INFLAMED BY THE WORLD: UNDERSTANDING THE ROLE OF BIOMARKERS ON SYSTEMIC INFLAMMATION

Cheryl Burdette, ND

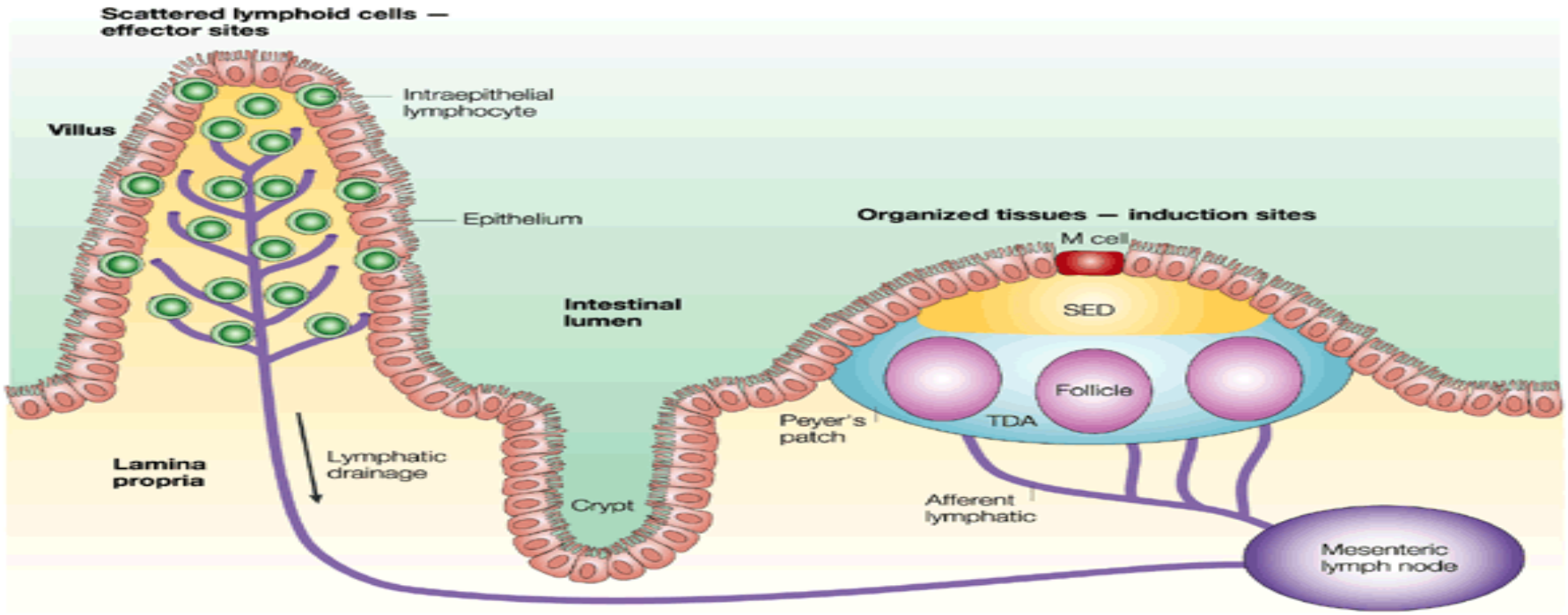
Dunwoody Labs, Director of Education

Organ of Immune tolerance

The intestinal mucosa forms the largest area of the body in direct contact with the exterior environment. If expanded, the surface of the small intestine alone can reach roughly the size of a tennis court, or 100 times the area of the skin.

Immune regulation by the gut

As expected, the intestinal mucosa is filled with a diverse and large number of immune cells. The gut-associated lymphoid-tissue (GALT) includes the Peyer's patches (PP) and isolated lymphoid follicles (ILFs). However, most of the immune cells in the intestine are associated with the intestinal villi, either in the intraepithelial or lamina propria



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588-Complete
Dietary Antigen Testing

Dunwoody Labs is an innovator of testing solutions that assist in the diagnosis and management of conditions.

PATIENT INFO

NAME: **SAMPLE REPORT**
REQUISITION ID: R#
SAMPLE ID: Sample #
DOB: -
SAMPLE DATE: -
RECEIVE DATE: -
REPORT DATE: 9/7/2017

CLINIC INFO

DUNWOODY LABS
ADDRESS: 9 DUNWOODY PARK
SUITE 121
DUNWOODY, GA 30338
PHONE: -
FAX: -

SUMMARY | 1/2

	588E - ALLERGIES					588G - SENSITIVITIES		
DIETARY ANTIGEN	RESULT	IgE	RESULT	IgG4	BLOCKING POTENTIAL	RESULT	TOTAL IgG	COMPLEMENT C3d
Almond		0.00 ng/ml		0.00 ng/ml			0.00 ng/ml	
Apple	MODERATE	3.50 ng/ml		0.00 ng/ml			14.08 ng/ml	
Asparagus	MODERATE	2.70 ng/ml		0.54 ng/ml			92.91 ng/ml	
Aspergillus Mix	HIGH	36.09 ng/ml		0.00 ng/ml		HIGH	1535.75 ng/ml	
Avocado		0.04 ng/ml		0.00 ng/ml			0.00 ng/ml	
Banana		0.35 ng/ml		0.22 ng/ml			63.34 ng/ml	
Barley		0.66 ng/ml	MODERATE	2.82 ng/ml	YES	MODERATE	154.84 ng/ml	YES
Basil	MODERATE	5.90 ng/ml		0.14 ng/ml			209.74 ng/ml	
Beef		0.00 ng/ml		0.00 ng/ml			0.00 ng/ml	
Black Pepper	HIGH	8.69 ng/ml		0.00 ng/ml			291.39 ng/ml	
Blueberry		1.51 ng/ml		0.00 ng/ml			80.24 ng/ml	
Brewer's Yeast	HIGH	17.92 ng/ml		0.00 ng/ml		MODERATE	525.06 ng/ml	
Broccoli	HIGH	10.69 ng/ml		0.00 ng/ml		MODERATE	426.52 ng/ml	
Cabbage	MODERATE	5.70 ng/ml		0.00 ng/ml			8.45 ng/ml	YES
Cacao	MODERATE	5.95 ng/ml		0.00 ng/ml			104.17 ng/ml	
Candida	HIGH	18.00 ng/ml	MODERATE	0.62 ng/ml		MODERATE	678.49 ng/ml	
Cantaloupe		0.02 ng/ml		0.00 ng/ml			38.01 ng/ml	
Carrot		0.00 ng/ml		0.00 ng/ml			60.53 ng/ml	
Casein	MODERATE	5.41 ng/ml		0.00 ng/ml			306.87 ng/ml	
Celery		1.53 ng/ml		0.00 ng/ml			32.38 ng/ml	
Cherry		0.02 ng/ml		0.00 ng/ml			0.00 ng/ml	
Chicken		0.00 ng/ml		0.00 ng/ml			0.00 ng/ml	
Cinnamon		0.00 ng/ml		0.00 ng/ml			289.98 ng/ml	
Clam	HIGH	26.63 ng/ml		3.14 ng/ml		MODERATE	163.29 ng/ml	YES
Coconut		0.00 ng/ml		0.00 ng/ml			35.19 ng/ml	
Codfish		0.00 ng/ml		0.05 ng/ml	YES		49.27 ng/ml	
Coffee	MODERATE	3.04 ng/ml		0.00 ng/ml			85.87 ng/ml	
Corn		0.00 ng/ml		0.00 ng/ml			19.71 ng/ml	
Cottonseed		0.00 ng/ml		0.00 ng/ml			26.75 ng/ml	
Cow's Milk	HIGH	13.46 ng/ml		2.09 ng/ml			685.53 ng/ml	
Crab		0.00 ng/ml		0.00 ng/ml			133.73 ng/ml	
Cucumber		1.31 ng/ml		0.00 ng/ml			14.08 ng/ml	
Dill Seed	MODERATE	3.50 ng/ml		0.00 ng/ml			91.50 ng/ml	
Egg Albumin		0.00 ng/ml		0.00 ng/ml			0.00 ng/ml	
Egg Yolk		0.00 ng/ml		0.00 ng/ml			221.00 ng/ml	YES
English Walnut		0.00 ng/ml		0.00 ng/ml			0.00 ng/ml	
Flounder		0.00 ng/ml		0.00 ng/ml			5.63 ng/ml	
Garlic		0.00 ng/ml		0.00 ng/ml			40.82 ng/ml	

Antibodies and Immunity

- IgE – Atopic, Allergies, Eczema, Asthma
- IgG4- Blocks IgE, Contributes to EoE, Thyroid, Ovarian, Prostate Issues
- IgG Total-Low grade chronic inflammation contributes to most chronic conditions, also drives a histaminergic response
- C3d-Complement, Activates complement cascade, creating more inflammation, particularly potent when bound to IgG

PATIENT	SAMPLE REPORT	REQUSITION	R#	REPORT DATE:	9/7/2017

MORE RESTRICTIVE DIET

We provide the diet found on this page as an alternative option with higher restrictive dietary recommendations where all moderate and high reactions are removed completely. This diet also introduces a **Rotate** category.

Low IgG reactions with complement are recommended to be rotated every 72 hours or to be reduced in amount of overall intake. While not all foods with complement are removed, a clinician may consider taking out anything that has complement present to further reduce reactions.

NO LIMITATION

These foods produce no immune reaction within your system at this time.

- Almond
- Avocado
- Banana
- Beef
- Blueberry
- Cantaloupe
- Carrot
- Celery
- Cherry
- Chicken
- Cinnamon
- Coconut
- Codfish
- Corn
- Cottonseed
- Crab
- Cucumber
- Egg Albumin
- English Walnut
- Flounder
- Garlic
- Green Pea
- Green Pepper
- Halibut
- Honeydew Melon
- Horseradish
- Lemon
- Lime
- Lobster
- Mushroom
- Mustard
- Navy Bean
- Oat
- Peanut
- Pear
- Pineapple
- Plum
- Pork
- Rice
- Rye
- Salmon
- Scallops
- Shrimp
- Soybean
- Squash Mix
- Strawberry
- Sunflower Seed
- Tomato
- Tuna
- Turkey
- White Potato
- Whole Wheat

ROTATE

These foods should be rotated out of your diet for a period of 72 hrs or reduced in overall intake.

- Egg Yolk
- Vanilla

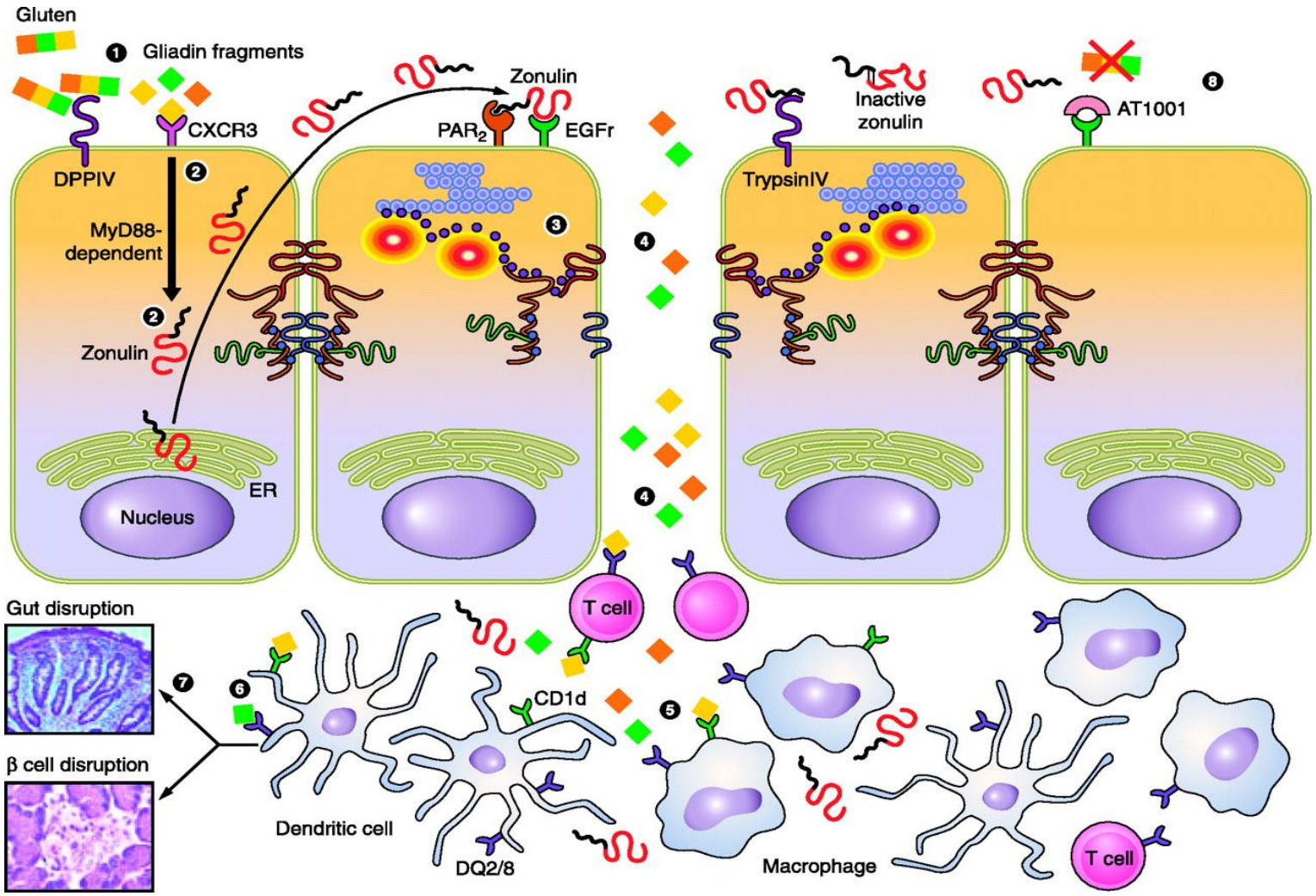
ELIMINATE

Remove these foods entirely from your diet.

- Apple
- Asparagus
- Aspergillus Mix
- Barley
- Basil
- Black Pepper
- Brewer's Yeast
- Broccoli
- Cabbage
- Cacao
- Candida
- Casein
- Clam
- Coffee
- Cow's Milk
- Dill Seed
- Gluten
- Goat's Milk
- Grapefruit
- Grapes
- Green Olive
- Kidney/Pinto
- Lettuce
- Onion
- Orange
- Oregano
- Peach
- Pecan
- Peppermint
- Sesame
- Spinach
- Sweet Potato
- Tea
- Watermelon

Complaint	Number Of Patients Reporting For Initial Test	Number Of Patients Reporting For Second Test
Memory/Concentration	22	3
Anxiety/Mood/Depression	20	3
Bloating/Stomach Pain	18	2
Fatigue	18	4
Joint Pain / Stiffness / Swelling	13	1
Muscle Aches	13	1
Craving Sugar	12	2
Sleeplessness/Insomnia	12	0
Lightheaded/Dizzy	11	2
Allergies/Sinus	9	2
Cold Intolerance	9	3
Inability to lose weight	9	2

Mechanisms of gliadin-induced zonulin release, increased intestinal permeability, and onset of autoimmunity.



Fasano A Physiol Rev 2011;91:151-175

Physiological Reviews

Antibodies and Immunity

- IgE – Atopic, Allergies, Eczema, Asthma
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- Corn
- Cottonseed
- Crab
- Cucumber
- Egg Albumin
- English Walnut
- Flounder
- Garlic
- Green Pea
- Green Pepper
- Halibut
- Honeydew Melon
- Horseradish
- Lemon
- Lime
- Lobster
- Mushroom
- Mustard
- Navy Bean
- Oat
- Peanut
- Pear
- Pineapple
- Plum
- Pork
- Rice
- Rye
- Salmon
- Scallops
- Shrimp
- Soybean
- Squash Mix
- Strawberry
- Sunflower Seed
- Tomato
- Tuna
- Turkey
- White Potato
- Whole Wheat

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- Egg Yolk
- Vanilla

ELIMINATE

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- Barley
- Basil
- Black Pepper
- Brewer's Yeast
- Broccoli
- Cabbage
- Cacao
- Candida
- Casein
- Clam
- Coffee
- Cow's Milk
- Dill Seed
- Gluten
- Goat's Milk
- Grapefruit
- Grapes
- Green Olive
- Kidney/Pinto
- Lettuce
- Onion
- Orange
- Oregano
- Peach
- Pecan
- Peppermint
- Sesame
- Spinach
- Sweet Potato
- Tea
- Watermelon

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588E
Dietary Antigen-Specific IgE & IgG4

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PATIENT INFO	
NAME:	SAMPLE REPORT
REQUISITION ID:	R#
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REPORT DATE:	9/7/2017

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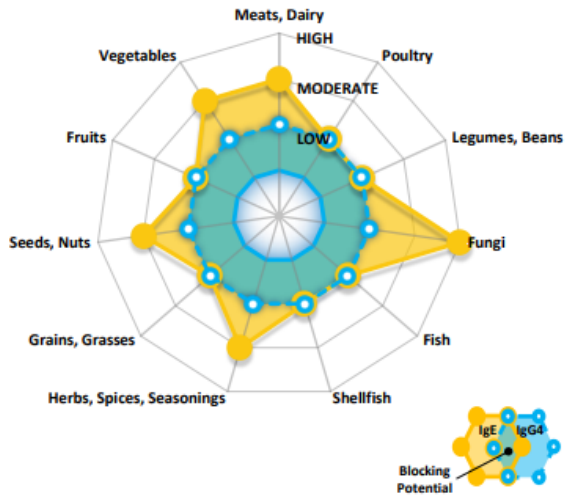
PHONE:	-
FAX:	-

588E - Dietary Antigen Testing | 1/4

Dietary Antigen Exposure by Food Group

	IgE	IgG4
Meats, Dairy	MODERATE	LOW
Poultry	LOW	LOW
Legumes, Beans	LOW	LOW
Fungi	HIGH	LOW
Fish	LOW	LOW
Shellfish	LOW	LOW
Herbs, Spices, Seasonings	MODERATE	LOW
Grains, Grasses	LOW	LOW
Seeds, Nuts	MODERATE	LOW
Fruits	LOW	LOW
Vegetables	MODERATE	LOW



Dietary Antigen Exposure by Food Group

In this test, a human serum sample is probed for the presence of IgE and IgG4 antibodies which have an exact affinity for specific dietary allergens. Dietary allergens are clustered by the food groups shown in the table and graph above. The quantitative summation of the IgE and IgG4 results within the offending food groups are expressed graphically. The exclusion of the offending food group(s) from the diet has been shown to reduce the severity of symptoms associated with food allergies.

Blocking Potential

In high levels, IgG4 antibodies alone can trigger an immune response within the body. However, data is available that provides support for the notion that IgG4 can serve another specific function of controlling antigen recognition by IgE and consequently regulating anaphylatic reactions and IgE-mediated immunity. IgG4 can act as a blocking agent by preventing IgE from binding to targeted receptor sites and releasing histamine. We refer to this as the blocking potential.

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588G
Dietary Antigen-Specific IgG with Complement

Dunwoody Labs is an innovator of testing solutions that assist in the diagnosis and management of conditions.

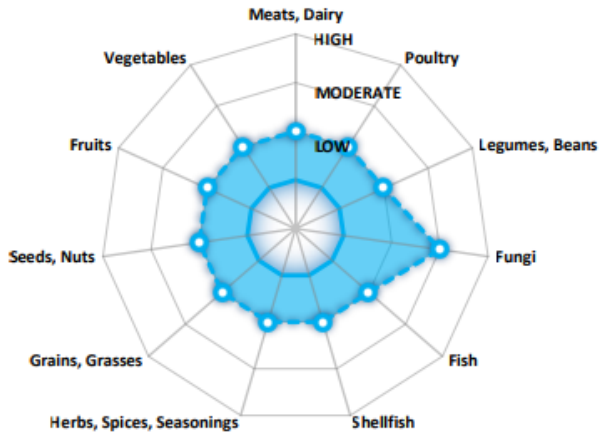
PATIENT INFO	
NAME:	SAMPLE REPORT
REQUISITION ID:	R#
SAMPLE ID:	Sample #
DOB:	-
SAMPLE DATE:	-
RECEIVE DATE:	-
REPORT DATE:	9/7/2017

CLINIC INFO	
	DUNWOODY LABS
ADDRESS:	9 DUNWOODY PARK
	SUITE 121
	DUNWOODY, GA 30338
PHONE:	-
FAX:	-

588G - Dietary Antigen Testing | 1/4

Dietary Antigen Exposure by Food Group

	IgG
Meats, Dairy	LOW
Poultry	LOW
Legumes, Beans	LOW
Fungi	MODERATE
Fish	LOW
Shellfish	LOW
Herbs, Spices, Seasonings	LOW
Grains, Grasses	LOW
Seeds, Nuts	LOW
Fruits	LOW
Vegetables	LOW



Dietary Antigen Exposure by Food Group

In this test, a human serum sample is probed for the presence of IgG antibodies which have an exact affinity for specific dietary allergens. Dietary allergens are clustered by the food groups shown in the table and graph above. The quantitative summation of the IgG results within the offending food groups are expressed graphically. The exclusion of the offending food group(s) from the diet has been shown to reduce the severity of symptoms associated with food allergies.

IgG

The IgG antibody response creates sensitivity to a particular food. Symptoms may be less severe than with IgE allergic reaction and can manifest anywhere from 3-72 hours after exposure. IgG reactions create inflammation that makes many pathologies worse. The delayed response makes sensitivities difficult to identify without a diagnostic test. Sensitivities can improve with treatment and improved gut health.

C3d

C3d is a complement antigen and an activator of our complement cascade system. Reaction to the specified food will worsen if C3d activation is present along with an IgG antibody response. The C3 protein attaches to the antigen and amplifies the IgG response, increasing the inflammatory potential of IgG titer. Complement is not dependent on exposure or antibody presence, and represents innate immune function.

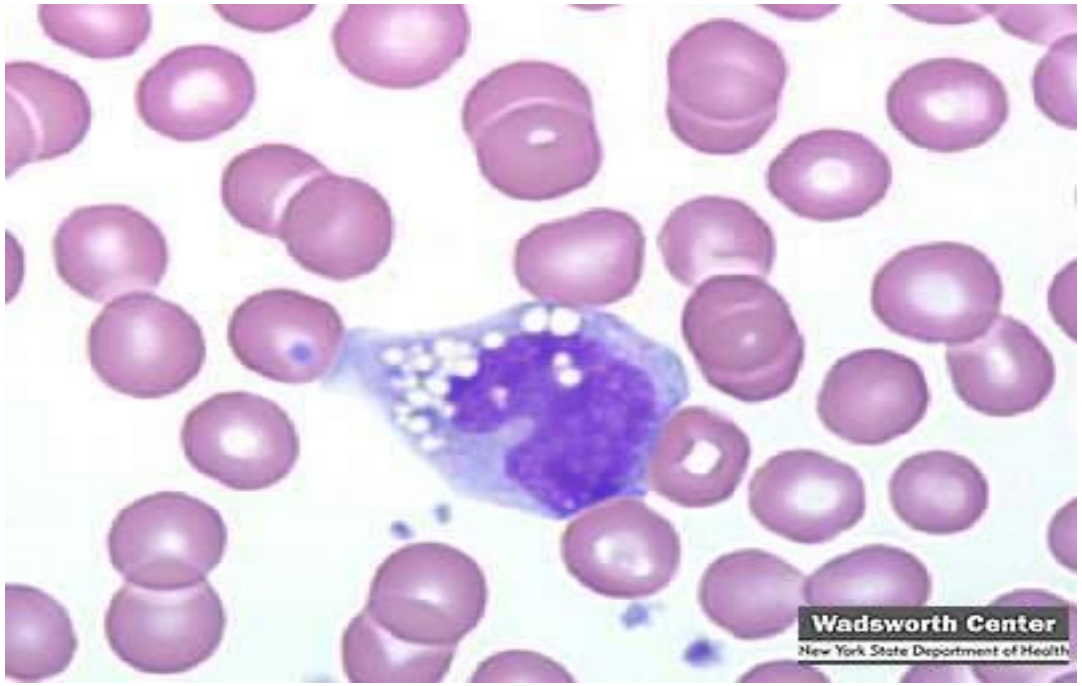
Patient Results

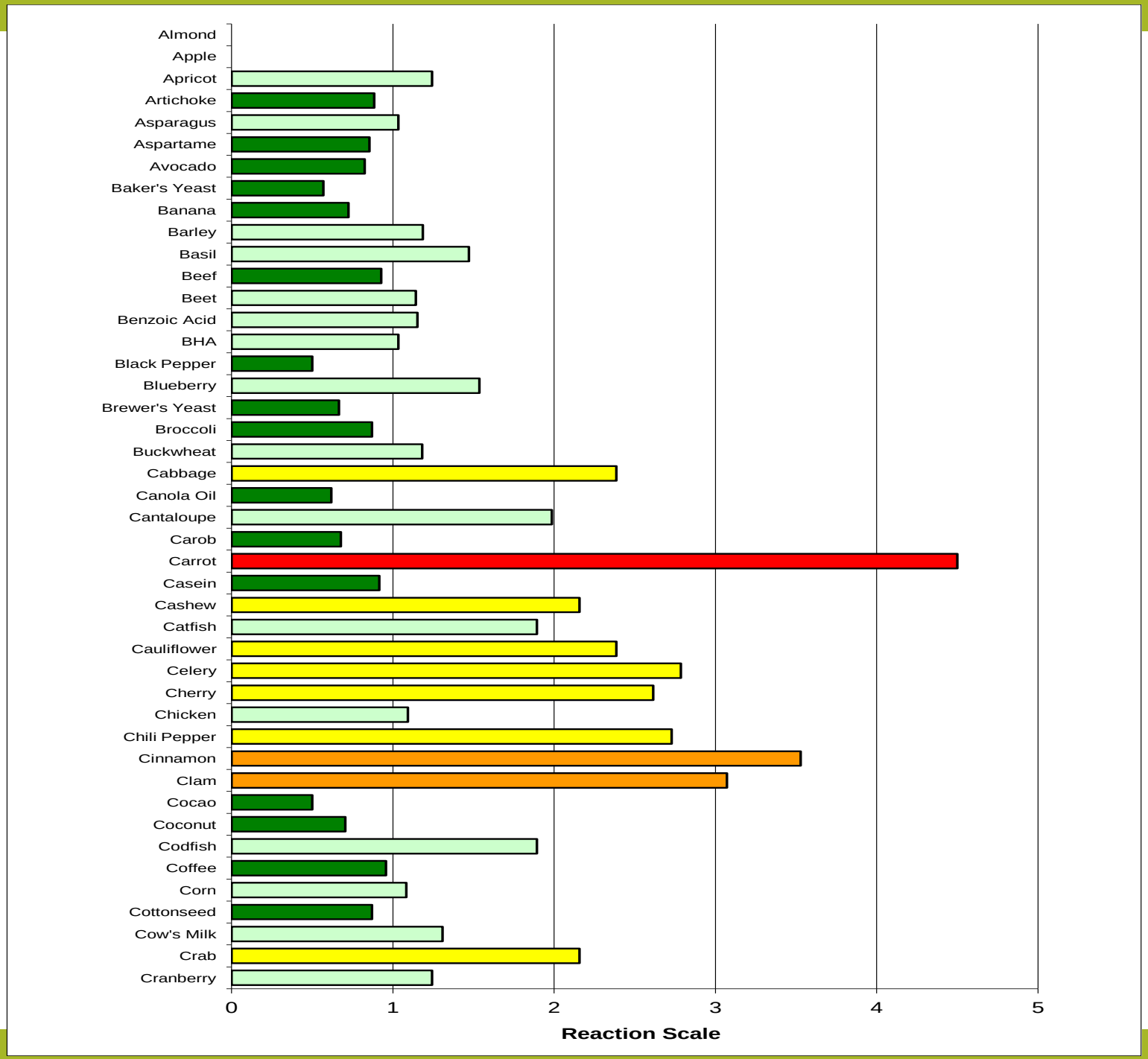
ANTIGEN	RESULT	IgG		REF. RANGE
MEATS, DAIRY				
Beef		0.00	ng/ml	0.00 - 50 ng/ml
Casein		306.87	ng/ml	0.00 - 1095 ng/ml
Cow's Milk		685.53	ng/ml	0.00 - 1388 ng/ml
Goat's Milk		398.37	ng/ml	0.00 - 1300 ng/ml
Pork		0.00	ng/ml	0.00 - 150 ng/ml
POULTRY				
Chicken		0.00	ng/ml	0.00 - 80 ng/ml
Egg Albumin		0.00	ng/ml	0.00 - 1160 ng/ml
Egg Yolk		221.00	ng/ml	0.00 - 820 ng/ml
Turkey		0.00	ng/ml	0.00 - 105 ng/ml
LEGUMES, BEANS				
Green Pea		0.00	ng/ml	0.00 - 240 ng/ml
Kidney/Pinto		15.48	ng/ml	0.00 - 480 ng/ml
Navy Bean		0.00	ng/ml	0.00 - 630 ng/ml
Peanut		0.00	ng/ml	0.00 - 950 ng/ml
Soybean		4.22	ng/ml	0.00 - 520 ng/ml
FUNGI				
Aspergillus Mix	HIGH	1535.75	ng/ml	0.00 - 2207 ng/ml
Brewer's Yeast	MODERATE	525.06	ng/ml	0.00 - 811 ng/ml
Candida	MODERATE	678.49	ng/ml	0.00 - 1949 ng/ml
Mushroom		0.00	ng/ml	0.00 - 230 ng/ml
FISH				
Codfish		49.27	ng/ml	0.00 - 275 ng/ml
Flounder		5.63	ng/ml	0.00 - 300 ng/ml
Halibut		0.00	ng/ml	0.00 - 100 ng/ml
Salmon		0.00	ng/ml	0.00 - 140 ng/ml
Tuna		0.00	ng/ml	0.00 - 190 ng/ml
SHELLFISH				
Clam	MODERATE	163.29	ng/ml	0.00 - 300 ng/ml
Crab		133.73	ng/ml	0.00 - 710 ng/ml
Lobster		0.00	ng/ml	0.00 - 240 ng/ml
Scallops		0.00	ng/ml	0.00 - 75 ng/ml
Shrimp		15.48	ng/ml	0.00 - 180 ng/ml

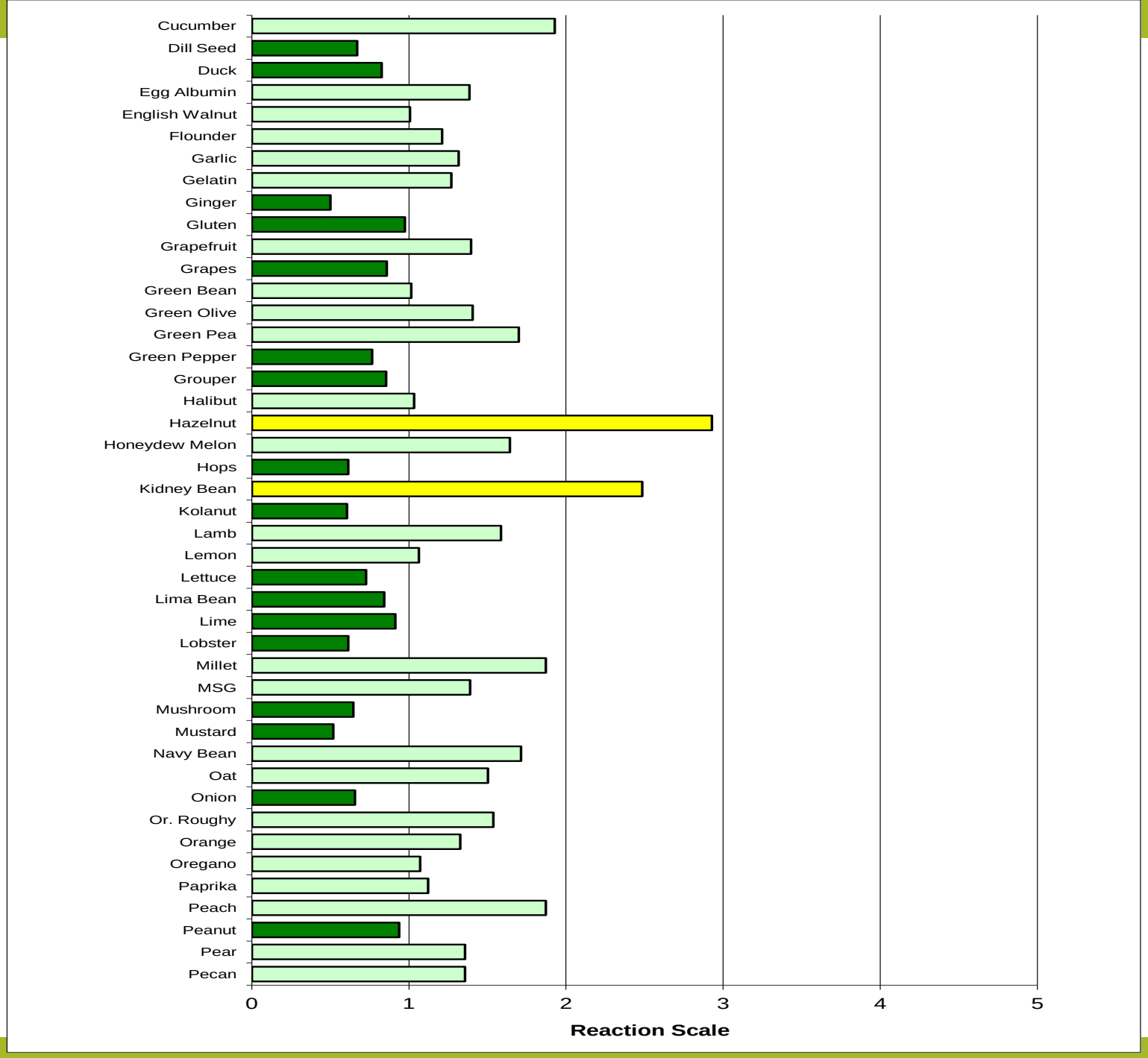
ANTIGEN	RESULT	COMPLEMENT		CUTOFF
MEATS, DAIRY				
Beef		0.00	ng/ml	60 ng/ml
Casein		3078.45	ng/ml	7650 ng/ml
Cow's Milk		1148.23	ng/ml	12400 ng/ml
Goat's Milk		2781.49	ng/ml	12900 ng/ml
Pork		3167.53	ng/ml	5500 ng/ml
POULTRY				
Chicken		0.00	ng/ml	25 ng/ml
Egg Albumin		0.00	ng/ml	3400 ng/ml
Egg Yolk	YES	584.01	ng/ml	4300 ng/ml
Turkey		0.00	ng/ml	110 ng/ml
LEGUMES, BEANS				
Green Pea		0.00	ng/ml	670 ng/ml
Kidney/Pinto		0.00	ng/ml	1200 ng/ml
Navy Bean		0.00	ng/ml	2100 ng/ml
Peanut		0.00	ng/ml	350 ng/ml
Soybean		0.00	ng/ml	4500 ng/ml
FUNGI				
Aspergillus Mix		0.00	ng/ml	7300 ng/ml
Brewer's Yeast		0.00	ng/ml	1800 ng/ml
Candida		0.00	ng/ml	2700 ng/ml
Mushroom		0.00	ng/ml	1050 ng/ml
FISH				
Codfish		0.00	ng/ml	1100 ng/ml
Flounder		0.00	ng/ml	800 ng/ml
Halibut		0.00	ng/ml	1100 ng/ml
Salmon		0.00	ng/ml	550 ng/ml
Tuna		0.00	ng/ml	630 ng/ml
SHELLFISH				
Clam	YES	108.88	ng/ml	2300 ng/ml
Crab		0.00	ng/ml	1500 ng/ml
Lobster		0.00	ng/ml	1050 ng/ml
Scallops		0.00	ng/ml	300 ng/ml
Shrimp		0.00	ng/ml	1300 ng/ml

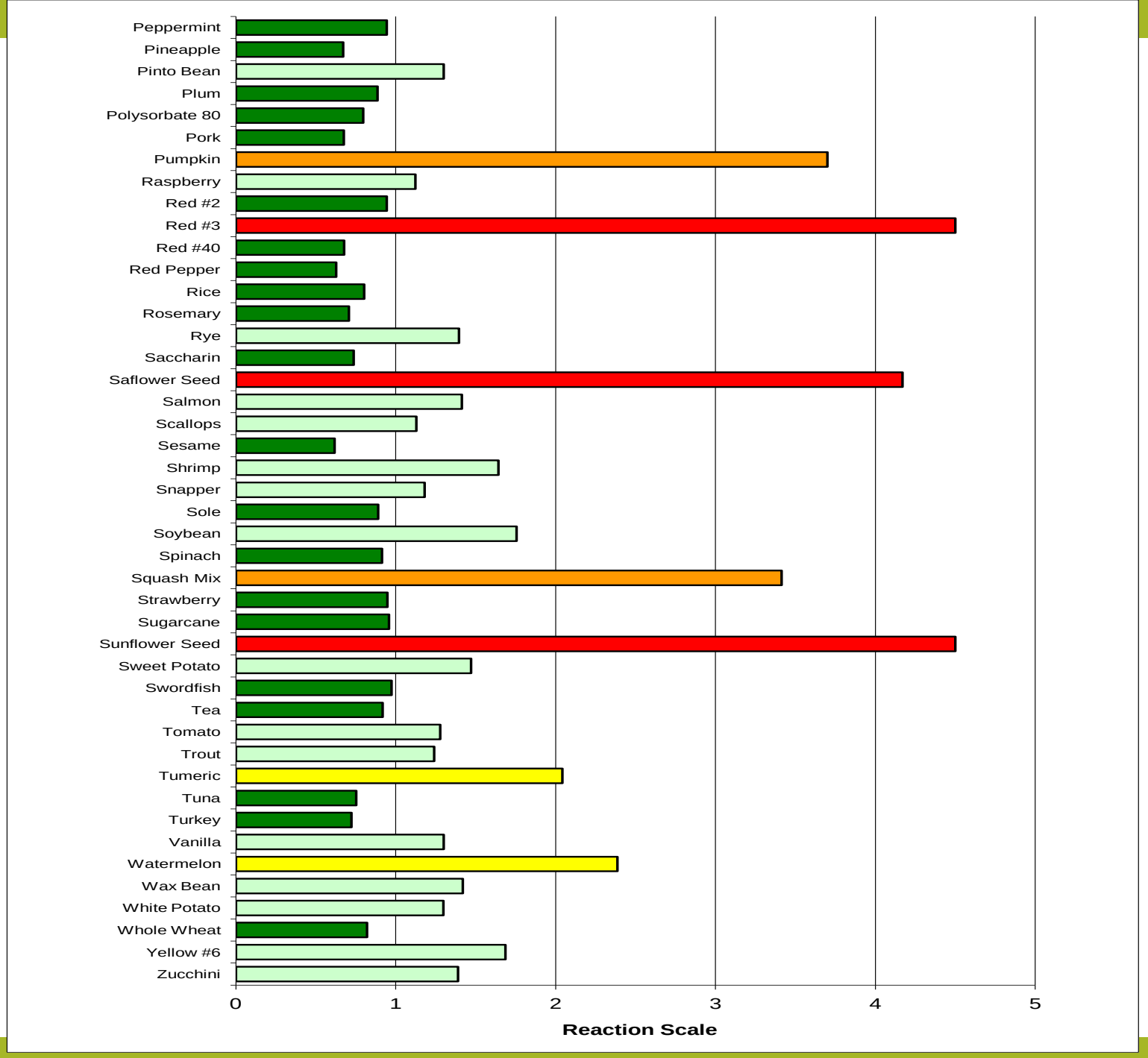
GL: 10/16/1955

- CC: fatigue and stomach issues
- Standard blood work: elevated monocytes




Almond
Apple
Apricot
Artichoke
Asparagus
Aspartame
Avocado
Baker's Yeast
Banana
Barley
Basil
Beef
Beet
Benzoic Acid
BHA
Black Pepper
Blueberry
Brewer's Yeast
Broccoli
Buckwheat
Cabbage
Canola Oil
Cantaloupe
Carob
Carrot
Casein
Cashew
Catfish
Cauliflower
Celery
Cherry
Chicken
Chili Pepper
Cinnamon
Clam
Cocao
Coconut
Codfish
Coffee
Corn
Cottonseed
Cow's Milk
Crab
Cranberry
0
1
2
3
4
5
Reaction Scale


Cucumber
Dill Seed
Duck
Egg Albumin
English Walnut
Flounder
Garlic
Gelatin
Ginger
Gluten
Grapefruit
Grapes
Green Bean
Green Olive
Green Pea
Green Pepper
Grouper
Halibut
Hazelnut
Honeydew Melon
Hops
Kidney Bean
Kolanut
Lamb
Lemon
Lettuce
Lima Bean
Lime
Lobster
Millet
MSG
Mushroom
Mustard
Navy Bean
Oat
Onion
Or. Roughy
Orange
Oregano
Paprika
Peach
Peanut
Pear
Pecan
0
1
2
3
4
5
Reaction Scale


Peppermint
Pineapple
Pinto Bean
Plum
Polysorbate 80
Pork
Pumpkin
Raspberry
Red #2
Red #3
Red #40
Red Pepper
Rice
Rosemary
Rye
Saccharin
Saflower Seed
Salmon
Scallops
Sesame
Shrimp
Snapper
Sole
Soybean
Spinach
Squash Mix
Strawberry
Sugarcane
Sunflower Seed
Sweet Potato
Swordfish
Tea
Tomato
Trout
Tumeric
Tuna
Turkey
Vanilla
Watermelon
Wax Bean
White Potato
Whole Wheat
Yellow #6
Zucchini
0
1
2
3
4
5
Reaction Scale

- Fiber
- Resveratrol, ALA, Arginine: A combination arginine, alpha lipoic acid and resveratrol for mitochondrial support
- S-acetyl glutathione: An orally absorbed form of glutathione
- Magnesium Chelate
- Functional Food: Functional food for blood sugar regulation
- Immunoglobulins in combination with probiotics
- Adrenal Support: A combination of nutrients for adrenal function (B5, B6, Vitamin C, carnitine)

Patient Information Sheet:

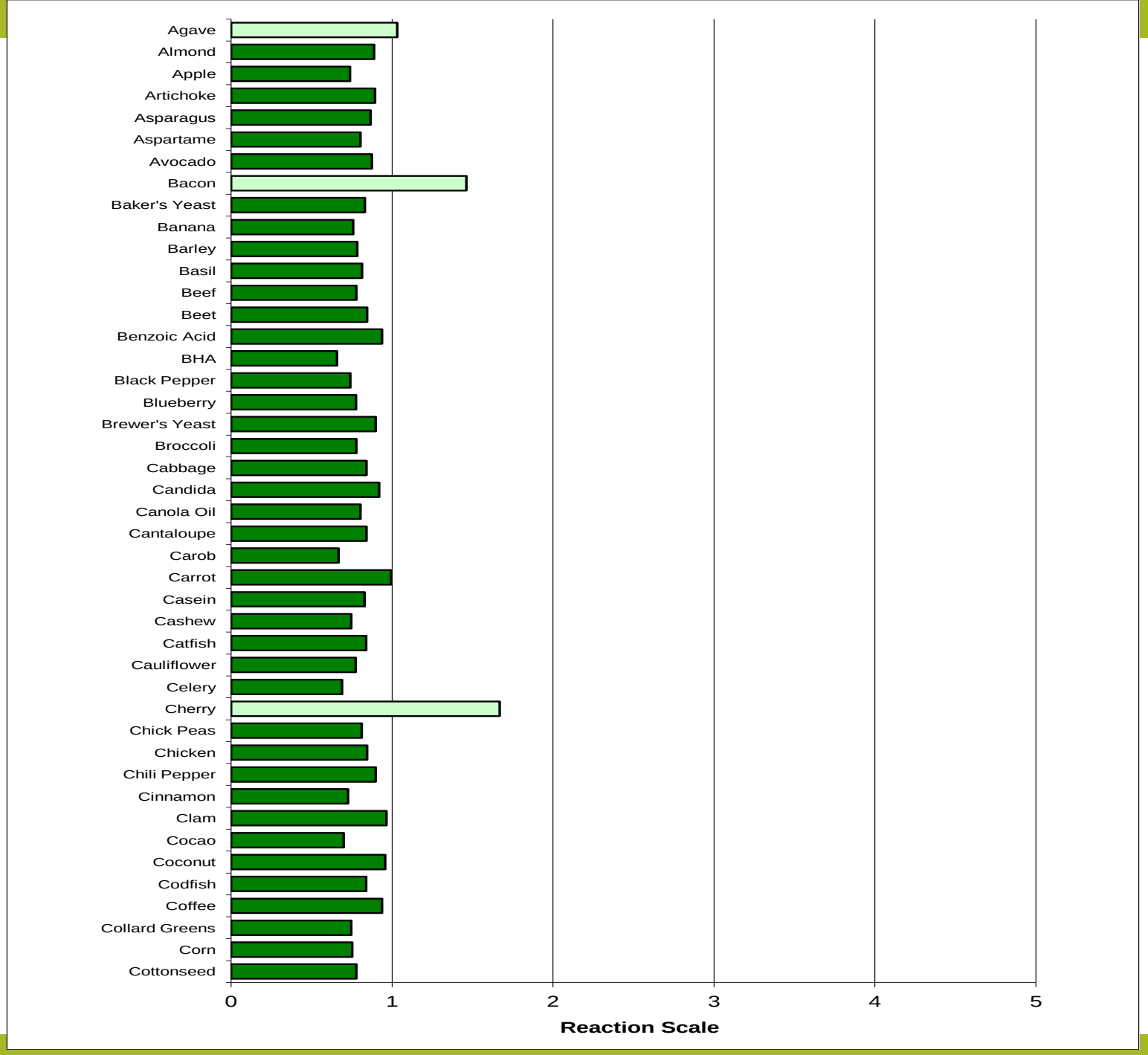
Name:	
Age:	NA
Date of Birth:	10/16/55
Date Drawn:	06/12/12
Date Test Completed:	07/04/12
Doctor:	Donaldson

Color Key:

	Severe Reaction	4+
	High Reaction	3+
	Moderate Reaction	2+
	Mild Reaction	1+
	No Reaction	Negative

Contact Information:

NutraTest
4646 North Shallowford Road, Suite N
Dunwoody, GA 30338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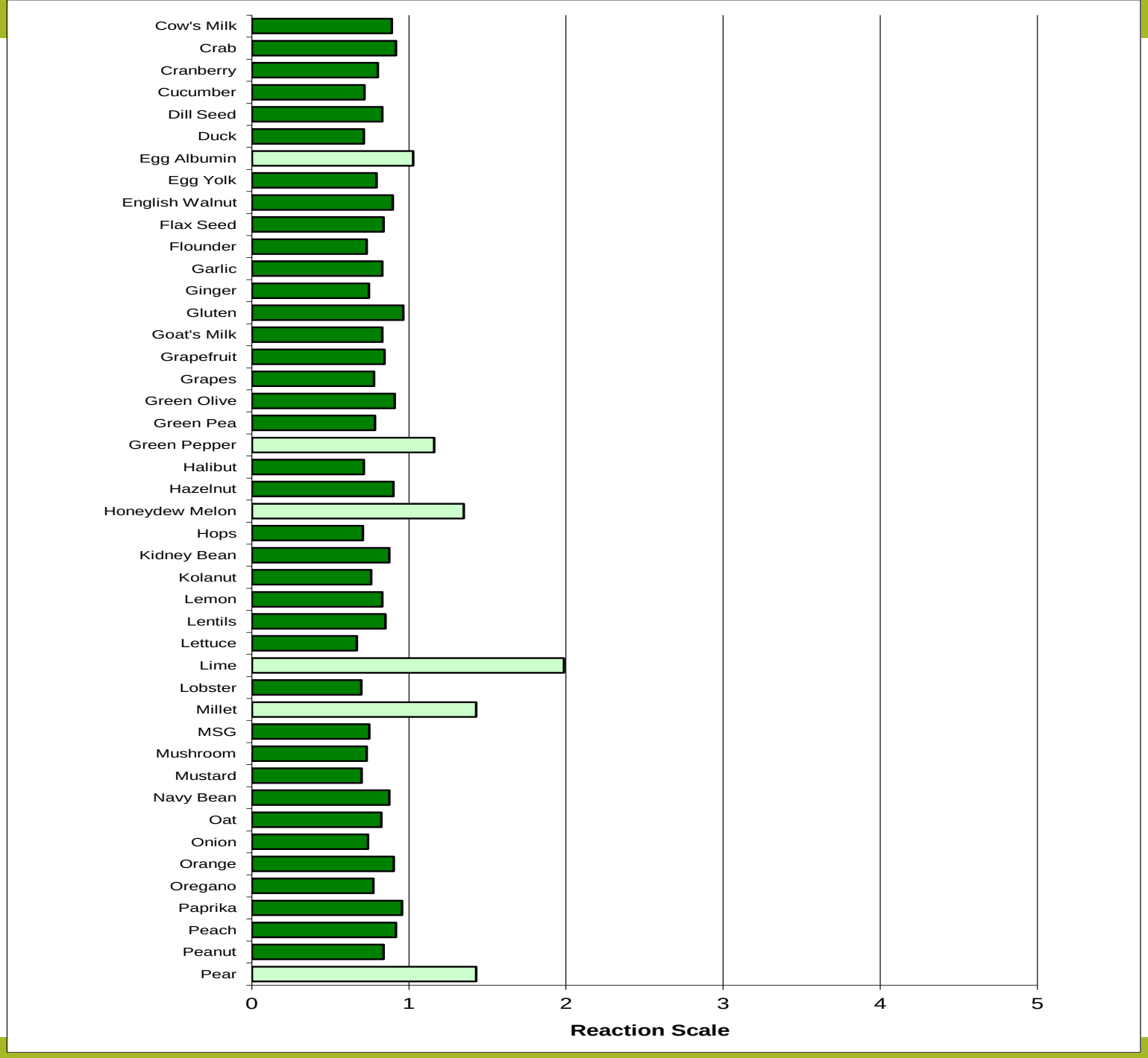
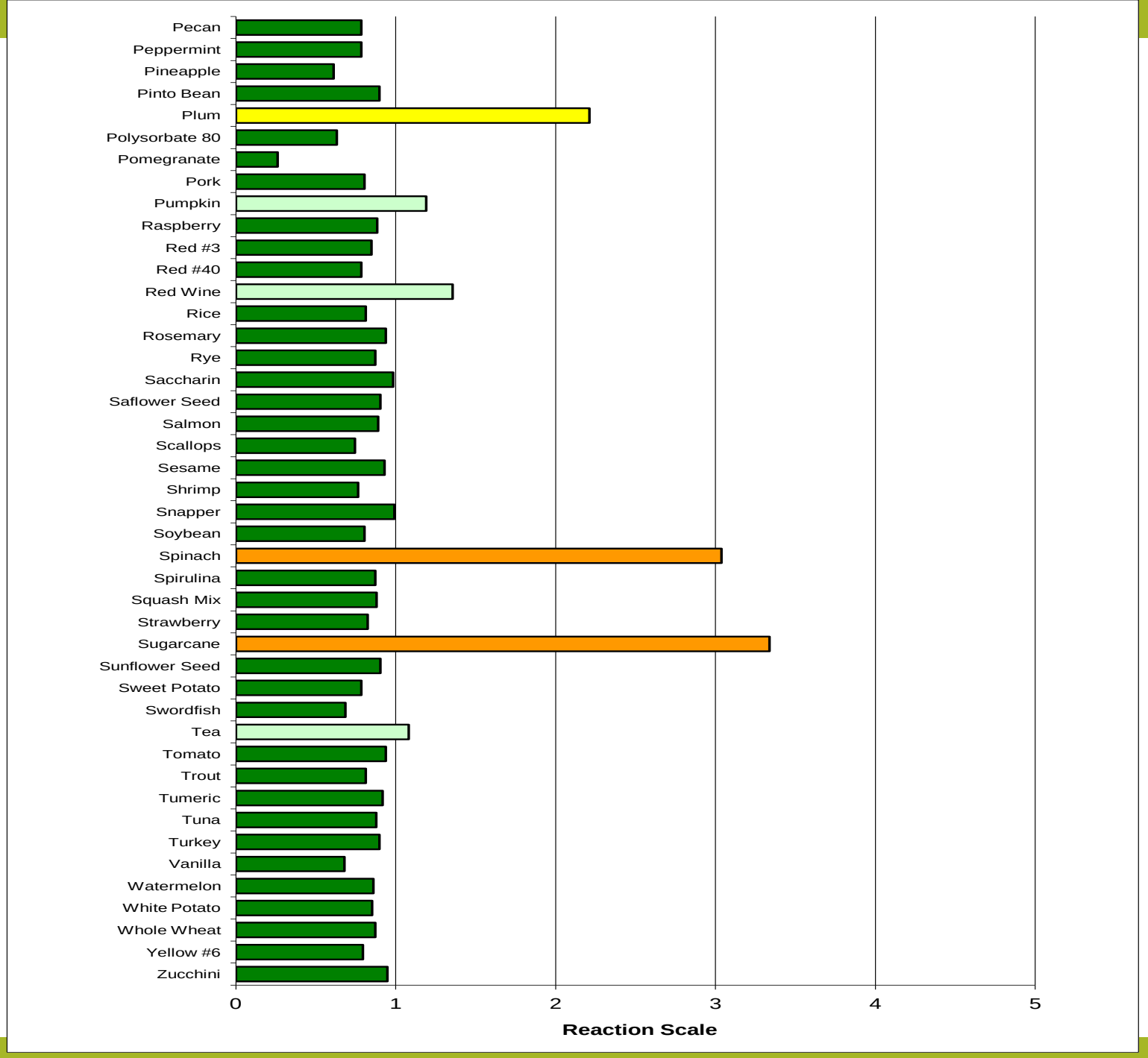
Black Pepper
Blueberry
Brewer's Yeast
Broccoli
Cabbage
Candida
Canola Oil
Cantaloupe
Carob
Carrot
Casein
Cashew
Catfish
Cauliflower
Celery
Cherry
Chick Peas
Chicken
Chili Pepper
Cinnamon
Clam
Cocao
Coconut
Codfish
Coffee
Collard Greens
Corn
Cottonseed
0
1
2
3
4
5
Reaction Scale


Cow's Milk
Crab
Cranberry
Cucumber
Dill Seed
Duck
Egg Albumin
Egg Yolk
English Walnut
Flax Seed
Flounder
Garlic
Ginger
Gluten
Goat's Milk
Grapefruit
Grapes
Green Olive
Green Pea
Green Pepper
Halibut
Hazelnut
Honeydew Melon
Hops
Kidney Bean
Kolanut
Lemon
Lentils
Lettuce
Lime
Lobster
Millet
MSG
Mushroom
Mustard
Navy Bean
Oat
Onion
Orange
Oregano
Paprika
Peach
Peanut
Pear
0
1
2
3
4
5
Reaction Scale


Pecan
Peppermint
Pineapple
Pinto Bean
Plum
Polysorbate 80
Pomegranate
Pork
Pumpkin
Raspberry
Red #3
Red #40
Red Wine
Rice
Rosemary
Rye
Saccharin
Saflower Seed
Salmon
Scallops
Sesame
Shrimp
Snapper
Soybean
Spinach
Spirulina
Squash Mix
Strawberry
Sugarcane
Sunflower Seed
Sweet Potato
Swordfish
Tea
Tomato
Trout
Tumeric
Tuna
Turkey
Vanilla
Watermelon
White Potato
Whole Wheat
Yellow #6
Zucchini
0
1
2
3
4
5
Reaction Scale

Follow-up

- Energy 7/10
- Feels much better
- Less hair loss
- BM: 2 a day
- Gas/Bloating-Resolved
- H. Pylori-negative
- Monocytes – in normal range

(Other treatment included working on treatment of parasite, identified with stool culture and concomitant high sIgA.

SIgA and IgE

- Pediatr Allergy Immunol. 2011 Aug;22(5):477-81. doi: 10.1111/j.1399-3038.2010.01106.x. Epub 2011 Feb 20.
- **High salivary secretory IgA antibody levels are associated with less late-onset wheezing in IgE-sensitized infants.**
- Low levels of secretory IgA (SIgA) and transient IgA deficiency have been associated with an increased risk for allergy, but data are conflicting. The aim was to assess the relationship between salivary SIgA antibody levels at 1 yr and wheezing at age four in a birth cohort, in particular the possible protective role of salivary SIgA in sensitized children. Saliva samples were obtained from all children (n=67) with a positive skin prick test (SPT) at 1 yr and 212 children with a negative SPT. In all, 200 of these children responded to questionnaires at 4 yrs and 183 were skin prick tested at that age. The levels of salivary SIgA and salivary IgA antibodies to the most common food allergen egg and inhalant allergen cat were analyzed by ELISA.
- In conclusion, high levels of SIgA antibodies in sensitized infants were associated with significantly less late-onset wheezing, supporting a protective role against development of asthmatic symptoms. Recurrent infections and other factors supporting an increased microbial pressure during infancy were associated with high levels of salivary SIgA.

Functions of sIgA

As the most abundant class of antibody found in the intestinal lumen of humans and most other mammals, secretory IgA (SIgA) has long been recognized as a first line of defense in protecting the intestinal epithelium from enteric pathogens and toxins.

SIgA production against specific mucosal antigens is dependent on the sampling by Peyer's patch M cells, processing by underlying antigen-presenting cells such as dendritic cells (DCs), T cell activation, and ultimately B cell class switch recombination in gut-associated lymphoid tissue (GALT), mesenteric lymph nodes, and possibly neighboring lamina propria (MLNs)

Multiple cytokines, including IL-4, TGF-β, IL-5, IL-6, IL-10 are instrumental in intestinal stimulating SIgA production.

A subset of these cytokines, notably TGF-β and IL-10, are also required for maintaining mucosal tolerance, thus establishing one of the many links between SIgA production, immunity and intestinal homeostasis.

sIgA is less likely to bind to complement than IgG

- Because SIgA essentially resides within an external environment (*i.e.*, the intestinal lumen), it must combat microbial infections through mechanisms that are fundamentally different than those employed by antibodies in systemic compartments.
- Whereas IgG, for example, promotes the killing and clearance of pathogenic bacteria through the coordinated activity of complement and Fc-mediated uptake by macrophages and neutrophils, it generally assumed that SIgA primary acts through receptor blockade, steric hindrance and/or immune exclusion.

Agglutination – mechanism of sIgA

Agglutination, for example, is simply the formation of macroscopic clumps of bacteria (or viruses) as the result of antibody-mediated cross-linking via polyvalent surface antigens.

This may interrupt quorum sensing, disrupting virulence.

sIgA critical in controlling response to commensel flora

- Analysis of cytokine expression in Peyer's patches demonstrated that SIgA-coated *S. flexneri* results in down regulation of pro-inflammatory cytokines TNF-α, IL-6, IFN-γ, while maintaining a sustained level of regulatory IL-10.

- sIgA overutilized against foods means less ability to mark commensel flora as normal

sIgA and Foods

- Neutralization of allergen occurred with the abundant SIgA found in mucosal secretions and contributed towards limiting the access of allergen to the lamina propria and thus the inflammatory responses.

- sIgA goes up in response to foods to neutralize it

sIgA –The Trojan Horse

- In genetically susceptible individuals with CD, complexes of luminal specific SIgA antibodies and gluten-derived deamidated gliadin peptides are retro-transcytosed across epithelial cells, leading to the basal delivery of intact, highly reactive peptides that stimulate inflammatory processes via activation of target $CD4^+$ T cells.

- This abnormal intestinal transport is mediated by the recognition of SIgA-gliadin complexes by the transferrin receptor (TfR, CD71) expressed at high levels on the apical surface of intestinal epithelial cells in CD patients.

Zonulin

SAMPLE DATE:	
RECEIVE DATE:	
REPORT DATE:	

Nine Dunwoody Park, Suite 121
Dunwoody, GA 30338
Phone: 678-736-6374 | Fax: 770-674-1701
Email: info@dunwoodylabs.com

ADVANCED INTESTINAL BARRIER ASSESSMENT: PROFILE 5150 (PLASMA)

Zonulin

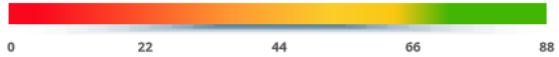
PATIENT RESULT
0.2
ng/ml
REPORTABLE RANGE: <4.0 ng/ml

OPTIMAL

Diamine Oxidase (DAO)

PATIENT RESULT
1.0
ng/ml
REPORTABLE RANGE: 0-88 ng/ml

ABNORMALLY LOW



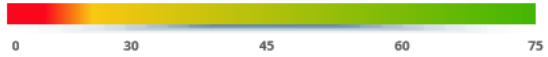
Histamine

PATIENT RESULT
0.84
ng/ml
REPORTABLE RANGE: 0.0–2.4 ng/ml

BORDERLINE

DAO: Histamine Ratio

1



A high DAO-to-Histamine ratio suggests that there is sufficient DAO present to degrade any free histamine.

A low ratio, on the other hand, may be indicative of histamine intolerance. The lower the ratio, and particularly the closer it gets to 1, the stronger that indication.

Inflammation, the fire behind The pathology

- Allergy and related diseases affect at least 100 million people worldwide. (hidden allergy symptoms)
- In the USA alone about 50 million people suffer from allergies at a cost of 18 billion dollars per year.
- In general, the prevalence of food allergies has increased to more than 50% in adults and more than 70% in children in the past few years.
- Food-related allergies cause a wide variety of illnesses ranging from skin rashes and headaches to chronic intestinal diseases.
- Although the symptoms of allergy may differ, allergens (antigens) from food, food additives or environmental sources cause the production of antibodies (IgM, IgA, IgG, IgE and IgD) or interact with the mucosa or epidermis and stimulate T-cells.

The Gut's Role in Inflammation

The cells in the intestinal mucosa consist of mainly activated or antigen experienced T cells (CD45RBlo, CD44hi, CD69hi, CD62Llo) that are capable of producing several proinflammatory cytokines such as IL-4, IFN-*γ*, *IL-17A/F, IL-22, and TNF-α [6–15].*

Living Life on the Edge of the Wall

- Physiological, Pathological, and Therapeutic Implications of Zonulin-Mediated Intestinal Barrier Modulation
  - Am J Pathol. 2008 November; 173(5): 1243–1252.
- Human zonulin, a potential modulator of intestinal tight junctions
  - J Cell Sci 113, 4435-4440. December 15, 2000

Leaky gut and autoimmune diseases.

Leaky gut and autoimmune diseases. Mucosal Biology Research Center, University of Maryland School of Medicine, Baltimore, MD 21201, USA. afasano@mbrc.umaryland.ed

Autoimmune diseases are characterized by tissue damage and loss of function due to an immune response that is directed against specific organs. This review is focused on the role of impaired intestinal barrier function on autoimmune pathogenesis. Together with the gut-associated

This new paradigm subverts traditional theories underlying the development of these diseases and suggests that these processes can be arrested if the interplay between genes and environmental triggers is prevented by re-establishing the zonulin-dependent intestinal barrier function.

Clin Rev Allergy Immunol. 2012 Feb;42(1):71-8. doi: 10.1007/s12016-011-8291-x.
PMID: 22109896 [PubMed - in process]

Leaky gut and type II diabetes

Leaky gut and diabetes mellitus: what is the link?

de Kort S, Keszthelyi D, Masclee AA.

Department of Internal Medicine, Division of Gastroenterology-Hepatology, Maastricht University Medical Centre+, Maastricht, the Netherlands.

Abstract

Diabetes mellitus is a chronic disease requiring lifelong medical attention. With hundreds of millions suffering worldwide, and a rapidly rising incidence, diabetes mellitus poses a great burden on healthcare systems. Recent studies investigating the underlying mechanisms involved in disease development in diabetes point to the role of the dys-regulation of the intestinal barrier. Via alterations in the intestinal permeability, intestinal barrier function becomes compromised whereby access of infectious agents and dietary antigens to mucosal immune elements is facilitated, which may eventually lead to immune reactions with damage to pancreatic beta cells and can lead to increased cytokine production with consequent insulin resistance. Understanding the factors regulating the intestinal barrier function will provide important insight into the interactions between luminal antigens and immune response elements. This review analyses recent advances in the mechanistic understanding of the role of the intestinal epithelial barrier function in the development of type 1 and type 2 diabetes. Given our current knowledge, we may assume that reinforcing the intestinal barrier can offer and open new therapeutic horizons in the treatment of type 1 and type 2

The Gut is more than a filter

Physiol Rev. 2011 Jan;91(1):151-75.

Zonulin and its regulation of intestinal barrier function: the biological door to inflammation, autoimmunity, and cancer.

Fasano A.

Sour

Mucc

The

Zonulin is the only physiological modulator of intercellular tight junctions described so far that is involved in trafficking of macromolecules and, therefore, in tolerance/immune response balance.

Zonulin and its regulation of intestinal barrier function: the biological door to inflammation, autoimmunity, and cancer. Physiol Rev. 2011 Jan;91(1):151-75.

Zonulin, the lens to immune tolerance

Gut 2009;**58**:1152-1167 doi:10.1136/gut.2008.163667

Recent advances in basic science

Crohn's disease: Th1, Th17 or both? The change of a paradigm: new immunological and genetic insights implicate Th17 cells in the

Crohn's disease: Th1, Th17 or both? The change of a paradigm: new immunological and genetic insights implicate Th17 cells in the pathogenesis of Crohn's disease

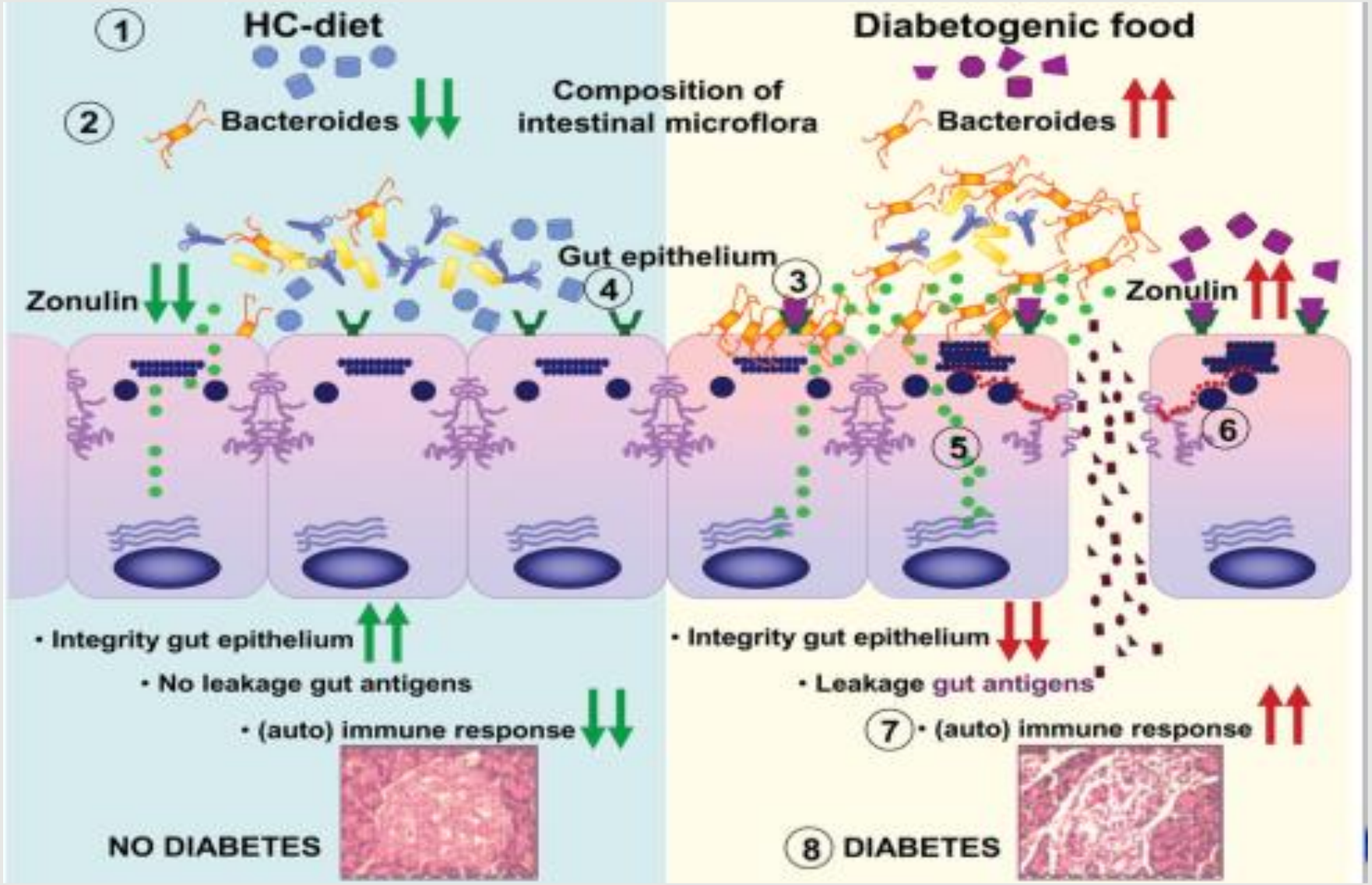
Gut 2009;**58**:1152-1167 doi:10.1136/gut.2008.163667

is

IL1β, IL6, IL21 and IL23. Recent studies indicate that TGFβ is essential not only for the development of murine Th17 cells but also for differentiation of human Th17 cells. TGFβ reciprocally regulates the differentiation of inflammatory Th17 cells and suppressive Treg subsets, with the concomitant presence of proinflammatory cytokines favouring Th17 cell differentiation. Several studies demonstrated an important role of Th17 cells in intestinal inflammation, particularly in Crohn's disease. Genome-wide association studies indicate that *IL23R* and five additional genes involved in Th17 differentiation (*IL12B*, *JAK2*, *STAT3*, *CCR6* and*TNFSF15*) are associated with susceptibility to Crohn's disease and partly also to ulcerative colitis. Taken together, both Th1 and Th17 cells are important mediators of inflammation in Crohn's disease, although activities previously ascribed to IL12 may be mediated by IL23. Anti-IL12/IL23p40 antibody therapy, which targets both Th1 and Th17 cells, is effective in Crohn's disease. However, the complex relationship between Th1 and Th17 cells has not been completely analysed. This will be of great importance to delineate the specific contributions of these cells to Crohn's disease and other autoimmune diseases.

Dysbiotic Diet and LPS

Alter intestinal tight junction function



Degradation of tight junctions determines symptoms/virulence

Biochim Biophys Acta. 2009 Apr;1788(4):832-41. Epub 2008 Nov 14.

Tight junctions as targets of infectious agents.

Guttman JA, Finlay BB.

Source

Simon Fraser University, Department of Biological Sciences, Shrum Science Centre, Burnaby, BC, Canada V5A 1S6. jguttman@sfu.ca

Abstract

The epithelial barrier is a critical border that segregates luminal material from entering tissues. Essential components of this epithelial fence are physical intercellular structures termed tight junctions. These junctions use a variety of transmembrane proteins coupled with cytoplasmic adaptors, and the actin cytoskeleton, to attach adjacent cells together thereby forming intercellular seals. Breaching of this barrier has profound effects on human health and disease, as barrier deficiencies have been linked with the onset of inflammation, diarrhea generation and pathogenic effects. Although tight junctions efficiently restrict most microbes from penetrating into deeper tissues and contain the microbiota, some pathogens have developed specific strategies to alter or disrupt these structures as part of their pathogenesis, resulting in either pathogen penetration, or other consequences such as diarrhea. Understanding the strategies that microorganisms use to commandeer the functions of tight junctions is an active area of research in microbial pathogenesis. In this review we highlight and overview the tactics bacteria and viruses use to alter tight junctions during disease. Additionally, these studies have identified novel tight junction protein functions by using pathogens and their virulence factors as tools to study the cell biology of junctional structures.

Zonulin Treatment

- Immunoglobulins
- Gluten Removal
- Antimicrobials

LPS

ADVANCED INTESTINAL BARRIER ASSESSMENT: PROFILE 5150 (PLASMA)

PATIENT RESULT

1.0
ng/ml

REPORTABLE RANGE:
<41.5 ng/ml

ABNORMALLY LOW

LPS IgA

PATIENT RESULT

6.5
ng/ml

REPORTABLE RANGE:
<41.5 ng/ml

ABNORMALLY LOW

LPS IgG

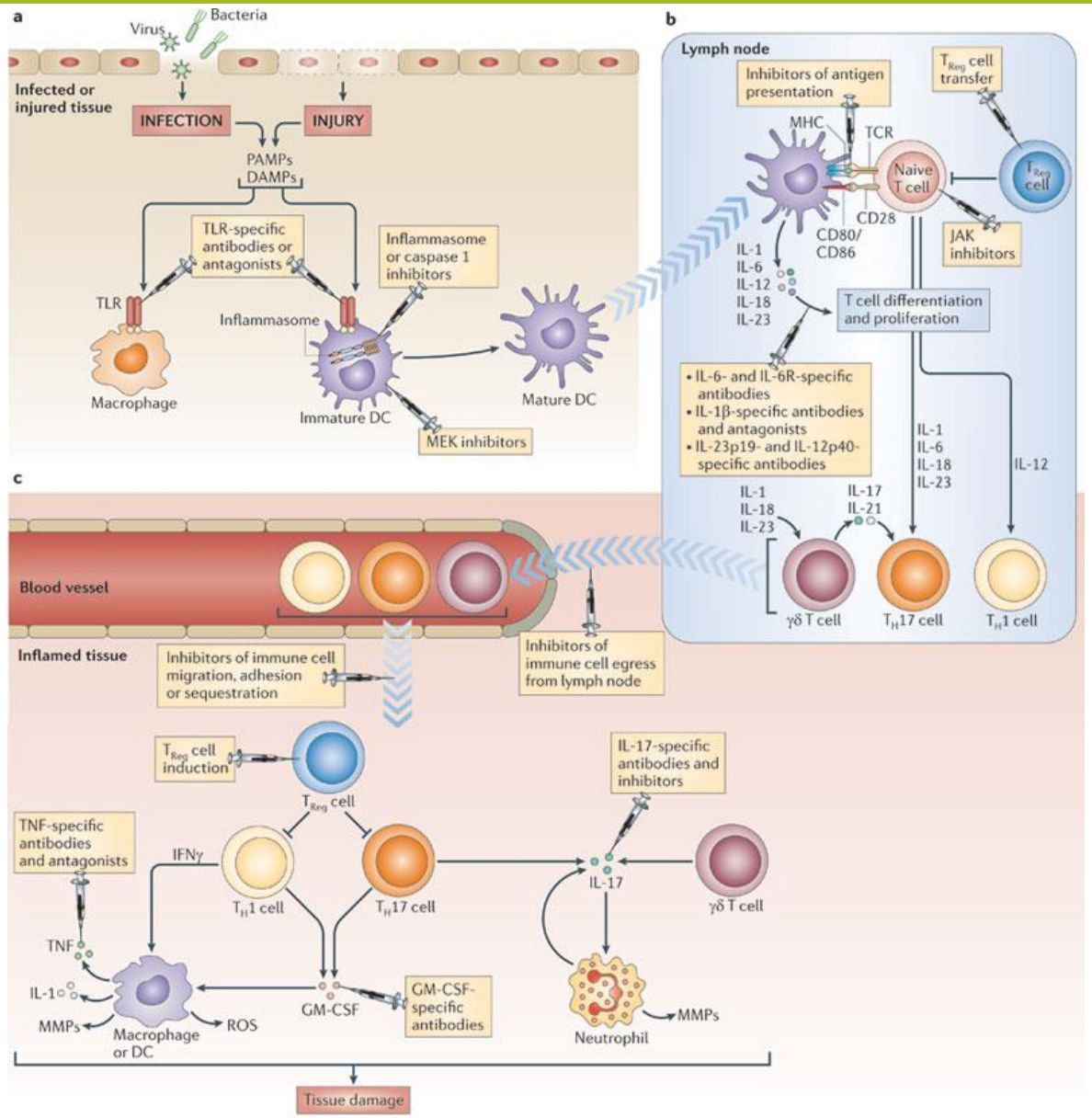
PATIENT RESULT

15.6
ng/ml

REPORTABLE RANGE:
<75.1 ng/ml

BORDERLINE HIGH

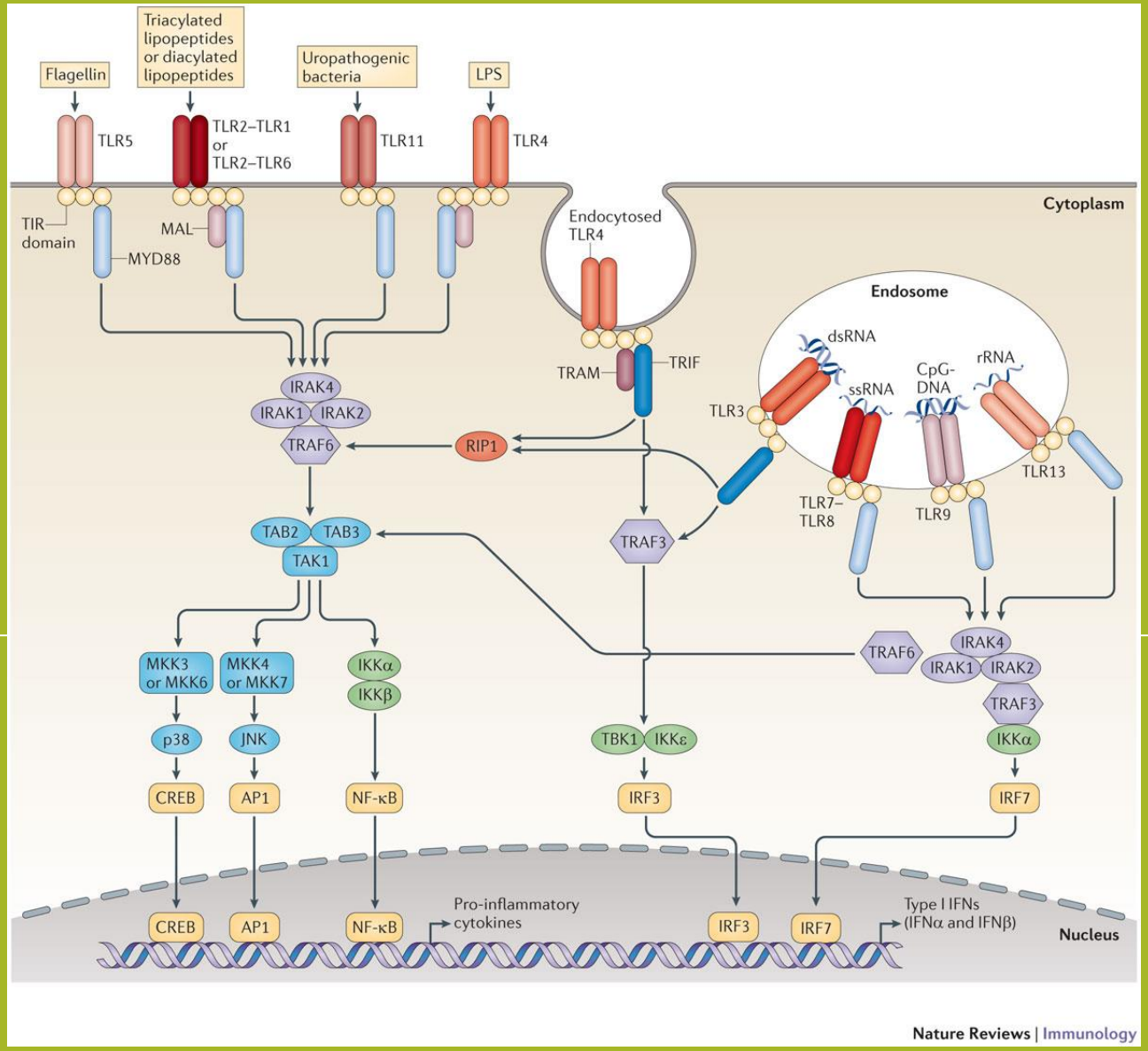
LPS IgM



Nature Reviews | Immunology

LPS

- Compared to the classic exotoxins of bacteria, endotoxins are less potent and less specific in their action, since they do not act enzymatically. Endotoxins are heat stable, boiling for 30 minutes does not destabilize endotoxin
- But certain powerful oxidizing agents such as superoxide, peroxide and hypochlorite, have been reported to neutralize them. Endotoxins, although antigenic, cannot be converted to toxoids.


Flagellin
Triacylated lipopeptides or diacylated lipopeptides
Uropathogenic bacteria
LPS
TLR5
TLR2–TLR1 or TLR2–TLR6
TLR11
TLR4
TIR domain
MAL
MYD88
Cytoplasm
Endocytosed TLR4
Endosome
dsRNA
rRNA
CpG-DNA
ssRNA
TLR3
TLR13
TLR7–TLR8
TLR9
TRAM
TRIF
IRAK4
IRAK1
IRAK2
TRAF6
RIP1
TAB2
TAB3
TAK1
TRAF3
MKK3 or MKK6
MKK4 or MKK7
IKKα
IKKβ
p38
JNK
CREB
AP1
NF-κB
TBK1
IKKε
IRF3
IRF7
Pro-inflammatory cytokines
Type I IFNs (IFNα and IFNβ)
Nucleus
Nature Reviews | Immunology

LPS is a factor in inducing Autoimmunity

- Lipopolysaccharide (LPS) is a component of the Gram-negative bacterial cell wall that activates B cells, resulting in marked production of polyclonal antibodies.

LPS is also a potent substance that secretes various kinds of mediators, including interleukin-12 (IL-12) and interferon-γ (IFN-γ)

- Therefore, a number of studies have demonstrated that LPS plays a role in some diseases in which autoantibodies or self antigen-specific T cells are involved.
- LPS enhances nephritis, experimental autoimmune uveitis, experimental autoimmune myocarditis and experimental autoimmune enterocolitis, and autoimmune arthritis.

LPS Treatment

- Antimicrobials
- Leaky Gut Treatments
- Immune Support: Immunoglobulins

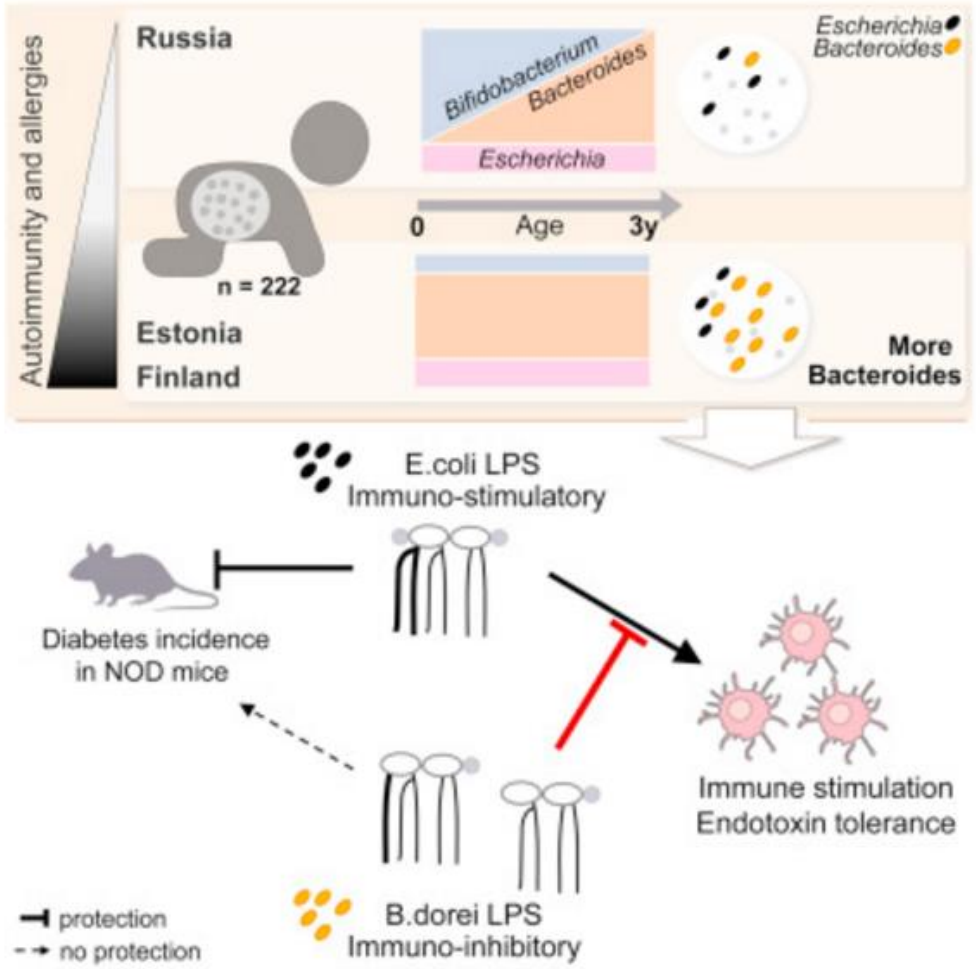
Normalizing Treg function

- Eliminate LPS
- Andrographis
- Curcuminoids
- Resveratrol
- Vitamin D
- Vitamin A
- Omega 3 fatty acids

LPS

- **Endotoxins** are part of the outer membrane of the cell wall of Gram-negative bacteria.
- Endotoxin is invariably associated with Gram-negative bacteria whether the organisms are pathogenic or not. Although the term "endotoxin" is occasionally used to refer to any cell-associated bacterial toxin, in bacteriology it is properly reserved to refer to the **lipopolysaccharide** complex associated with the outer membrane of Gram-negative pathogens such as *Escherichiacoli*, *Salmonella*, *Shigella*, *Pseudomonas*, *Neisseria*, *Haemophilus influenzae*, *Bordetella pertussis* and *Vibrio cholerae*.

Graphical Abstract



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of immune education.

LPS, Zinc and Alkaline Phosphatase

- The making of LPS can be modified in order to present a specific sugar structure. Those can be recognized by either other LPS (which enables to inhibit LPS toxins) or glycosyltransferases that use those sugar structure to add more specific sugars.
- It has recently been shown that a specific enzyme in the intestine (alkaline phosphatase) can detoxify LPS by removing the two phosphate groups found on LPS carbohydrates

- Bates JM, Akerlund J, Mittge E, Guillemin K (2007). "Intestinal alkaline phosphatase detoxifies lipopolysaccharide and prevents inflammation in zebrafish in response to the gut microbiota". *Cell Host Microbe.* **2** (6): 371–82.

World Journal of Gastrointestinal Pathophysiology

Reversed with Zinc

PMC full text: World J Gastrointest Pathophysiol. 2014 Nov 15; 5(4): 496–513.
Published online 2014 Nov 15. doi: 10.4291/wjgp.v5.i4.496

Table 1

Gastrointestinal morbidities associated with Zinc deficiency

Condition	Model used	Reversibility with Zn supplementation	Ref.
Esophageal cancer	Rodent	Yes	Fong et al[27], 2011
Diarrhea	Human	Yes	Hambidge[72], 1992
Inflammatory bowel diseases	Porcine	Yes	Sturniolo et al[82], 2002
Celiac disease	Human	Not determined	Wierdsma et al[143], 2013
Alcoholic liver disease	Mouse	Yes	Lambert et al[198], 2003
Malnutrition	Guinea pig	Yes	Rodriguez et al[65], 1996

Bacterial Endotoxin

- LPS-A marker of transcellular leaky gut
- Profound research with heart disease
- Connects gut to systemic inflammatory problems
- Higher in auto-immune conditions (worse with Mercury)

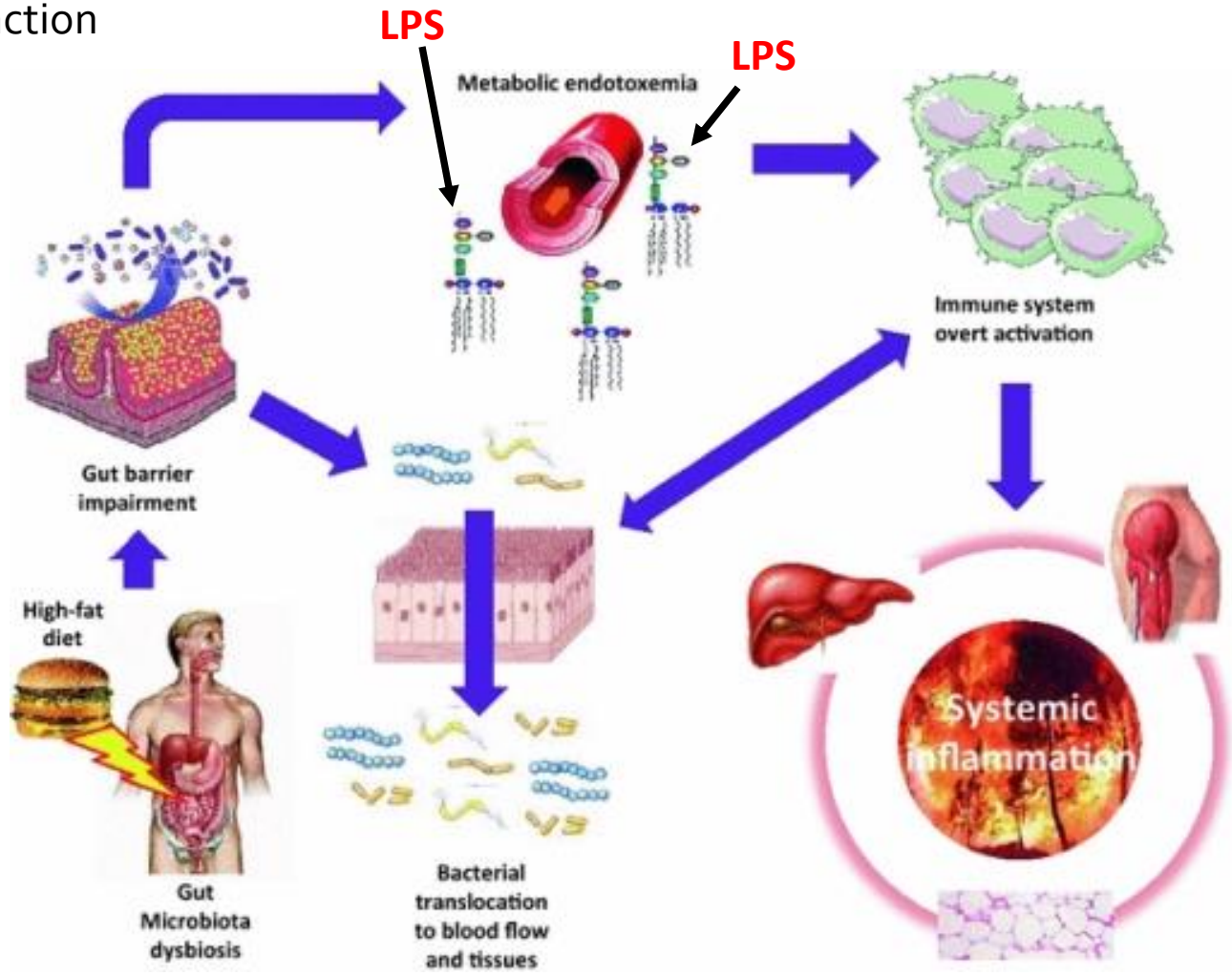
LPS antibodies

- LPS IgM
- LPS IgA
- LPS IgG

- High: Under high level of attack
- Low Levels: Immune System has no bottomed out

Metabolic Endotoxemia – Increased Systemic LPS

- **Elevated plasma levels of endotoxin associated with:**
  - ❖ Shock
  - ❖ Multiple organ dysfunction
  - ❖ Depression
  - ❖ Anxiety
  - ❖ Sepsis
  - ❖ Atherosclerosis
  - ❖ Obesity
  - ❖ Type 2 diabetes
  - ❖ Alzheimer's
  - ❖ Autoimmunity
  - ❖ Infertility
  - ❖ Hypogonadism



Neviere R. Pathophysiology of sepsis. In: UpToDate, Manaker, S (Ed), UpToDate, Waltham, MA, 2014;
Erridge, et al. Am J Clin Nutr. 2007;86:1286-1292;

METABOLIC ENDOTOXEMIA AND ELEVATED LPS IN DISEASE

Metabolic Endotoxemia Initiates Obesity and Insulin Resistance
Patrice D. Cani, Jacques Amar, et al.
Diabetes 2007 Jul; 56(7): 1761-1772. https://doi.org/10.2337/db06-1491

Metabolic endotoxemia directly increases the proliferation of adipocyte precursors at the onset of metabolic diseases through a CD14-dependent mechanism
Elodie Luche, Béatrice Cousin, et al.
Mol Metab. 2013 Aug; 2(3): 281–291.

Lipopolysaccharide Causes an Increase in Intestinal Tight Junction Permeability in Vitro and in Vivo by Inducing Enterocyte Membrane Expression and Localization of TLR-4 and CD14
Shuhong Guo, Rana Al-Sadi, Hamid M. Said, and Thomas Y. Ma
The American Journal of Pathology, Vol. 182, No. 2, February 2013

Elevated endotoxin levels in non-alcoholic fatty liver disease
Alison L Harte et al.
Journal of Inflammation 20107:15
Received: 3 September 2009Accepted: 30 March 2010Published: 30 March 2010

CONDITION	MECHANISM
Leptin Resistance	LPS enters and causes inflammation in the enteric nervous system leading to a disruption in the gut-brain axis of communication.
Chronic Constipation	LPS enters the enteric nervous system and causes disruption in signals for gastric emptying and bowel motility.
Mood and Appetite Disorders	LPS disrupts ghrelin function which has a direct impact on appetite and mood,
Depression	LPS can migrate to the blood-brain barrier and cause inflammation along with inhibition of dopamine receptors.
Cognitive Decline	Inflammation in the blood brain barrier leads to cognitive decline
Loss of Memory and Recall	LPS can get into the amygdala and hippocampus which disrupts memory function
Depression	LPS can increase the turnover of serotonin in the synapse and CNS reducing the concentration in those regions
Anorexia	The reduction of serotonin in the synapse and CNS is proposed as a possible mechanism for anorexia.
Anxiety	LPS disrupts key communication between the hypothalamic-adrenal-pituitary axis thereby increasing the expression of corticosteroid releasing hormone
Chronic Pain	Elevated LPS in sensory neurons in the dorsal root stimulate nociceptors.
Parkinson's	Intra-cranially LPS causes microglial activation and neuronal loss
Hypogonadism (low testosterone)	Increased circulating LPS and the subsequent chronic immune activation has feedback inhibition of testosterone production. GELDING theory.
Autoimmunity	Chronic activation of the innate immune system in various tissues leads to the by-stander effect where self-tissues inadvertently become targeted by the immune system.

Diamine Oxidase Evaluation

SAMPLE DATE:	
RECEIVE DATE:	
REPORT DATE:	

Nine Dunwoody Park, Suite 121
Dunwoody, GA 30338
Phone: 678-736-6374 | Fax: 770-674-1701
Email: info@dunwoodylabs.com

ADVANCED INTESTINAL BARRIER ASSESSMENT: PROFILE 5150 (PLASMA)

Zonulin

PATIENT RESULT
0.2
ng/ml
REPORTABLE RANGE: <4.0 ng/ml

OPTIMAL

0 1 2 3 4

Diamine Oxidase (DAO)

PATIENT RESULT
1.0
ng/ml
REPORTABLE RANGE: 0-88 ng/ml

ABNORMALLY LOW

0 22 44 66 88

Histamine

PATIENT RESULT
0.84
ng/ml
REPORTABLE RANGE: 0.0–2.4 ng/ml

BORDERLINE

0.0 0.6 1.2 1.8 2.4

DAO: Histamine Ratio

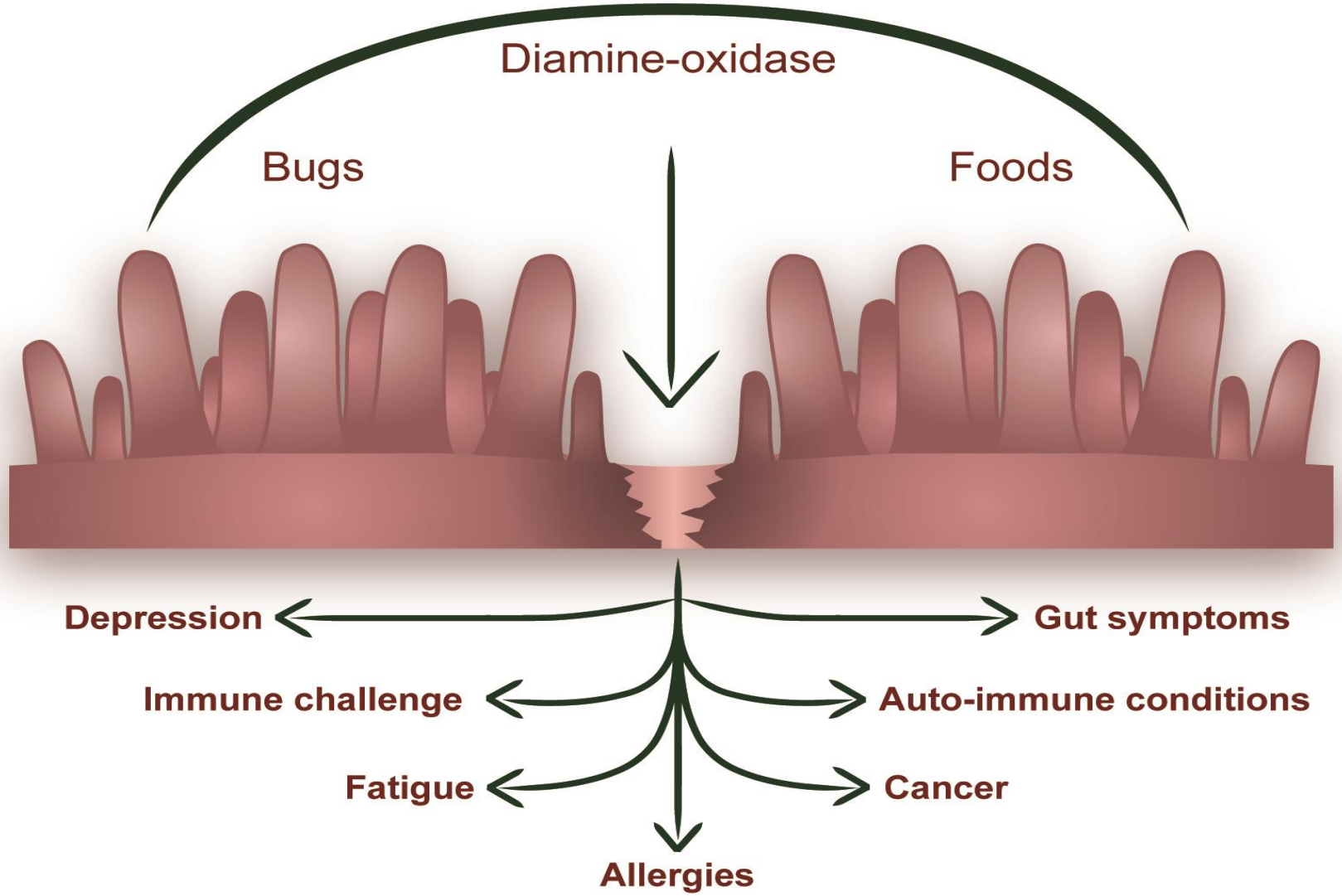
1

0 30 45 60 75

A high DAO-to-Histamine ratio suggests that there is sufficient DAO present to degrade any free histamine.

A low ratio, on the other hand, may be indicative of histamine intolerance. The lower the ratio, and particularly the closer it gets to 1, the stronger that indication.

Triggers of Gut Permeability



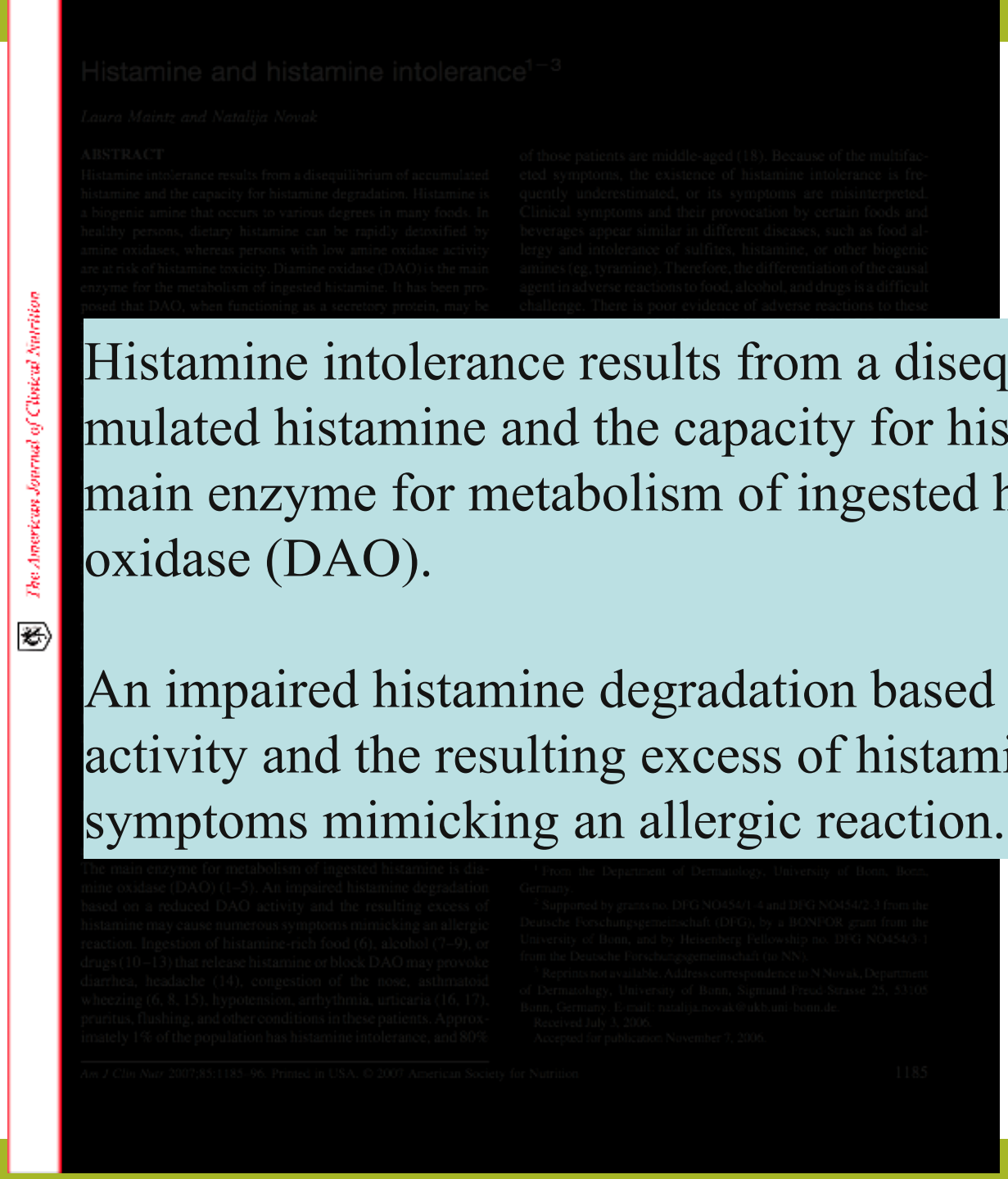
Diamine oxidase is a meaningful marker in newborns

Journal of Applied Clinical Pediatrics》 2008-06

Significance of Determining Serum Diamine Oxidase and D-Lactate in Newborn Infant with Critically Ill

WEI Qiu-wen,WANG Lin-lin,LI Xiao-rong (Department of Pediatrics,the First Affiliated Hospital of Guangxi Medical University,Nanning 530021,China)

Objective To explore the changes of levels of serum diamine oxidase(DAO) and D-lactate in neonates with critically ill and those clinical significances.Methods Fifty-two newborn infants with critical ill were selected as study group,and 15 cases of no-critical and no-gastrointestinal dysfunction were selected as control group.The study group was divided into gastrointestinal dysfunction group(n=18) and no-gastrointestinal dysfunction group(n=34).All cases were required to sample the blood from vein to determine the levels of serum DAO and D-lactate by using spectrophoto metry admission,and the differences in all groups were analyzed.Results The level of serum DAO in study group was significantly higher than that in control group(t=-4.706 P0.01),and the level in gastrointestinal dysfunction group was higher than that in no-gastrointestinal dysfunction group and control group,ANOVA analysis in 3 groups had statistic significance(F=16.694 P0.01).There was no statistic significances of serum DAO in gastrointestinal dysfunction patient whether he was severe or mild(t=0.633 P0.05).The levels of serum D-lactate in study group was significantly higher than that in control group(t=-2.332 P0.05),and that in gastrointestinal dysfunction group was higher than that in control group(t=0.814 P0.05),but there was no statistic difference between no-gastrointestinal dysfunction group and control group(t=0.679 P0.05).There was no statistic significance of serum D-lactate in gastrointestinal dysfunction patient whether he was severe or mild(t=0.561 P0.05).Conclusions Serum DAO can be used as a sensitive marker to early diagnose gastrointestinal dysfunction in critical neonates.Serum D-lactate will be of high specific clinical significance in diagnosis,the change of D-lactate may have relations to the features of intestinal microflora in early neonates.



Histamine and histamine intolerance[1–3]

Laura Maintz and Natalija Novak

ABSTRACT

Histamine intolerance results from a disequilibrium of accumulated histamine and the capacity for histamine degradation. Histamine is a biogenic amine that occurs to various degrees in many foods. In healthy persons, dietary histamine can be rapidly detoxified by amine oxidases, whereas persons with low amine oxidase activity are at risk of histamine toxicity. Diamine oxidase (DAO) is the main enzyme for the metabolism of ingested histamine. It has been proposed that DAO, when functioning as a secretory protein, may be

of those patients are middle-aged (18). Because of the multifaceted symptoms, the existence of histamine intolerance is frequently underestimated, or its symptoms are misinterpreted. Clinical symptoms and their provocation by certain foods and beverages appear similar in different diseases, such as food allergy and intolerance of sulfites, histamine, or other biogenic amines (eg, tyramine). Therefore, the differentiation of the causal agent in adverse reactions to food, alcohol, and drugs is a difficult challenge. There is poor evidence of adverse reactions to these

The main enzyme for metabolism of ingested histamine is diamine oxidase (DAO) (1–5). An impaired histamine degradation based on a reduced DAO activity and the resulting excess of histamine may cause numerous symptoms mimicking an allergic reaction. Ingestion of histamine-rich food (6), alcohol (7–9), or drugs (10–13) that release histamine or block DAO may provoke diarrhea, headache (14), congestion of the nose, asthmatoid wheezing (6, 8, 15), hypotension, arrhythmia, urticaria (16, 17), pruritus, flushing, and other conditions in these patients. Approximately 1% of the population has histamine intolerance, and 80%

[1] From the Department of Dermatology, University of Bonn, Bonn, Germany.

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Received July 3, 2006.

Accepted for publication November 7, 2006.

The American Journal of Clinical Nutrition

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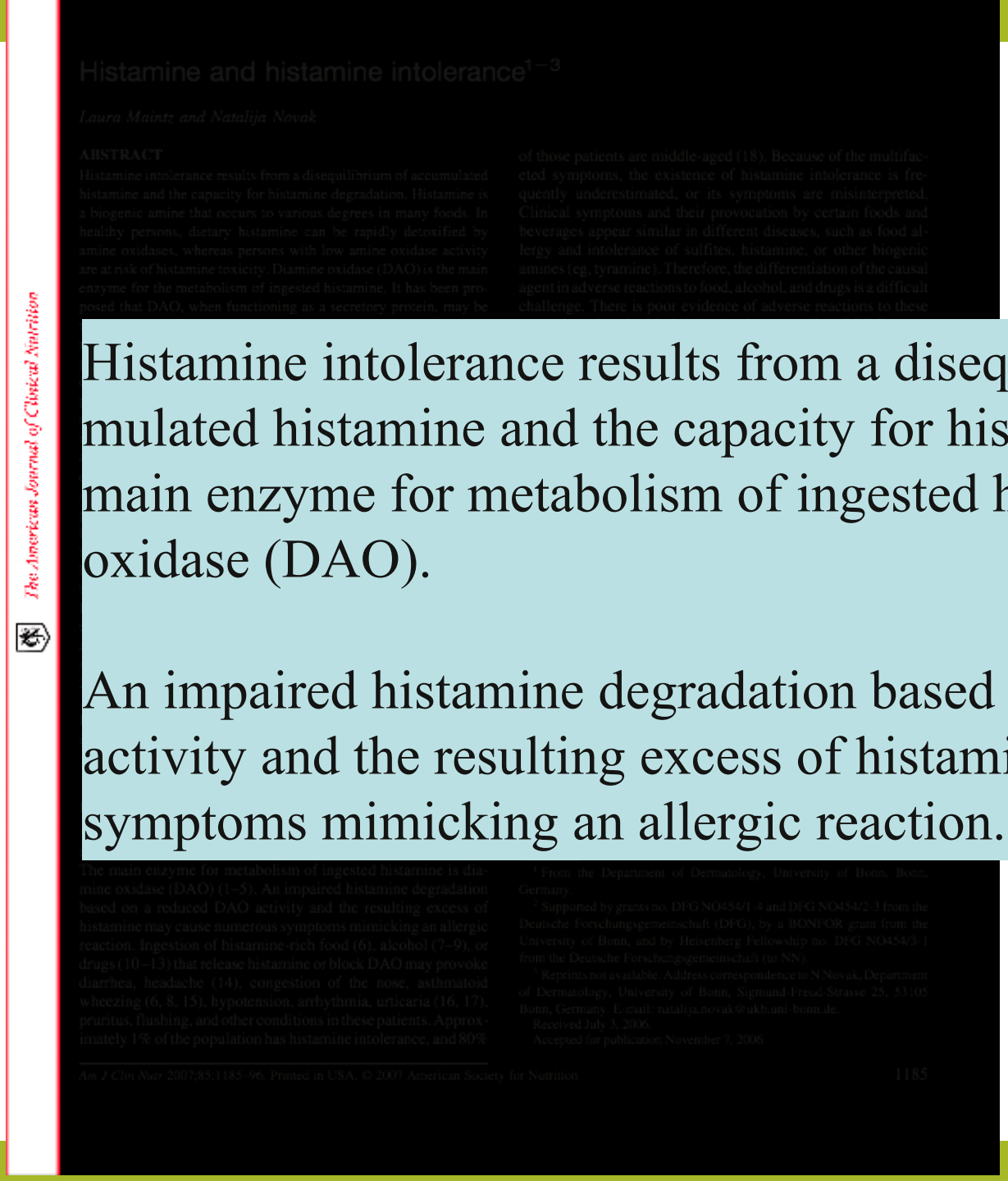

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Besides headache, gastrointestinal ailments including diffuse stomach ache, colic, flatulence, and diarrhea are leading symptoms of histamine intolerance. Elevated histamine concentrations and diminished DAO activities have been shown for various inflammatory and neoplastic diseases such as Crohn disease, ulcerative colitis, allergic enteropathy, food allergy, and colorectal neoplasmas.

KEY WORDS Histamine intolerance, histamine, diamine oxidase, food intolerance, allergy

INTRODUCTION

Histamine intolerance results from a disequilibrium of accumulated histamine and the capacity for histamine degradation. The main enzyme for metabolism of ingested histamine is diamine oxidase (DAO) (1–5). An impaired histamine degradation based on a reduced DAO activity and the resulting excess of histamine may cause numerous symptoms mimicking an allergic reaction. Ingestion of histamine-rich food (6), alcohol (7–9), or drugs (10–13) that release histamine or block DAO may provoke diarrhea, headache (14), congestion of the nose, asthmatoid wheezing (6, 8, 15), hypotension, arrhythmia, urticaria (16, 17), pruritus, flushing, and other conditions in these patients. Approximately 1% of the population has histamine intolerance, and 80%

cytokines, hyperosmolarity, lipoproteins, adenosine, superoxidases (22), hypoxia, chemical and physical factors (eg, extreme temperatures, traumas) (23), or alcohol and certain food and drugs, may activate mast cells.

Histamine exerts its effects by binding to its 4 receptors [histamine 1 receptor (H1R), H2R, H3R, and and H4R] on target cells in various tissues (**Figure 1**, **Table 1**). It causes smooth

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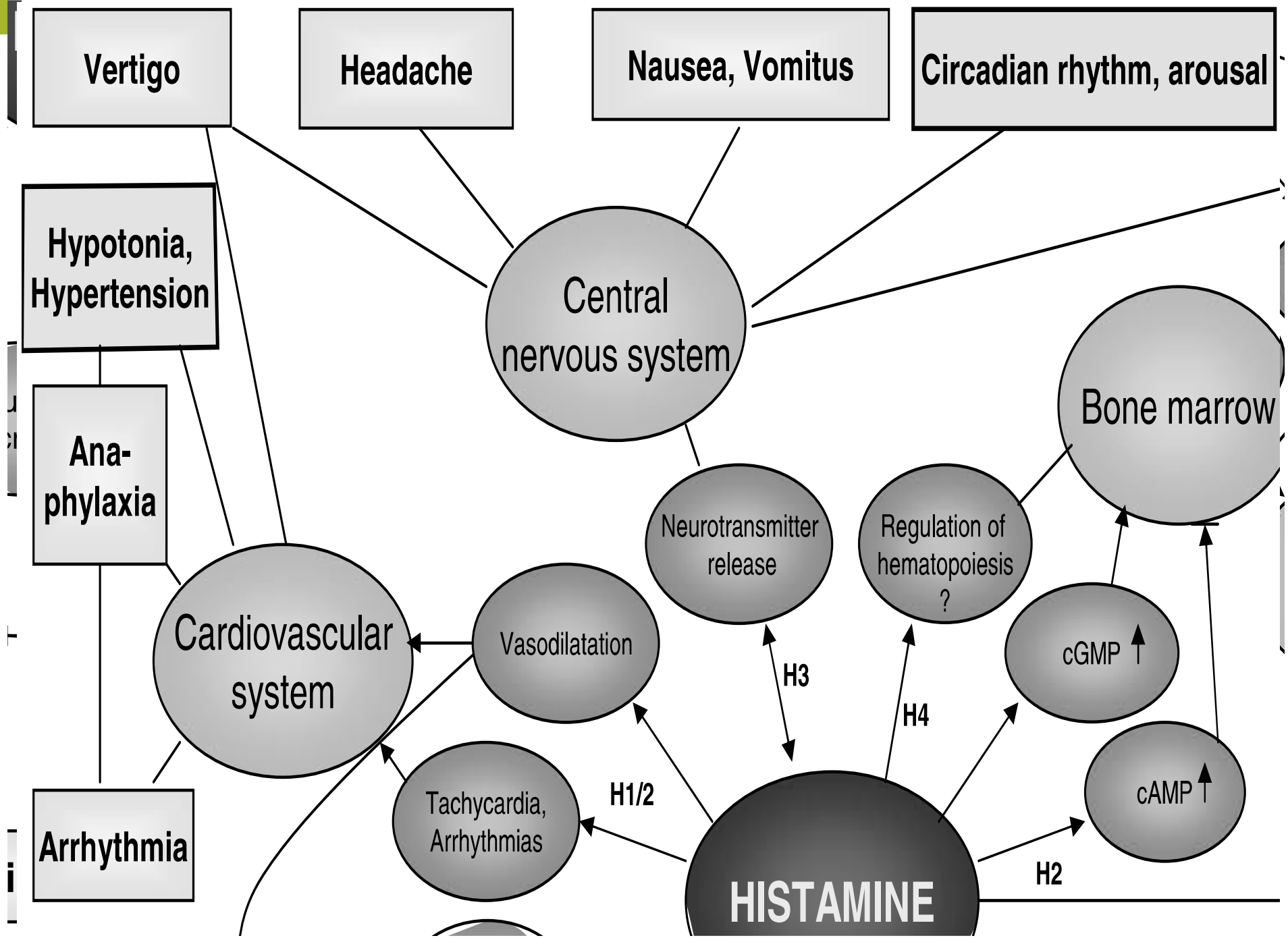

Adapted from Maintz L et al. Dtsch Artzebl 2006;103:A3477-83

DAO varies with menstrual cycle

Clin Biochem. 2012 Oct 22. pii: S0009-9120(12)00568-1. doi: 10.1016/j.clinbiochem.2012.10.013. [Epub ahead of print]

Effect of the menstrual cycle on serum diamine oxidase levels in healthy women.

Hamada Y, Shinohara Y, Yano M, Yamamoto M, Yoshio M, Satake K, Toda A, Hirai M, Usami M.

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RESULTS:

Biochemical parameters, except for DAO levels, were comparable between the two phases. However

Serum diamine oxidase (DAO) level is employed as a useful marker of intestinal mucosal integrity.

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J Clin Invest. 1980 July; 66(1): 66–70.
doi: 10.1172/JCI109836

PMCID: PMC371506

Diamine oxidase (histaminase). A circulating marker for rat intestinal mucosal maturation and integrity.

G D Luk, T M Bayless, and S B Baylin

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29, P less than 0.04). Diamine oxidase activity is thus unique among intestinal mucosal enzymes studied to date in that circulating levels can serve as a marker of mucosal maturation and integrity.

"With increasing mucosal damage, there was a progressive decrease in the enzyme activities studied; first, lactase levels fell, then maltase and sucrase, and finally mucosal and plasma diamine oxidase activity levels fell.

The decrease in plasma diamine oxidase reflected the degree of mucosal damage (n = 29, P less than 0.04). Diamine oxidase activity is thus unique among intestinal mucosal enzymes studied to date in that circulating levels can serve as a marker of mucosal maturation and integrity."

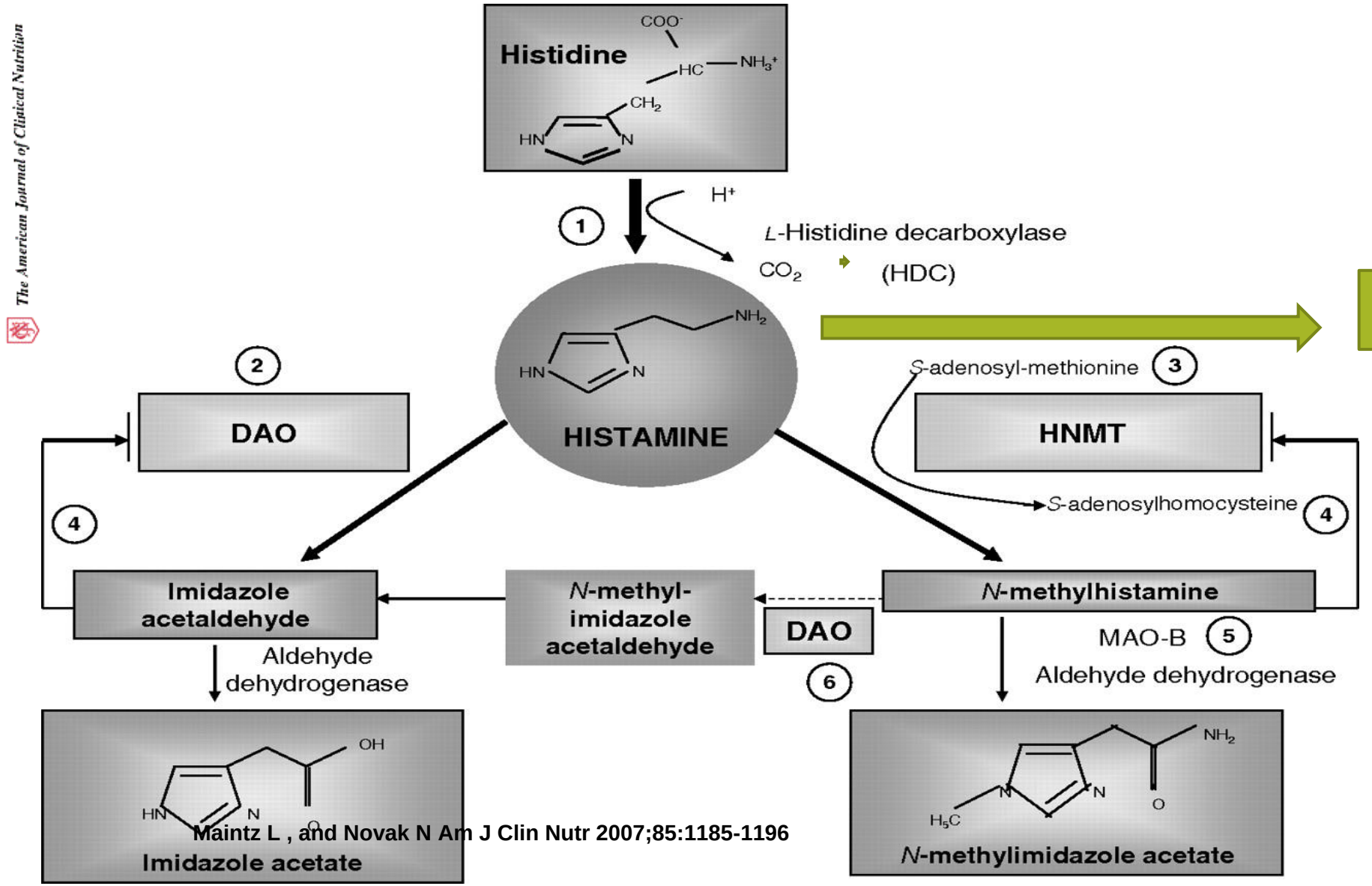
Factors That Contribute To Histamine Excess

- Allergies
- Mastocytosis
- Bacteria
- GI bleeding
- Ingestion of histidine or histamine by food or alcohol
- DAO deficiency

Impact of Histamine

- Smooth muscle cell contraction
- Vasodilatation
- Increased vascular permeability
- Mucus secretion
- Tachycardia
- Alterations of blood pressure
- Arrhythmias
- Nociceptive nerve fibers
- Neurotransmission
- Immunomodulation
- Hematopoiesis
- Wound healing
- Day-night rhythm
- Angiogenesis in tumor models
- Intestinal ischemia

Summary of the histamine metabolism.



Maintz L , and Novak N Am J Clin Nutr 2007;85:1185-1196

Patient KF

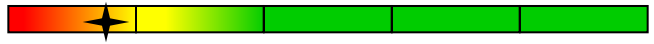
- Chronic hives
- Gut issues
- Only maintained on prednisone

4646 N. Shallowford Rd., Suite N
Dunwoody, GA 30338
678-736-6374
678-736-6390 (fax)
contact@nutratestlabs.com

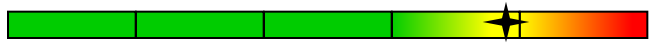
Patient Name: KF Pre
Patient DOB:
Clinic Name:
Ordering Physician:
Sample Date:
Date of Report:

Zonulin:DAO Profile 5100

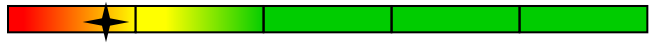
	Patient Results	Reference Range
Diamine Oxidase	21.2	21.2-46.4 ng/mL



	Patient Results	Reference Range
Histamine	2.1	0.9-2.2 ng/mL



	Patient Results	Reference Range
DAO:Histamine Ratio	9.9	11.9-33.2



not expect the same results as those found in case studies alone.

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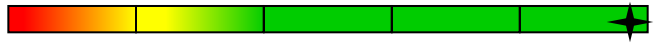
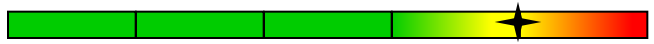
Patient DOB:
Clinic Name:
Ordering Physician:
Sample Date:
Date of Report:

Zonulin:DAO Profile 5100

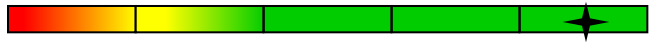
	Patient Results	Reference Range
Diamine Oxidase	66.5	21.2-46.4 ng/mL



	Patient Results	Reference Range
Histamine	2.2	0.9-2.2 ng/mL



	Patient Results	Reference Range
DAO:Histamine Ratio	30.2	11.9-33.2



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Follow up with KF

- Able to back down prednisone, now off prednisone
- Gut feels better
- Energy is better
- “This is the first time I feel better, not worse, I have hope”

DAO Treatment

- DAO
- Omega 3 fatty acid
- B6, Vitamin C, Copper

THANK YOU