

Diabetes and Inflammation

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Nutrients in Food

- Influence the integrity & function of GIT
- Detoxify endogenous & exogenous toxins
- Control oxidative stress
- Affect immune & inflammatory activities



- Inflammation is linked to oxidative stress
- Diabetes-fat and sugar problem
- Foods and chemicals can trigger and combat inflammation
- Diabetes:
 - Increased oxidative stress
 - Decreased antioxidant defenses
- “Our health always seems much more valuable after we lose it”

~author unknown

Cytokines

- Proteins
- Regulate immune response
- Intercellular mediators
- Growth
- Immunoregulatory
- Proinflammatory




Oxidative Stress


- Pro-oxidants [free radicals] outnumber antioxidants
- Pro-oxidants highly reactive
- Inflammation and oxidative stress linked

- Triggers for chronic inflammation
- Combating inflammation

Triggers for chronic Inflammation

1. **Toxin exposure**
 2. **Dysglycemia**
 3. **Oxygen metabolism**
 4. **Immune-mediated adverse food reactions**
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Toxin Exposure

- Exotoxins
 - Endotoxins
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Toxin exposure

- A high-fat meal induces low-grade endotoxemia: Evidence of PP inflammation.
- Inflammation may contribute to the development of endothelial cell activation, and early events of atherosclerosis.

American Journal of Clinical Nutrition, Vol. 86, No. 5, 1286-1292, November 2007 © 2007 [American Society for Nutrition](#) Clett Erridge, Teresa Attina, Corinne M Spickett and David J Webb

Dysglycemia

Trigger and mediator of chronic inflammation

- “PP dysmetabolism induces immediate oxidant stress, which correlates with increased glucose and triglycerides after a meal.”
- “Transient increase in free radicals triggers atherogenic changes including inflammation, endothelial dysfunction, hypercoagulability, and sympathetic hyperactivity.”
- “Markers of inflammation and CV health improve with improvement in PP glucose and lipids.”

O’Keefe, James H, MD, from the Mid America Heart Institute and University of Missouri– Kansas City, and colleagues. Improve Postprandial Glucose with “Anti-inflammatory Diet” Markers of inflammation and cardiovascular health show improvement with the improvement of postprandial glucose and lipid profiles. J Am College of Cardiology, 2008;51:249-255.

Anti-inflammatory Diet

Improve PP glucose, TG, and inflammation:

- Select minimally processed, high-fiber CHO with low glycemic index, vegetables, fruits, whole grains, legumes, and nuts
- Linear relationship between IGT and mortality
- A fatty meal leads to immediate increases in serum TG levels. However, reducing TG levels can reduce the risk for coronary artery disease by as much as 40%.”

O’Keefe, James H, MD, from the Mid America Heart Institute and University of Missouri–Kansas City, and colleagues. Improve Postprandial Glucose with “Anti-Inflammatory Diet” Markers of inflammation and cardiovascular health show improvement with the improvement of postprandial glucose and lipid profiles. J Am College of Cardiology, 2008;51:249-255.

Dysglycemia

- Low-Fat Vegan Diet Improves Glycemic Control and Cardiovascular Risk Factors.
- Both a low-fat vegan diet and a diet based on ADA guidelines improved glycemic and lipid control in type 2 diabetic patients.
- These improvements were greater with a low-fat vegan diet.

Neal D. Barnard, MD1,2, Joshua Cohen, MD1, David J.A. Jenkins, MD, PHD3, Gabrielle Turner-McGrievy, MS, RD4, Lise Gloede RD, CDE5, Brent Jaster, MD2, Kim Seidl, MS, RD2, Amber A. Green, RD2 and Stanley Talpers, MD1. A Low-Fat Vegan Diet Improves Glycemic Control and Cardiovascular Risk Factors in a Randomized Clinical Trial in Individuals With Type 2 Diabetes. Diabetes Care 29:1777-1783, 2006, DOI: 10.2337/dc06-0606 © 2006 by the American Diabetes Association

Oxygen Metabolism

Oxidative stress is both a trigger and a mediator of chronic inflammation

Interventions focused on restoring balance in oxidative metabolism work simultaneously to reduce the effects of oxidative stress as an inflammatory trigger, as well as release of reactive oxygen species as a mediating response of the body.

Lila, Mary Ann, PhD, From beans to berries and beyond: teamwork between plant chemicals for protection of optimal human health, *Ann N Y Acad Sci.* 2007, Oct;1114:372-80, Division of Nutritional Sciences, University of Illinois, 211 Mumford Hall MC 710, 1301 W. Gregory Drive, Urbana, IL 61801, USA.

Foods From Plants Protect Us From Disease

Phytochemicals block activation of pro-inflammatory genes

Inflammation and You: How Foods From Plants Protect Us From Disease. Daniel H Hwang, *Agricultural Research*/April 2009, 6-7

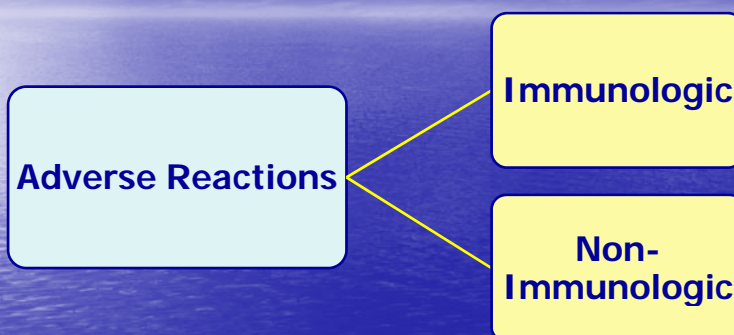
- Intake of Dietary Flavonoids Inversely Associated with Marker of Inflammation
- The authors conclude, "Intake of flavonoid-rich foods may thus reduce inflammation-mediated chronic diseases."

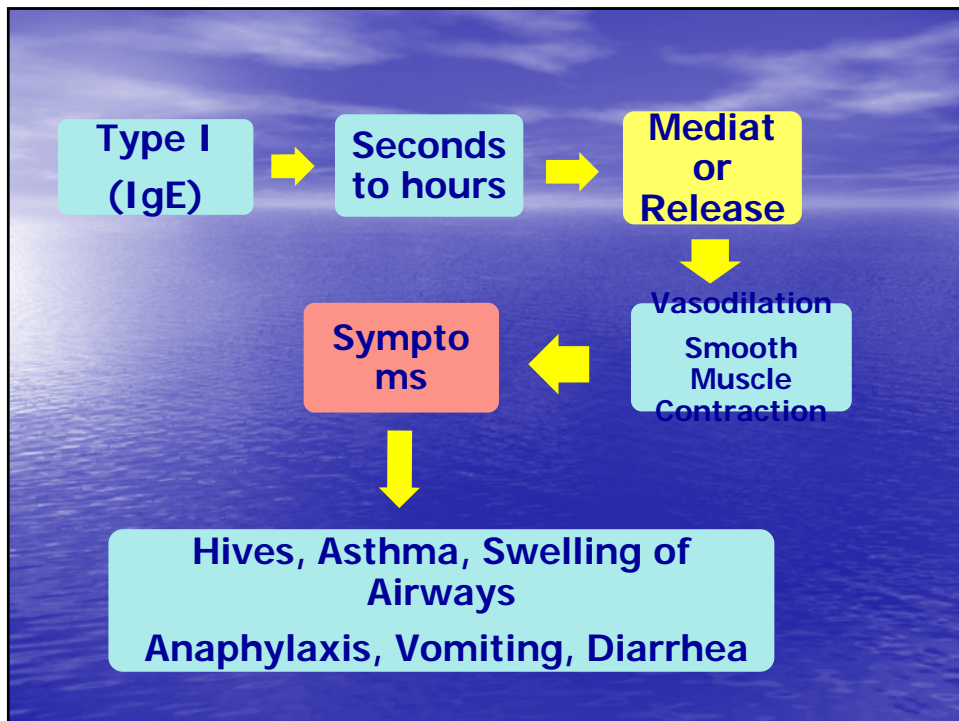
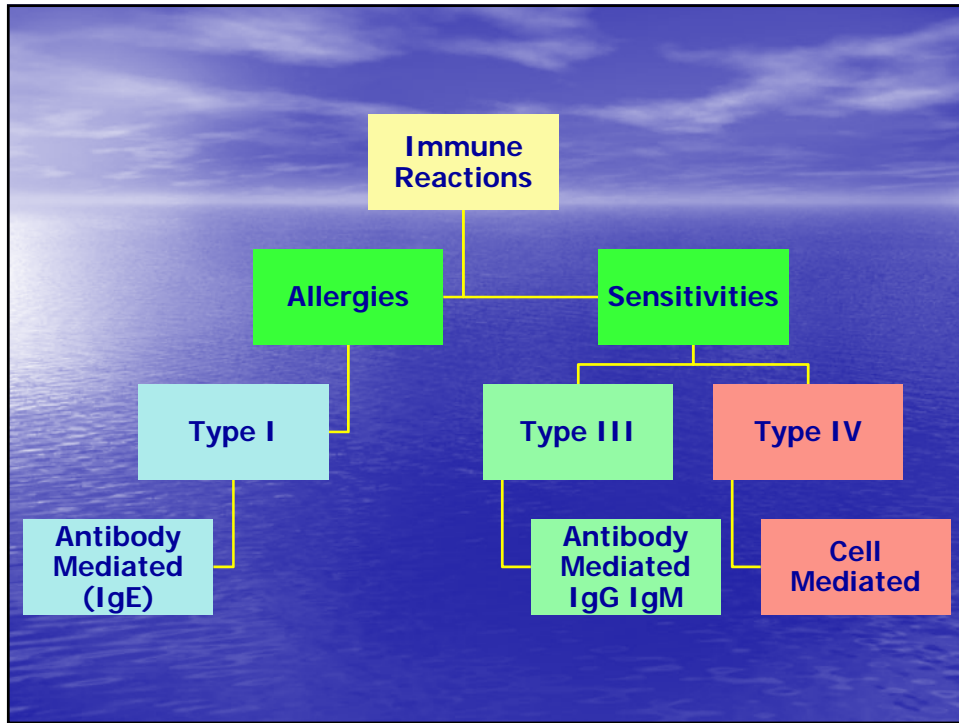
Reference: "Serum C-Reactive Protein Concentrations Are Inversely Associated with Dietary Flavonoid Intake in U.S. Adults," Chun OK, Chung SJ, et al, J Nutr, 2008; 138(4): 753-60.
(Address: Won O. Song, Department of Food Science and Human Nutrition, Michigan State University, East Lansing, MI 48824, USA.

Immune-mediated adverse food reactions

Gut Immunology

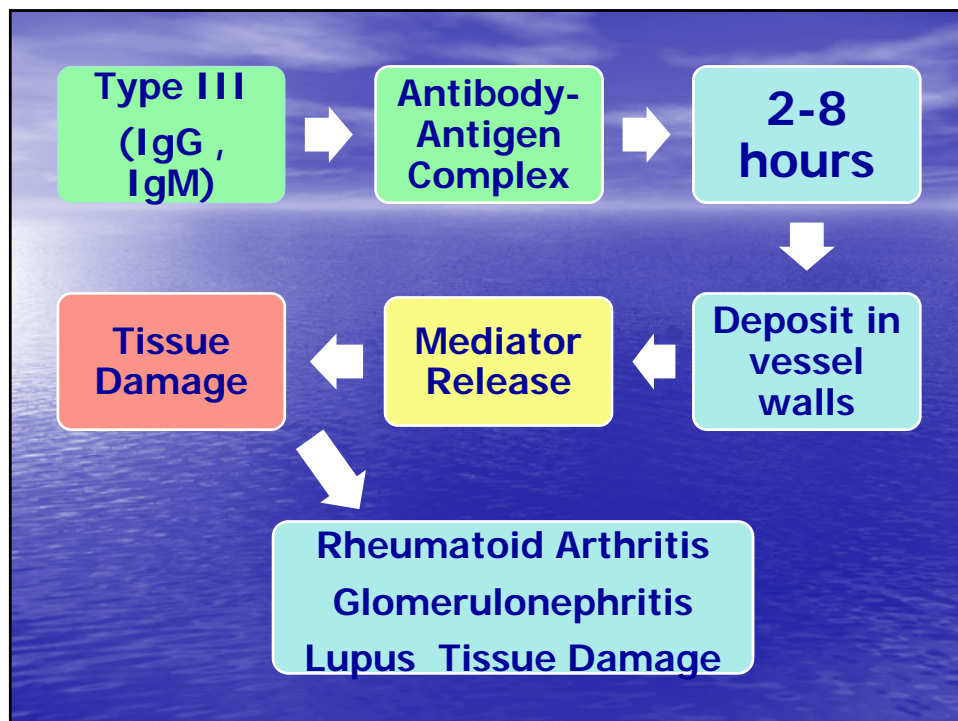
- GI Tract has 2 major roles:
 - Digestion and uptake of nutrients
 - Immune homeostasis
- Bombarded with chemicals, proteins, bacteria, antigens
- Gut must decide what's friend or foe





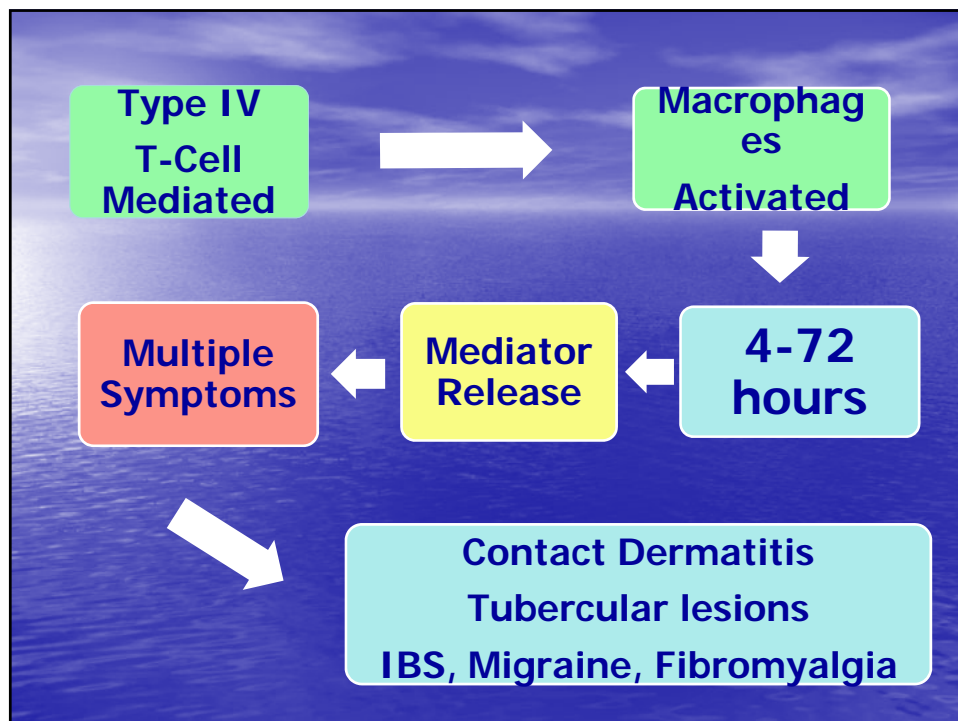
Food Allergy –Type 1

- IgE
- Usually immediate
- Can result in anaphylaxis
- Overall, a relatively small number of patients with IgE mediated allergies - 2-4%
- Peanut, milk, egg, fish, wheat, nuts, soy
- TESTING: RAST, ELISA, Skin Prick Test, Oral Challenge



Food Allergy –Type 3

- Non-IgE
- Immune Complex Mediated
- Delayed Response – 2-8 hours
- IgG may be protective
- Testing: IgG ELISA – poor reliability



Food Allergy –Type 4

- T-Cell Mediated Reaction
- Non-IgE, non-IgG
- Delayed up to 72 hours
- Cytokines/mediators released from T-cells
- Testing: MRT/LEAP - Mediator Release Test, Alcat, Elisa-LRA

Type IV Hypersensitivity Reaction

- Foods and food additives trigger non-allergic (non-IgE mediated) immune reaction causing mediator release by immunologic cells
 - Cytokines (eg. Interleukins and TNF-a)
 - Histamine
 - Serotonin
 - Prostaglandins
 - Leukotrienes
 - Dopamine
 - Many others



Type IV Hypersensitivity Reaction

Physiologic effects of released pro-inflammatory and pro-algesic mediators:

- Inflammation
- Fatigue
- Infection
- Muscle and joint aches and pain
- Depression
- Food cravings

Scientific Studies:

The Role of Mediator Release
&
Diabetes

Inflammatory Cytokines and Risk of Type 2 Diabetes

- European Prospective Investigation
- Examined TNF- α , IL-6 and CRP
- 27,548 Individuals
- 2.3 year f/u – 192 cases of new DM identified

Conclusion: Combined elevation of IL-1b and IL-6 increases risk of type 2 DM

Spranger, Kroke, et al., Diabetes 2003; 52(3):812-817

Women's Health Initiative Study- Inflammatory Cytokines and DM

- 82,069 women
- Examined TNF- α , IL-6 and CRP
- 5.9 years f/u - 1584 developed DM

Conclusion: Elevated IL-6 and CRP were consistently and significantly associated with increased risk of diabetes

Liu, Tinker et al, Arch Intern Med 2007; 167(15):1676-85

Cytokines as Mediators of Autoimmune DM and complications

- 1995
- Cytokines – regulate beta-cell destruction

Summary: Rapidly expanding field of study should have a major impact on our understanding of diabetogenesis and our ability to intervene in the disease process.

Pankewycz, et al., Endocrine Reviews 1995; 16(2):164-176

Role of Inflammatory Cytokines in Diabetic Neuropathy

- Brief Review – 134

Summary:

Inflammatory cytokines, mainly IL-1, IL-6, and IL-18, as well as TNF- α , are involved in the development and progression of diabetic neuropathy.

Navarro-Gonzalez, et al., J Am Soc Nephrol 2008; 19:433-442

Type 1 DM Asso. with Increased Cytokine Mediated Inflammation

- CRP, PGF, SAA and IL-6 measured
- 38 T1D; 41 healthy controls

Conclusions:

Low grade inflammatory process reflected by elevated levels of TGF-2a and IL-6 are involved in T1D

Basu, Vessey, et al., Diabetes Care 2005; 28; 6:1371-1375

Antioxidants

- In the process of breaking down and metabolizing foods, our bodies generate free radicals.
- “We’re learning that antioxidants should be consumed with every meal,” says Prior.
- “And if you routinely skip antioxidants in your diet, over time, the excess number of free radicals being produced may begin damaging cellular components, ultimately leading to cancer, atherosclerosis, and other diseases.

Prior, Ronald L, A Daily Dose of Antioxidants? Agricultural Research/March 2008, 4-5.

"High intake of fruit and vegetables is related to low oxidative stress and inflammation in a group of patients with type 2 diabetes,"

Fruit and Vegetable Intake May Reduce Oxidative Stress and Inflammation in Type 2 Diabetics.

Asgard R, Rytter E, et al, Scandinavian Journal of Food and Nutrition, 2007; 51(4): 149-158. (Address: Department of Biosciences and Nutrition, Karolinska Institutet, Huddinge, Sweden).

Fat

- Stored or burned
- Saturated fat—pro-inflammatory
- EFAs –
 - Cell membranes
 - Eicosanoid precursors
 - Anti-inflammatory

At Pennington Biomedical Research center in Baton Rouge, researchers saw after just 3 days on a high-fat diet, significant increase in intramyocellular lipids. Evidence shows that diet changes can reduce the intramyocellular lipids. We can see diabetes is not just a sugar problem; it is also a fat problem.

Barnard, Neal D, MD. Dr. Neal Barnard's program for reversing Diabetes. The scientifically proven system for reversing Diabetes without drugs. 2007.

Fat

“A fatty meal can lead to immediate increases in serum triglyceride levels. However, reducing triglyceride levels can reduce the risk for coronary artery disease by as much as 40%.”

O'Keefe, James H, MD, from the Mid America Heart Institute and University of Missouri–Kansas City, and colleagues. Improve Postprandial Glucose with "Anti-Inflammatory Diet" Markers of inflammation and cardiovascular health show improvement with the improvement of postprandial glucose and lipid profiles. J Am College of Cardiology, 2008;51:249-255.



Adiponectin

- Adipose tissue secreted cytokine
- Regulates fat and glucose metabolism
- Levels decrease as fat stores increase
- Is antiatherogenic and antidiabetic
- Improves insulin sensitivity by reducing blood free fatty acids
- Stimulates glucose utilization
- Increases hepatic fatty acid oxidation
- Decreases hepatic fatty acid synthesis

Adiponectin

- Circulating adiponectin is associated with a better lipid profile, better glycemic control, and reduced inflammation in diabetic patients.
- Fiber increases circulating adiponectin concentrations in patients with type 2 diabetes.

Qi L, Meigs JB, Liu S, Manson JA, Mantzoros C, Hu FB. Dietary Fibers and Glycemic Load, Obesity, and Plasma Adiponectin levels in Women with Type 2 Diabetes. *Diabetes Care*. July 2006;29(7):1501-1505.

Persons with higher levels of adiponectin, that has anti-inflammatory and insulin-sensitizing properties, have an associated lower risk of type 2 diabetes, according to an analysis of previous studies, reported in the July 8 issue of JAMA. (Embargo expired on 07-Jul-2009 at 16:00 ET)

JAMA, 8-Jul-2009 -American Medical Association (AMA)

Fiber

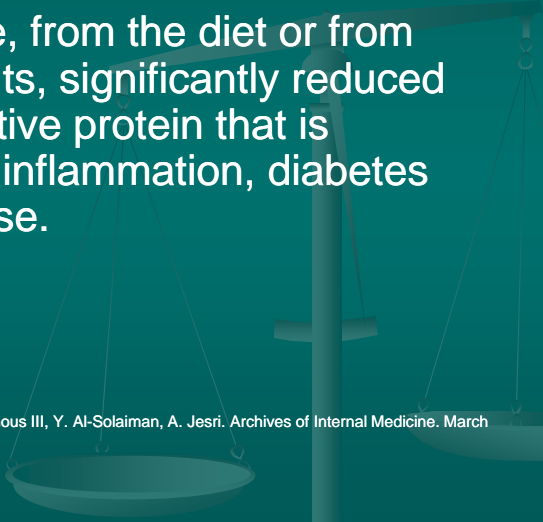
- Soluble
- Insoluble
- Resistant Starch

Cereal fiber improves whole-body insulin sensitivity in overweight and obese women.

M.O. Weickert, M. Mohlig, C. Schofl, A.M. Arafat, B. Otto, H. Viehoff, C. Koebnick, A. Kohl, J. Spranger, A.F.H. Pfeiffer, *Diabetes Care* 4/2006


- Consumption of a high-fiber diet (~50g/d) reduces glycemia, hyperinsulinemia and lipemia in subjects with type 2 diabetes and glycemia in type 1 diabetes.
- Resistant starch may modify postprandial glycemia, prevent hypoglycemia and reduce hyperglycemia.

[David J. A. Jenkins, Cyril W. C. Kendall, Augustine Marchie, Andrea R. Josse, Tri H. Nguyen, Dorothea A. Faulkner, Karen G. Lapsley, and Jeffrey Blumberg. Almonds Reduce Biomarkers of Lipid Peroxidation in Older Hyperlipidemic Subjects. *Journal of Nutrition*, May 1, 2008, University of Toronto and Tufts University.]



High fiber intake, from the diet or from fiber supplements, significantly reduced levels of C-reactive protein that is associated with inflammation, diabetes and heart disease.

D.E. King, B.M. Egan, R.F. Woolson, A.G. Mainous III, Y. Al-Solaiman, A. Jesri. Archives of Internal Medicine. March 12 2007, Volume 167, Pages 502-506.



For every additional serving of green leafy vegetables, the risk of developing diabetes may be reduced by almost 10 percent.

American Diabetes Association: Clinical Practice Recommendations 2008. Diabetes Care, volume 31, Supplement 1, January 2008, S12.