The evolution of dietary inflammation

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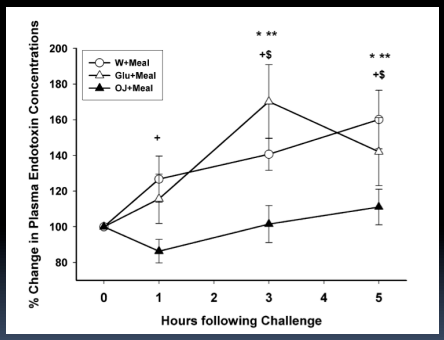
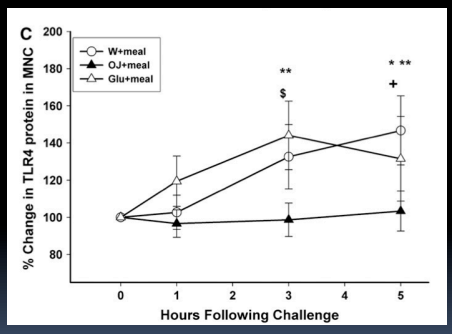
The Problem: Obesity, Metabolic Syndrome, And Cardiovascular Disease

- Responsible for >50% deaths
- Cost > $400 billion
- Lifestyle

Within minutes of your Grand Slam..

Proximate cause: endotoxemia





Ghanim et al. Am J Clin Nutr 2010;91:940–9.

Paradox: why are commonly ingested nutrients so harmful?

- Inflammation involves a costly mobilization of resources
- Tissue damage
- Why doesn't natural selection eliminate harmful inflammatory pathways caused by diet?

I. Paleodiet

- Eaton and colleagues hypothesized that Paleolithic humans ate a radically different diet as hunter gatherers.
- Much more omega-3 fatty acid
- Mismatch

Prediction

Healthiest diets are those of hunter gatherers.

II. Kuzawa's developmental bottleneck

- Mobilization of visceral fat is beneficial during childhood infections
- Preserves nutrient delivery to the developing brain
- Harmful later in life

Prediction

inflammation should occur only in big brained animals.

III. Finch's Food Poisoning

- "The pro-inflammatory responses to fatty foods could have evolved as protection from infectious pathogens that have been common in food, until recently"

  C.E. Finch, 2007. *The Biology of Human Longevity*. Academic Press.

Prediction

Saturated fat should most often be found in foods that have heavy bacterial contamination.

Dietary Fat	Effect	Reference
Saturated	Increased obesity Increased CVD	(Mozaffarian et al. 2010) (Hu et al 1999)
Trans	Increased CVD Increased diabetes	(Remig et al. 2010) (Kummerow 2009)
PUFA	Reduced CVD Reduced obesity Improved insulin sensitivity	(Mozaffarian et al. 2010)
Omega 3	Reduced CVD Improved Insulin sensitivity	(Einvik et al. 2010)

IV. Nutrient Signaling Hypothesis

- *The vertebrate immune system uses nutrients as cues of the risk from the gut microbiome*
- *Who, where, what, how*

Prediction

- Impairment host defenses, dangerous microbiome require a compensatory mobilization of immune resources

Fats that feed pathogens will be pro-inflammatory

- Enhancement of host defense and safer microbiome requires less investment in immunity

Fats that are antimicrobial will be anti-inflammatory

Saturated Fat

Unsaturated fatty acids studied	Antimicrobial comparison	Saturated fatty acids studied	Pathogens inhibited by FA*	Are unsaturated lipids more antimicrobial?	References
even C14:1-C22:1 C18:1 elaidic C18:1 petroselinic C18:1 cis vaccenic C18:2, C18:3 C20:2, C20:3,C20:4 C20:5, C22:6	>	even C14:0 – C22:0	*Bacillus cereus* *Candida albicans* *Clostridium perfringens* *Clostridium botulinum* *Cryptosporidium parvum* *Giardia lamblia* *Enterococcus* *Helicobacter pylori* *Listeria monocytogenes* *Mycoplasma bovis* *Mycoplasma tuberculosis* *Salmonella typhimurium* *Staphylococcus aureus* *Streptococcus faecalis* *Streptococcus* Group A *Streptococcus* Group B	yes (29)	(Kodicek 1945; Hassinen et al. 1951; Willett and Morse 1966; Fuller and Moore 1967; Galbraith et al. 1971; Kabara et al. 1972; Kondo and Kanai 1972; Altenbern 1977b; Kabara and Vrable 1977; Kondo and Kanai 1977; Greenway and Dyke 1979; Carson and Daneo-Moore 1980; Dye and Kapral 1981; Knapp and Melly 1986; Reiner et al. 1986; Rohrer et al. 1986; Hogan et al. 1988; Ababouch et al. 1992; Wang and Johnson 1992; Petrone et al. 1998; Sprong et al. 1999; Sun et al. 2003; Skrivanova et al. 2005; Zheng et al. 2005; Kelsey et al. 2006; Sun et al. 2007; Schmidt and Kuhlenschmidt 2008; Babu et al. 2009; Huang and Ebersole 2010)*
even C6:1-C10:1 C16:1, C18:1 C18:2 MG C12:1 C18:1 elaidic C18:1 cis vaccenic	<	even C6:0-C10:0 C16:0, C18:0 MG C12:0	*Candida albicans* *Clostridium perfringens* *Aeromonas hydrophila* *Helicobacter pylori* *Listeria monocytogenes* *Staphylococcus aureus*	no (6)	(Canas-Rodriguez and Smith 1966; Butcher et al. 1976; Lacey and Lord 1981; van der Kooij and Hijnen 1988; Petschow et al. 1996; Mbandi et al. 2004)
MG C18:1 MG C18:2	=	MG C18:0	*Listeria monocytogenes*	no (1)	(Wang et al. 1993)

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Polyunsaturated Fat

Polyunsaturated fatty acids studied	Antimicrobial comparison	Monounaturated fatty acids studied	Pathogens inhibited by FA*	Are PUFA more antimicrobial?	References
C18:2, C18:3 C18:3 gamma linolenic C20:2, C20:3, C20:4, C20:5 C22:5	>	C18:1 C20:1 C22:1	*Bacteroides fragilis* *Bacillus cereus* *Campylobacter jejuni* *Clostridium botulinum* *Clostridium perfringens* *Cryptosporidium parvum* *Giardia lamblia* *Helicobacter pylori* *Enterococcus* *Listeria monocytogenes* *Mycoplasma bovis* *Mycoplasma tuberculosis* *Staphylococcus aureus* *Streptococcus* Group A *Streptococcus* Group B	yes (27)	(Fuller and Moore 1967; Kabara et al. 1972; Kondo and Kanai 1972; Kabara et al. 1973; Gutteridge et al. 1974; Butcher et al. 1976; Altenbern 1977b; Kondo and Kanai 1977; Naidoo 1981; Campbell et al. 1983; Knapp and Melly 1986; Rohrer et al. 1986; Hogan et al. 1988; Thompson et al. 1990; Crouch et al. 1991; Ababouch et al. 1992; Wang and Johnson 1992; Thompson et al. 1994; Khulusi et al. 1995; Petrone et al. 1998; Sprong et al. 2001; Sun et al. 2003; Sun et al. 2003; Kelsey et al. 2006; Schmidt and Kuhlenschmidt 2008)(Dilika et al. 2000; Zheng et al. 2005)
C16:3 C18:2, C18:3	<	C16:1 C18:1 oleic C18:1 ricinoleic	*Aeromonas hydrophila* *Bacillus cereus* *Candida* sp. *Clostridium perfringens* *Escherichia coli* *Listeria monocytogenes* *Salmonella enteriditis* *Staphylococcus aureus*	no (7)	(Willett and Morse 1966; Dye and Kapral 1981; van der Kooij and Hijnen 1988; Sprong et al. 1999; Mbandi et al. 2004; Skrivanova et al. 2005; Desbois et al. 2008)
MG C18:2 C18:2, C18:3	=	MG C18:1 C18:1	*Giardia lamblia* *Staphylococcus aureus*	no (3)	(Lacey and Lord 1981; Reiner et al. 1986; Wang et al. 1993)

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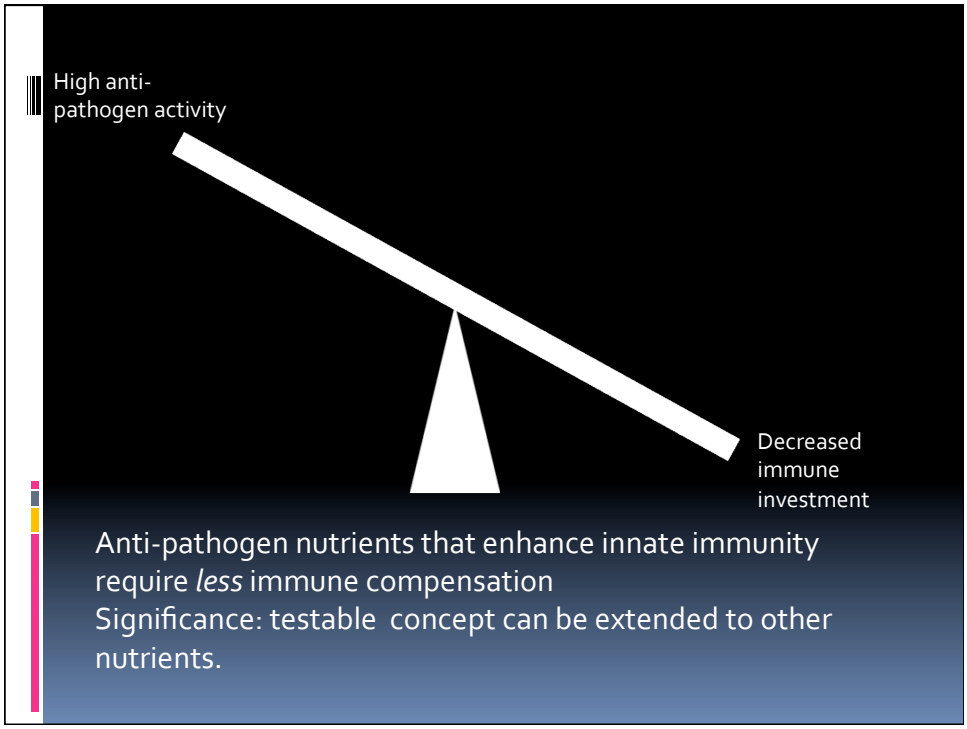
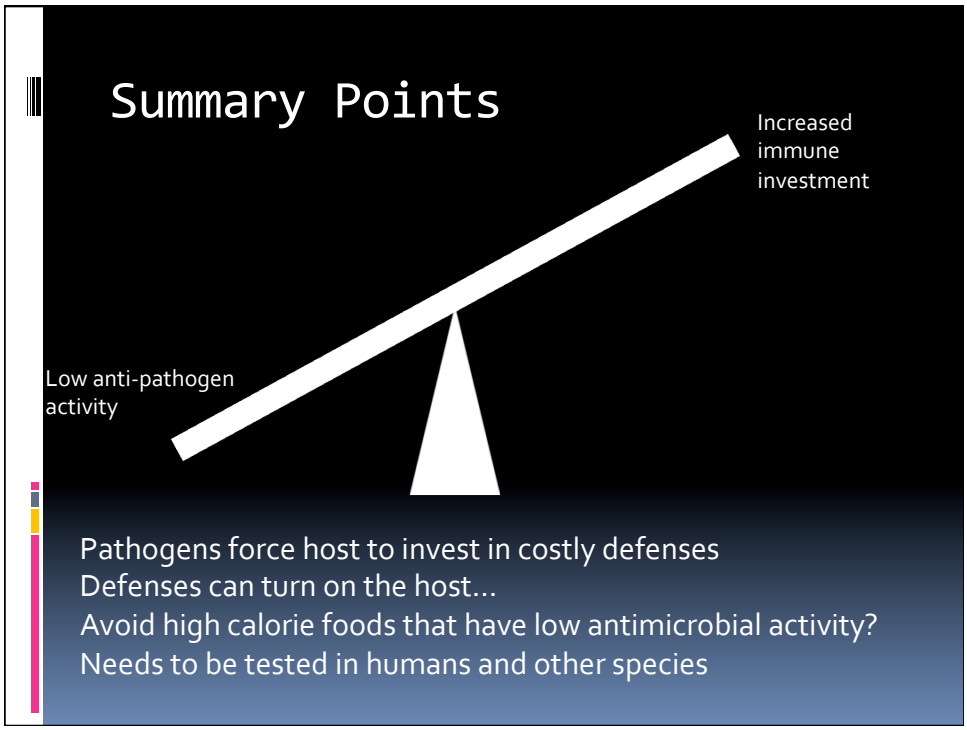
Independent effects?

Fatty acid	More Antimicrobial Lipid	More Inflammatory Lipid	p value (Fisher's exact test)
Saturated	7	8	p < 0.001
Unsaturated	29	0	
Long Chain Saturated	7	3	p = 0.03
Short/Medium Chain Saturated	34	1	
Monounsaturated	10	4	p = 0.010
Polyunsaturated	27	0	
Omega 6	7	7	p = 0.011
Omega 3	16	1	
trans fatty acid	1	4	p = 0.010
cis fatty acid	7	0	



Anti-pathogen nutrients that enhance innate immunity require *less* immune compensation
Significance: testable concept can be extended to other nutrients.



Pathogens force host to invest in costly defenses
Defenses can turn on the host…
Avoid high calorie foods that have low antimicrobial activity?
Needs to be tested in humans and other species