< 20 CU	20 - 30 CU	> 30 CU

CU = Chemiluminescent Unit

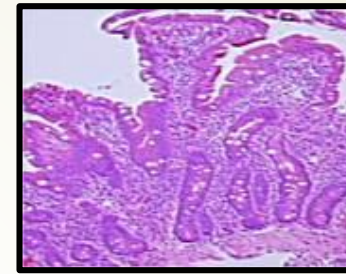
Biopsy: Histological Features



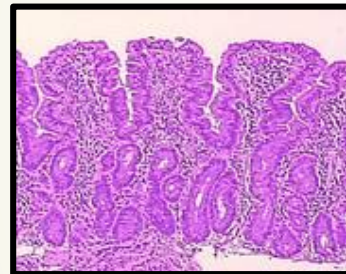
Normal 0



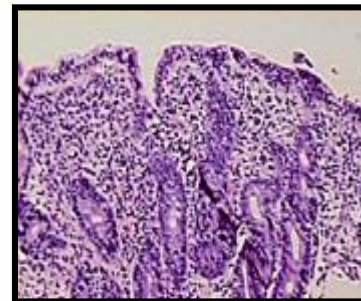
Infiltrative 1



Hyperplastic 2



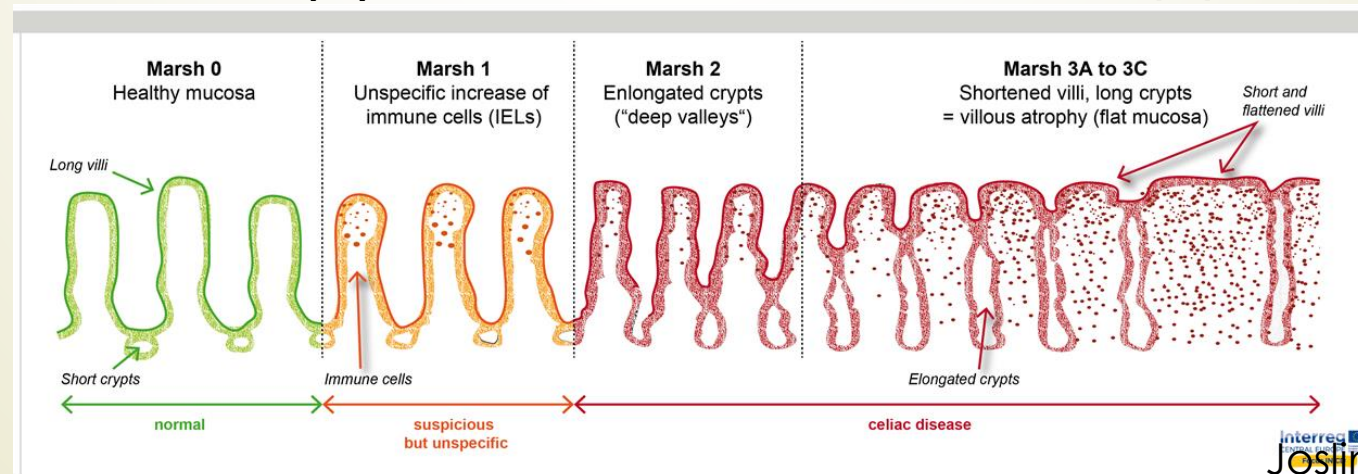
Partial atrophy 3a



Subtotal atrophy 3b



Total atrophy 3c





Biopsy

- ▶ Might miss the diagnosis because intestinal damage can be “patchy,” depends on how many samples are taken (4 is recommended), and who is reading the slide
- ▶ People are fearful of the procedure (but no preparation like colonoscopy)



Does a Biopsy Matter?

- ▶ Medical benefits
- ▶ Health benefits if CD is found and treated
- ▶ If positive, family members should be screened
- ▶ A false positive from blood tests alone can cause a string of unnecessary tests in relatives
- ▶ Without official diagnosis people with no symptoms may be less likely to follow a GFD
- ▶ The burden of the GFD is substantial



Biopsy

- ▶ 2012 ESPGHAN* “Guidelines for the Diagnosis of Coeliac Disease” states no biopsy is needed if:
 - ▶ Patient has “Classic Symptoms”
 - ▶ Antibody tests are >10 times the upper limit of normal (for example, 200 CU, if upper limit is 20 CU)
 - ▶ Verified by EMA positivity (a blood test)
 - ▶ And HLA-DQ2 and/or DQ8 positive (genetic test)
- ▶ Recent study confirmed that IgA-TTG at least 10 times normal can be used to diagnose CD *without* other tests/biopsy (repeat IgA-TTG test to exclude sample mix-up)

*European Society for Paediatric Gastroenterology Hepatology and Nutrition

Treatment of Celiac Disease

- Currently, the only treatment is a life-long gluten-free diet (GFD)
 - Eliminate gluten
 - Expand repertoire of GF foods
 - Optimize nutrient intake
- GFD should not be recommended until diagnosis is confirmed





Gluten-Containing Grains

Wheat

- ▶ Bran
- ▶ Bulgur
- ▶ Couscous
- ▶ Cracked Wheat
- ▶ Durum Flour
- ▶ Farina
- ▶ Graham Flour
- ▶ Matzo
- ▶ Semolina
- ▶ Wheat Bran
- ▶ Wheat Germ
- ▶ Wheat Starch

Wheat Varieties

- ▶ Einkorn
- ▶ Emmer
- ▶ Kamut
- ▶ Spelt (Dinkel)
- ▶ Triticale

Barley

- ▶ Malt
- ▶ Malt Beverages
- ▶ Malt Extract
- ▶ Malt Flavoring
- ▶ Malted Milk
- ▶ Malt Syrup
- ▶ Malt Vinegar

Rye



Food Labels

- ▶ Food Allergen Labeling and Consumer Protection Act (FALCPA), 2004
 - ▶ Labels must state if the food includes any of 8 common allergens (soy, wheat, milk, eggs, peanuts, tree nuts, crustacean shellfish and fish)
- ▶ FALCPA – 2014
 - ▶ Defined “gluten-free” for label claim
- ▶ However, USDA regulated foods, medications, supplements and other non-food items do not require identification of allergens; no regulation for “gluten-free”

Threshold for Safe Gluten Intake

Gluten (mg/day)	Relative to 1 Slice Bread
50 mg (villous atrophy by 90 days)	~1/70 th 0.014
10 mg (no villous atrophy)	1/350 th 0.003
0.4 mg (villous atrophy)	1/8750 th 0.000114
0.015 mg (clinical adverse effects)	1/233,333 th 0.0000043



Naturally Gluten-free Foods (If processed without gluten)

- ▶ Fresh, frozen or canned fruits and vegetables
- ▶ Fresh meats, poultry, seafood, fish, game, eggs, some processed meats, dried peas, beans, lentils, tofu
- ▶ Milk, yogurt, aged, natural cheese
- ▶ Oils, tree nuts, seeds, natural peanut butter, salad dressing, spreads
- ▶ Honey, sugar, pure maple syrup, corn syrup, jams, jellies, candy, ice cream
- ▶ Pure spices and herbs, salt, soy sauce without wheat, cider, wine, distilled and non-malt vinegars
- ▶ Coffee ground from whole beans, brewed tea, distilled alcoholic beverages

Gluten-Free Grains/Starches

- ▶ Amaranth
- ▶ Arrowroot
- ▶ Whole-bean flour
- ▶ Buckwheat
- ▶ Corn*, cornstarch
- ▶ Flax
- ▶ Job's tears
- ▶ Millet
- ▶ Nut flours
- ▶ Oats, oat bran, oat gum*
- ▶ Peas, pea flour
- ▶ Potato, sweet potato, yam, potato flour, potato starch
- ▶ Quinoa
- ▶ Rice, wild rice, rice bran, rice flour
- ▶ Sago
- ▶ Sorghum
- ▶ Soy
- ▶ Tapioca
- ▶ Teff

Underlined options are high in nutritional value

*Some with CD react to corn and/or oats



Nutritional Adequacy of the GFD

- ▶ Patients with no nutritional deficiencies have the same nutritional requirements as the general population
- ▶ Healing takes 6 months to years, although complete recovery in adults is rare
- ▶ Lactose intolerance is common at diagnosis, but may resolve
- ▶ Studies suggest that osteopenia and vitamin and mineral deficiencies resolve on the diet
- ▶ GF foods may be lower in B vitamins, iron, and fiber (not fortified); a GF daily multivitamin may be recommended in patients with CD
- ▶ The GFD may be high in lead, mercury, arsenic and cadmium

Nutrient Dense Gluten-free Foods

Nutrient	Vegetables	Fruits	Protein	Dairy	GF Grains
Thiamin			Pork, ham, bacon, liver, legumes, nuts		Whole grains
Riboflavin	Leafy greens vegetables		Meat	Milk, yogurt, cottage cheese	Whole-grain or enriched breads and cereals
Niacin			Eggs, meat, poultry, fish, nuts, other protein-rich foods	Milk	Whole-grain or enriched breads and cereals
Vitamin B6	Green and leafy vegetables	Fruits	Meats, fish, poultry, shellfish, legumes		Whole grains
Folate	Leafy green vegetables		Legumes, seeds, liver		
B-12			Animal products		
Fiber	Vegetables	Fresh fruits	Legumes, seeds		Whole grains


Nutrient Dense Gluten-free Foods

Nutrient	Vegetables	Fruits	Protein	Dairy	GF Grains
Calcium	Leafy greens, sea vegetables	Fortified orange juice, dried fruit	Calcium-rich soy products, beans, sardines (with bones)	Milk, yogurt, cheese, fortified soymilk	Quinoa , brown rice
Iron	Spinach, other leafy greens		Beef , poultry, fish, seafood (heme) Beans, tofu (non-heme)		Amaranth, teff, buckwheat, quinoa
Magnesium	Leafy greens, peas	Bananas, dried apricots, avocados			
Vitamin D	Plant oils (eg, olive)	Avocados	Salmon, nuts, enriched eggs	Fortified milk	
Vitamin E	Leafy greens, vegetable oils	Kiwi, mango	Nuts, seeds		GF whole grains
Vitamin K	Leafy greens, broccoli, soybean oil			Milk, dairy	




The GFD is Challenging

- ▶ Perceived burden of GFD is significant; second only to the perceived burden of kidney dialysis
- ▶ Gluten is found in ~ 90% of processed foods
- ▶ Recent study indicates one third of “gluten-free” restaurant foods contain gluten
- ▶ Hard to tell whether foods contain gluten
 - ▶ Labels can be difficult to understand
 - ▶ Gluten is a hidden ingredient in many non-food items (vitamins, cosmetics, other products)
 - ▶ Recent evidence indicates that it is rarely found in oral medications (<http://www.glutenfreedrugs.com> has links to lists)



The GFD is Challenging - Cross Contamination

- ▶ Cultivation of grains (leftover or wind-blown wheat in the field)
- ▶ Harvesting and shipping of grains (bins, rail cars, trucks)
- ▶ Processing (shared equipment)
- ▶ Grocery stores (bulk sale bins/scoops)
- ▶ Home
 - ▶ Shared kitchen items: toasters, counters, utensils (wooden spoons, wooden cutting boards, etc.), storage containers, jars of jam, peanut butter, and other spreads (no double-dipping), hand towels...



The GFD is Challenging - Cross Contamination

▶ Restaurants

- ▶ Substantial fraction of GF labeled restaurant foods contain detectable gluten
 - ▶ Gluten was detected in 32% of GF labeled foods
 - ▶ Differed by meal: 27.2% at breakfast and 34.0% at dinner
 - ▶ Gluten detected in 53.2% of pizza and 50.8% of pasta GF samples
 - ▶ GF labeled food was less likely to test positive for gluten in the West than in the Northeast United States
- ▶ Pans, grills, deep-fat fryers used for multiple foods
- ▶ Serving utensils used in buffets
- ▶ Kitchen and wait staff: “Educate, separate, sanitize”



The GFD is Challenging

- ▶ Cost of GF versions of foods are often 2-3 times higher than regular version
- ▶ Naturally GF foods cost less than GF substitutes
 - ▶ Potatoes, rice, corn, corn tortillas
 - ▶ Homemade foods may cost less than processed GF foods like bread, pizza, canned or frozen meals
- ▶ The cost of GF foods replaces the cost of “pills”
- ▶ The IRS allows a tax deduction for the increased cost of gluten-free foods and DNA tests can be counted as a medical expense if done specifically for screening for disease risk

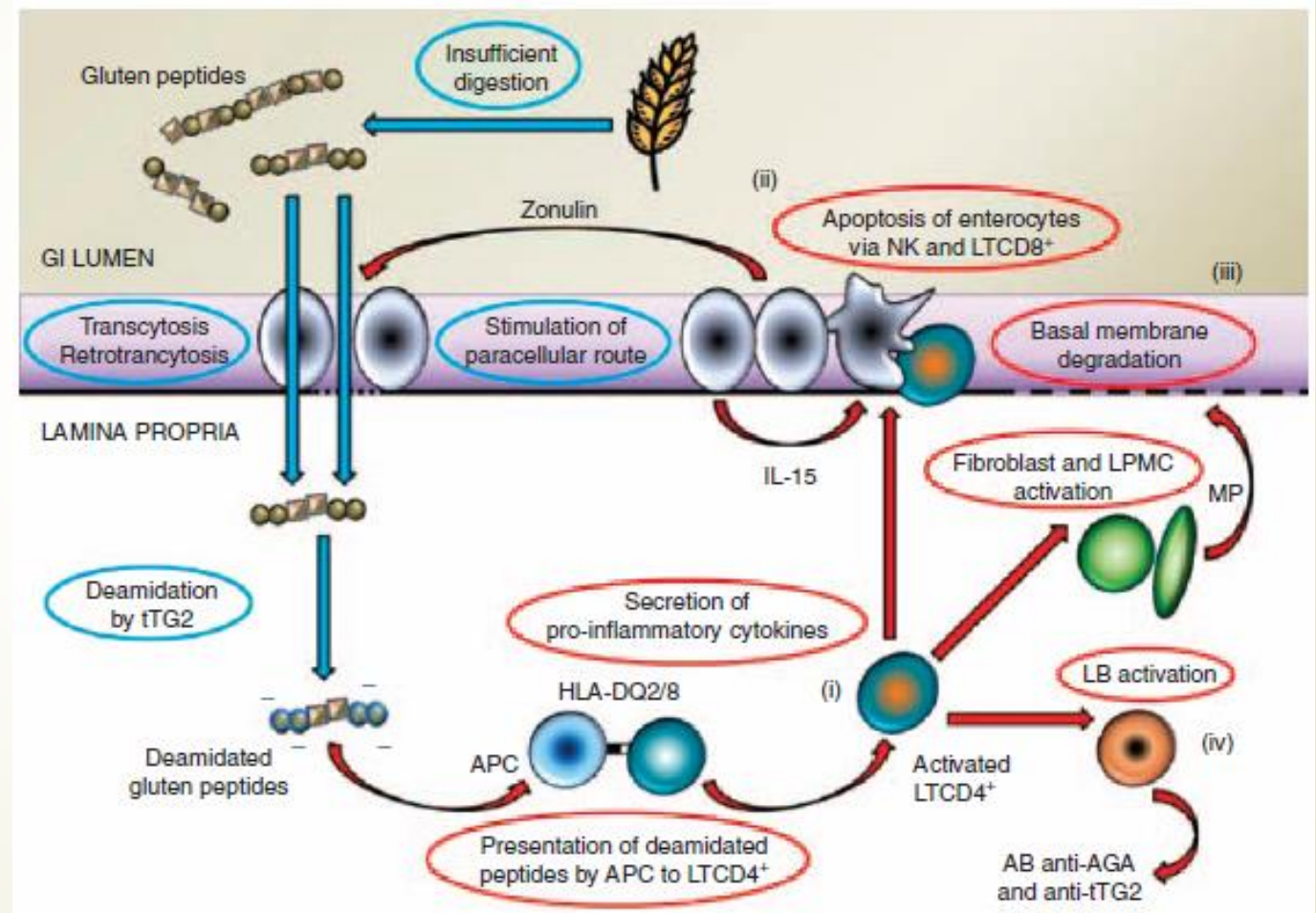


Benefits of the GFD in CD

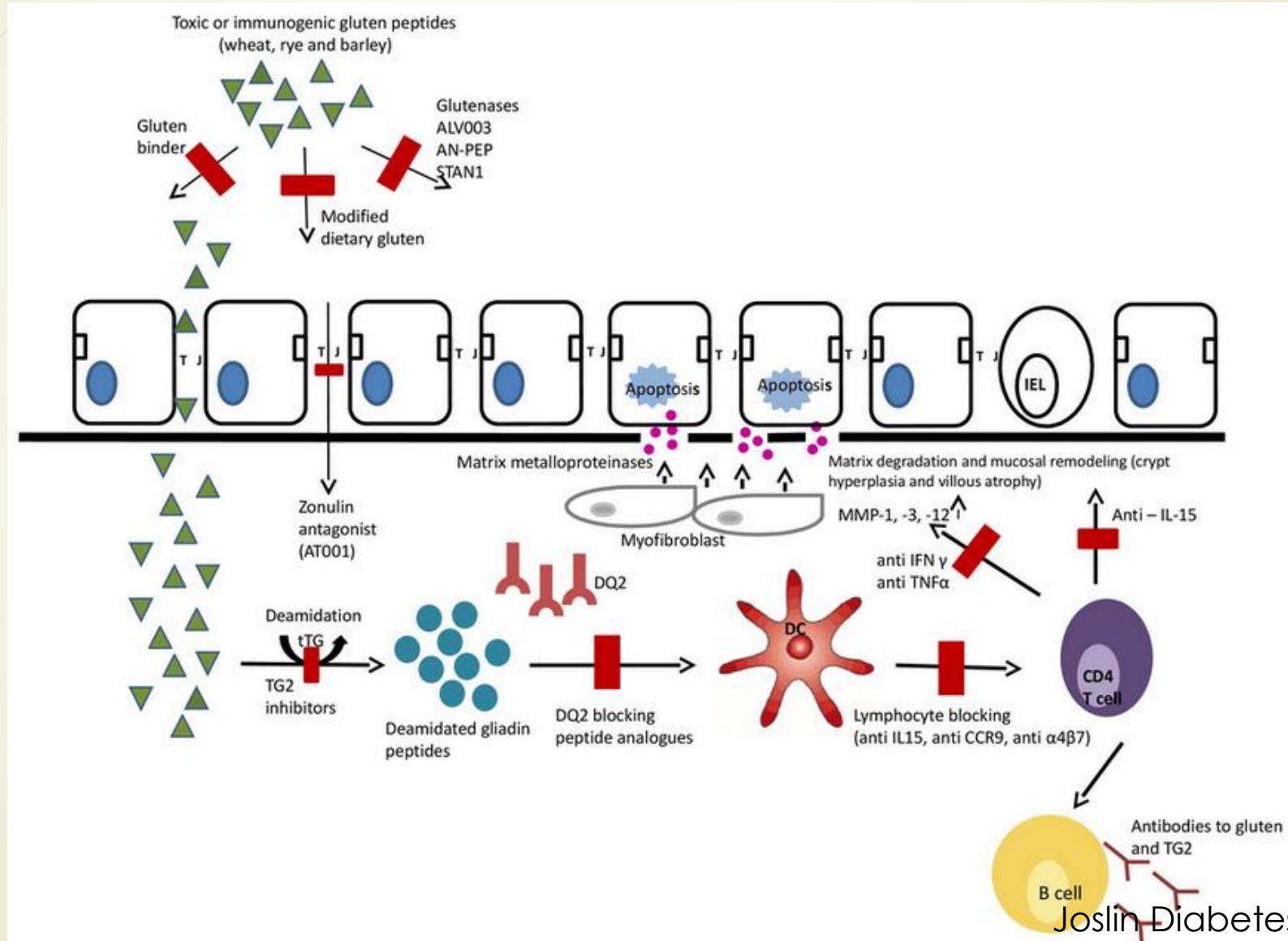
- ▶ Improve/resolve GI symptoms
- ▶ Resolve DH rash
- ▶ Resolve anemia
- ▶ Improve management of osteopenia, osteoporosis and hypothyroidism
- ▶ Might reduce the risk of other autoimmune disease
- ▶ Might improve mood and sense of well-being

Pathophysiology of CD

1. Gluten entry into submucosa
2. Deamidation of gluten by tissue transglutaminase
3. Immune activation



Research into CD Treatment





Summary



- ▶ The spectrum of wheat-related conditions include wheat allergy, intolerance and CD
- ▶ Celiac disease is autoimmune and is the only of the gluten spectrum that causes villous atrophy
- ▶ CD affects about 1% of the US population
- ▶ Having a family member with CD increases risk
- ▶ Blood tests are used to screen for CD, but biopsy of the small intestine is the gold standard for diagnosis
- ▶ The gluten-free diet is the only proven treatment for CD; it can be challenging
- ▶ A vaccine, pills to help break down gluten and immuno-therapy drugs are among treatment options being studied



Resources



- ▶ www.beyondceliac.org Celiac disease organization, lots of info about CD and diet
- ▶ www.glutenfreedrugs.com Site managed by a pharmacist and his students
- ▶ www.glutenfreewatchdog.org Tricia Thompson, MS, RD started this – they test foods for gluten



Questions?



Clinical Stages of Celiac Disease

Potential	Positive serological tests and normal intestinal biopsy
Asymptomatic	Absence of symptoms despite specific questioning regarding symptoms
Symptomatic	Presence of either intestinal or extra-intestinal symptoms
Classic	Diarrhea, signs and symptoms of malabsorption, or both
Non-classic	Lack of malabsorption symptoms, but other symptoms present (eg, anemia, osteoporosis)
Refractory	Persistent symptoms and villous atrophy despite adherence to a gluten-free diet

Estimation of Genetic Risk

HLA DQ2/DQ8 Genotype	Risk
DQ2+DQ8	1:7 (14.3%)
DQ2+DQ2 OR Homozygous DQB1*02	1:10 (10%)
DQ8+DQ8	1:12 (8.4%)
DQ8+DQB1*02	1:24 (4.2%)
Homozygous DQB1*02	1:26 (3.8%)
DQ2 alone	1:35 (2.9%)
DQ8 alone	1:89 (1.2%)
Population risk	1:100 (1%)
½ DQ2: DQB1*02	1:210 (0.5%)
½ DQ2: DQA1*05	1:1842 (0.05%)
No HLA-DQ2/DQB celiac susceptibility alleles	1:2518 (<0.04%)

Taylor, et. al., Gene Reviews accessed on-line 8/8/2018 at: <https://www.ncbi.nlm.nih.gov/books/NBK1727/>

Environmental Triggers - Gluten

- ▶ **Diabetes Autoimmunity Study in the Young (DAISY)**
 - ▶ 1875 of 2547 children genetically at risk for T1DM and CD and had dietary data and were screened for CD autoimmunity (blood tests)
 - ▶ 161 developed CDA
 - ▶ Lowest third of intake 6.4 gm/day - used as reference point
 - ▶ Middle third 10.9 gm/day – HR **1.96** (1.20-3.19), *P* = 0.01
 - ▶ Highest third 18.1 gm/day – HR **2.17** (1.22-3.88), *P* = 0.01
 - ▶ 85 diagnosed with CD
 - ▶ Lowest third - used as reference point
 - ▶ Middle third – HR 1.81 (0.94-3.49), *P* = 0.08
 - ▶ Highest third – HR 1.96 (0.9-4.24) *P* = 0.09
 - ▶ Gluten intake between 1 and 2 years (and to lesser extent, cumulative intake through childhood) were associated with CDA/CD

Screening Results

IgA-TTG	TOTAL IgA	IgG-TTG	IgA-DGP	IgG-DGP	DIAGNOSIS
<u>Positive</u>	<u>Normal</u>	Not performed	Not performed	Not performed	<u>Presumptive</u> CD
Negative	Normal	Negative	Negative	Negative	CD not likely
Negative	<u>Low</u>	<u>Positive</u>	Negative	<u>Positive</u>	Possible celiac disease
Negative	Normal	Negative	<u>Positive</u>	<u>Positive</u> (or not performed)	Possible celiac disease (may be seen in children less than 3 years old)