NUTRITION IN PCOS AND ROLE OF ANTI INFLAMMATORY DIETS

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Nutrition in PCOS

- A modest amounts of weight loss improve all of the manifestations of PCOS.
- Weight loss decreases insulin resistance, serum androgen concentrations, ovarian size, and the number of ovarian cysts; it increases ovulation and fertility; and it improves the concentrations of plasma lipids.
- **The optimal dietary treatment for PCOS is not known.**
- High-protein diets are being promoted because of their beneficial effects on satiety, lean body mass, weight maintenance.
- BUT ITS NOT EASY TO FOLLOW HIGH PROTEIN DIETS IN INDIA BECAUSE OF NATURAL DIETARY PATTERNS.

"Genes load the gun.
Lifestyle pulls the trigger"

Dr. Elliot Joslin

Scope

- PCOD is a inflammatory state
- Diet induced inflammation
- Anti-Inflammatory Diets
- Anti-Inflammatory Index
- Advance Glycation Endproducts in food and relation to inflammation.
- Probiotics

PCOS is a Proinflammatory state

- Chronic low-grade inflammation underpins the development of metabolic aberration and ovarian dysfunction.
- A strong association between hyperandrogenism and inflammation in PCOS.

- González F, Rote NS, Minium J, Kirwan JP. Increased activation of nuclear factor kB triggers inflammation and insulin resistance in polycystic ovary syndrome. Journal of Clin Endocrinol Metab. 2006; 91:1508–12. [PubMed: 16464947] 6.
- Piotrowski PC, Rzepczynska IJ, Kwintkiewicz J, Duleba AJ. Oxidative stress induces expression of CYP11A, CYP17, STAR and 3bHSD in rat theca-interstitial cells. J Soc Gynecol Invest. 2005; 12(2 Suppl):319A

Chronic low-grade inflammation in PCOS

- There is a genetic basis for the chronic low-grade inflammation observed in PCOS.
- Several proinflammatory genotypes including those that encode **TNF-α**, and the type **2 TNF** receptor as well as **interleukin-6 (IL-6)** and its signal transducer are associated with PCOS.
- **CRP** is also elevated in PCOS.

- Escobar-Morreale HF, Calvo RM, Villuendas G, Sancho J, San Millan JL. Association of polymorphisms in the interleukin 6 receptor complex with obesity and hyperandrogenism. Obes Res. 2003; 11:987–96. [PubMed: 12917504] 20. Peral B, San Millan JL, Castello R, Moghetti P, Escobar-Morreale HF.
- The methionine 196 arginine polymorphism in exon 6 of the TNF receptor 2 gene (TNFRSF1B) is associated with the polycystic ovary syndrome and hyperandrogenism. J Clin Endocrinol Metab. 2002; 87:3977–83. [PubMed: 12161545] .
- Villuendas G, San Millan JL, Sancho J, Escobar-Morreale HF. The -597 G->A and -174 G->C polymorphisms in the promoter of the IL-6 gene are associated with hyperandrogenism. J Clin Endocrinol Metab. 2002; 87:1134–41. [PubMed: 11889177] .
- Moshage HJ, Roelofs HM, van Pelt JF, Hazenberg BP, van Leeuwen MA, et al. The effect of interleukin-1, interleukin-6 and its interrelationship on the synthesis of serum amyloid A and Creactive protein in primary cultures of adult human hepatocytes. Biochem Biophys Res Commun. 1988; 155:112–117. [PubMed: 3261980]

Inflammation markers in PCOS

- Circulating mononuclear cells (MNC) and MNC-derived macrophages in tissue produce proinflammatory cytokines such as TNFα and IL-6.
- TNFα is a known mediator of insulin resistance.
- IL-6 is involved in the promotion of atherogenesis.

- Holmes AG, Mesa JL, Neill BA, Chung J, Carey AL, Steinberg GR, et al. Prolonged interleukin-6 administration enhances glucose tolerance and increases skeletal muscle PPARalpha and UCP2 expression in rats. J Endocrinol. 2008; 198:367–74. [PubMed: 18523033].
- Romano M, Sironi M, Toniatti C, Polentarutti N, Fruscella P, Ghezzi P, et al. Role of IL-6 and its soluble receptor in induction of chemokines and leukocyte recruitment. Immunity. 1997; 6:315– 25. [PubMed: 9075932]

Diet-Induced Silent Inflammation

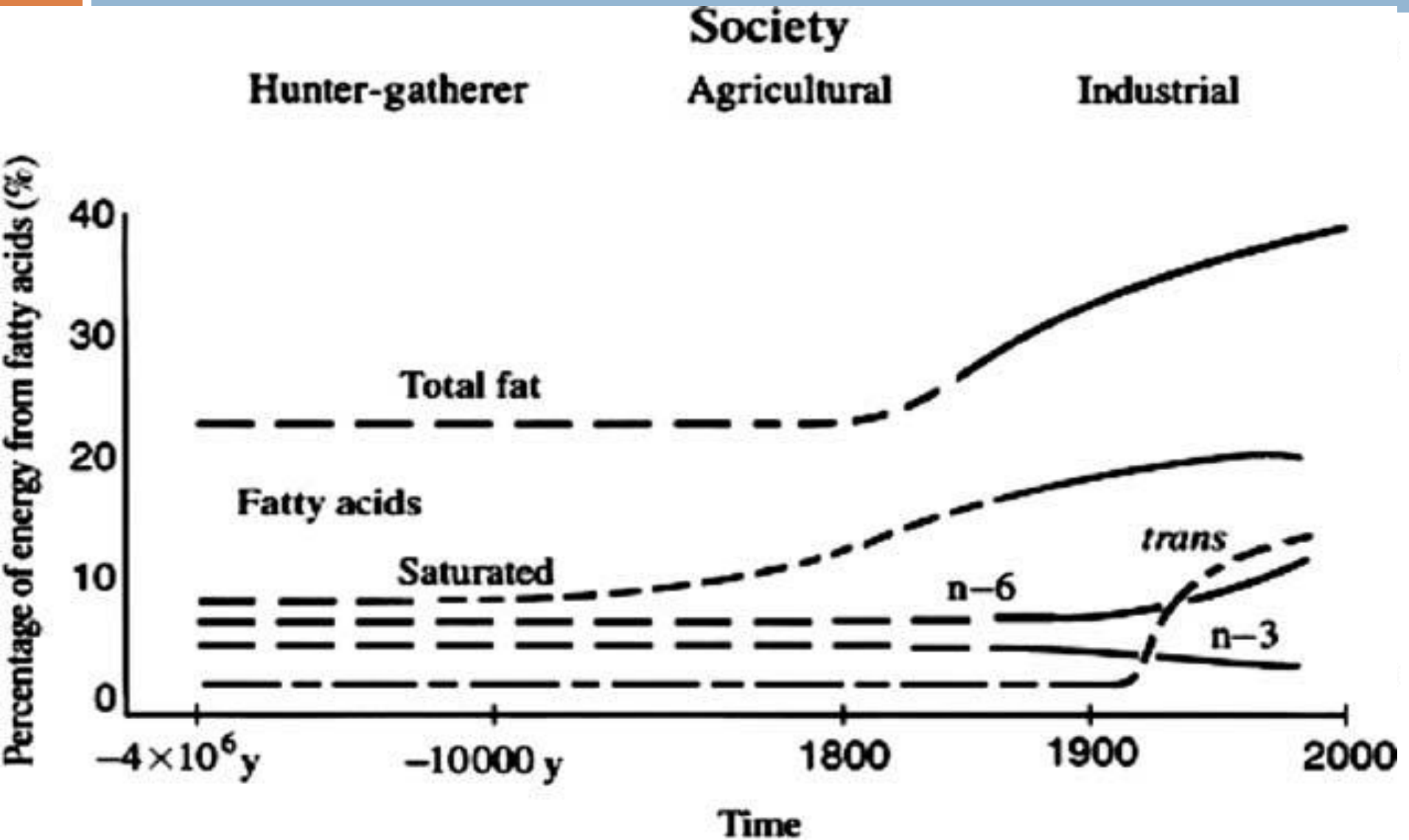
- "The Perfect Nutritional Storm"
- These dietary factors include

(1) increased consumption of refined high-glycemic load carbohydrates,

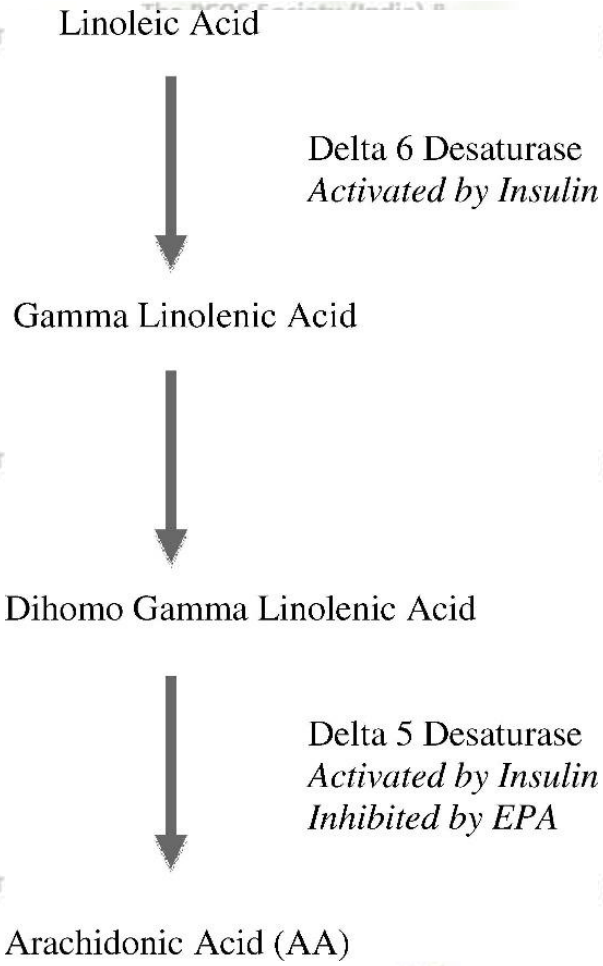
(2) increased consumption of refined vegetable oils rich in omega-6 fatty acids, and

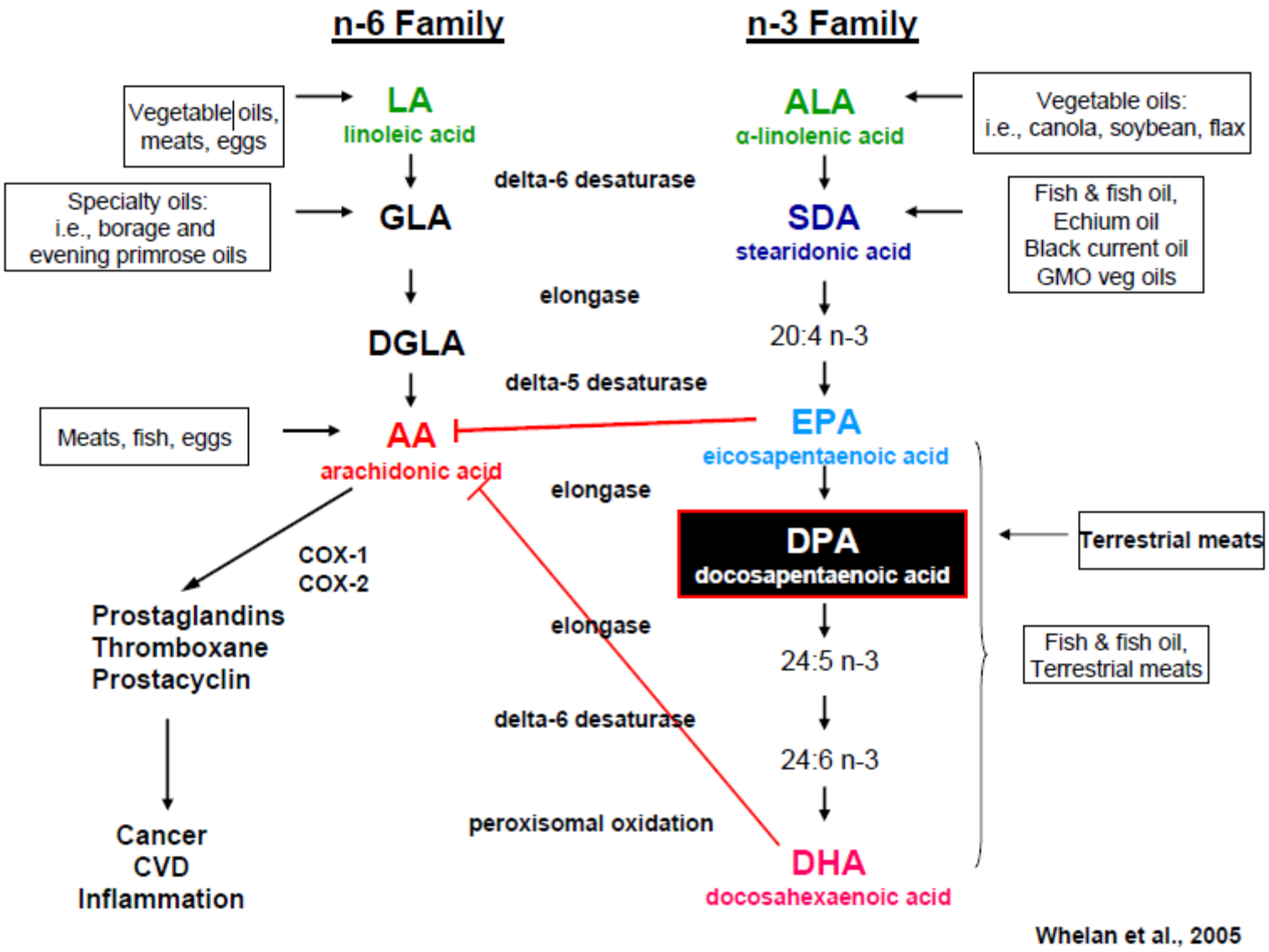
(3) decreased consumption of long-chain omega-3 fatty acids.

Historical schematic of relative percentages of fat and intake of different fatty acids in human beings.



Metabolism of omega-6 fatty acids





Whelan et al., 2005

The role of diet-induced inflammation in PCOS

- In PCOS, **glucose ingestion (High Glycemic Diets)** induces an inflammatory response as evidenced by increased ROS-related oxidative stress, and increased NFκB activation that are independent of obesity.
- The release of TNFα and IL-6 from circulating MNC is also altered in PCOS by glucose ingestion in vivo, and by glucose exposure in vitro .
- These markers of oxidative stress and inflammation are associated with glucose-challenged measures of insulin sensitivity and/or fasting measures of insulin resistance .
- Thus, diet-induced inflammation in PCOS culminates in proinflammatory signaling known to be involved in the development of insulin resistance and atherogenesis.

- González F, Rote NS, Minium J, Kirwan JP. In vitro evidence that hyperglycemia stimulates tumor necrosis factor-a release in obese women with polycystic ovary syndrome. J Endocrino. 2006; 188:521–9. 9.
- González F, Rote NS, Minium J, Kirwan JP. Reactive oxygen species-induced oxidative stress in the development of insulin resistance and hyperandrogenism in polycystic ovary syndrome. J Clin Endocrinol Metab. 2006; 91:336–40. [PubMed: 16249279]

Principles of Anti inflammatory Diets

- The principal dietary components of a proposed anti-inflammatory
- diet should be a low glycemic-load diet
- low in omega-6 fatty acids
- rich in EPA

Carbohydrates in Anti-inflammatory Diet

- The macronutrient composition of such a diet would provide about 150 g of carbohydrates (600Kcal) per day.
- The majority of carbohydrates should be coming from low glycemic-load sources that would significantly lower the production of insulin.
- This can be achieved by consuming approximately 10 servings of non-starchy vegetables (200Kcal) .
- limited amounts of fruits (because of their higher carbohydrate content) per day
- A relatively rigid (but not total) exclusion of high glycemic-load carbohydrates such as bread, pasta, rice, and potatoes.

- Djuric Z, Vanloon G, Radakovich K, Dilaura NM, Heibrun LK,Sen A: Design of a Mediterranean exchange list diet implemented by telephone counseling. J Am Diet Assoc 108:2059–2065, 2008.

Proteins in Anti-inflammatory Diet

- The protein requirements would be approximately 100 g of protein per day coming from
- low-fat sources such as fish and chicken
- vegetarian protein sources like tofu or
- Imitation soybean meat products.
- The higher levels of protein are required to help stimulate the release of the satiety hormone PYY from the gut.

- Batterham RL, Heffron H, Kapoor S, Chivers JE, Chandarana K,Herzog H, le Roux CW, Thomas EL, Bell JD, Withers DJ: Critical role for peptide YY in protein-mediated satiation and body-weig regulation. Cell Metab 4:223–233, 2006.

Fats in Anti-inflammatory Diet

- The fat content would be approximately 50 g per day.
- The composition of the fat in an anti-inflammatory diet should be low in both omega-6 and saturated fatty acids.
- The omega-6 fatty acids provide the driving force for increased AA formation and the resulting elevation of silent inflammation that drives new fat cell proliferation.
- Saturated fatty acids are likewise kept to low amounts since they can activate NF-kappa B via the TLR4 toll-like receptors to cause increased cellular inflammation.
- The bulk of the dietary fatty acids should consist of monounsaturated fats, which have virtually no effect on inflammation.
- These monounsaturated fats should also be supplemented by at least 5 g of long-chain omega-3 fatty acids per day.
- This level of long-chain omega-3 fatty acids would increase the secretion of adiponectin by the fat cells .
- Increased adiponectin production can have significant benefits in reducing insulin resistance in peripheral organs.

J BiolChem 278:37041–37051, 2003, J Biol Chem 279:16971–16799, 2004, Arterioscler Thromb Vasc Biol 27:84–91, 2007, J Nutr 139:1–4, 2009, J Clin Invest 116:3015–3025, 2006, Arterioscler Thromb Vasc Biol 27:1918–1925, 2007.

Macro-Nutrient Composition

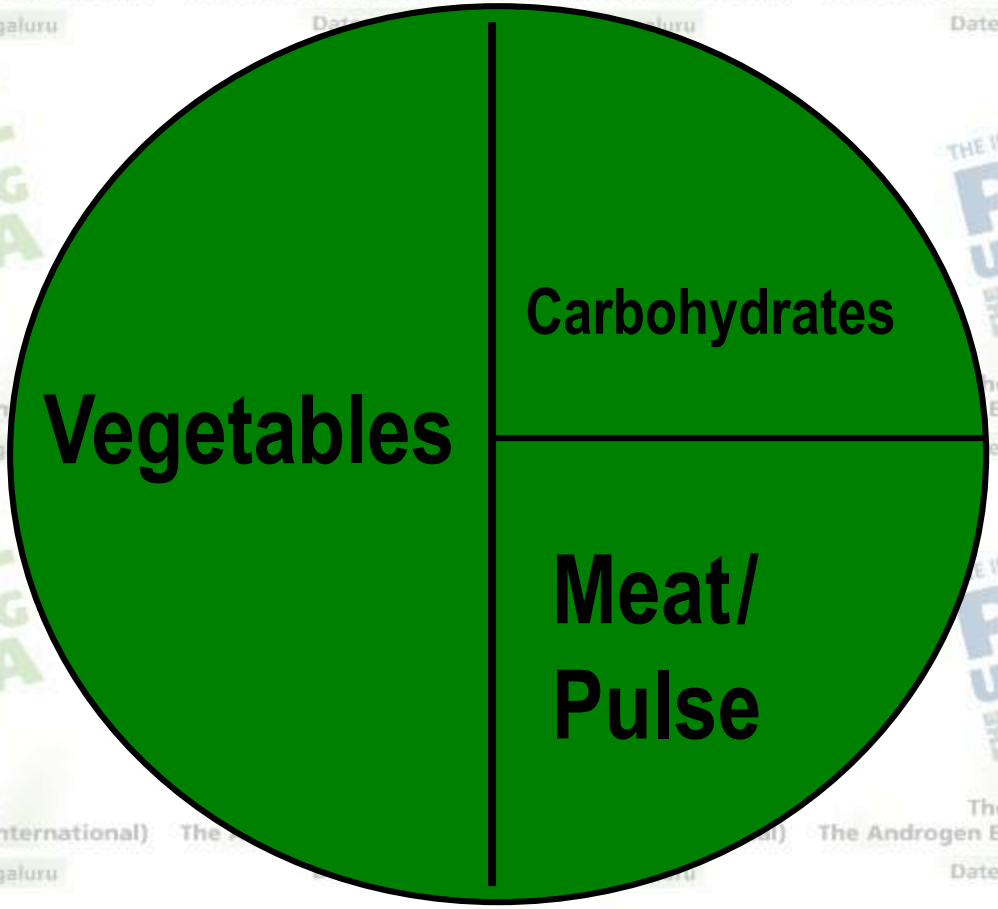
- An anti-inflammatory diet could be considered a 1-2-3 diet; meaning for *every one gram of fat consumed, the individual would consume two grams of protein, and three grams of carbohydrate*.
- This 1-2-3 ratio stabilizes post-prandial insulin levels, thus relieving the inhibition of the hormone-sensitive lipase in the fat cells.
- As a result, the release of stored fat for ATP production is enhanced.
- The 1-2-3 ratio has been shown to be superior in reducing hunger, reducing insulin and stabilizing blood lipid levels , reducing blood glucose levels , increasing weight loss in patients characterized by a high initial insulin secretion to carbohydrates , and ***reducing silent inflammation .***
- JAMA 292:2482–2490, 2004.

Calories in Anti –Inflammatory Diet

- Anti inflammatory diet also represents a calorie restricted diet providing approximately 1450 calories per day.
- It has been demonstrated that this level of calorie restriction is required to maintain weight loss .
- Furthermore, Markovic et al. has demonstrated that **calorie restriction at 1200 calories** per day can reverse insulin resistance in type 2 diabetics within 4 days, well before any fat loss had occurred .
- One potential mechanism of this rapid effect of calorie restriction on insulin resistance may lie in the reduction of the NF-kappa B activation in hypothalamic neurons.
- Maintaining such a calorie-restricted diet, however, depends on controlling hunger, primarily by increasing satiety.
- This is why an anti-inflammatory diet requires higher levels of protein (approximately 30% of total calories) to help stimulate the release of the satiety hormone PYY from the gut.

Ann Rev Nutr 21:323–341, 2001, Diabetes Care 21:687–694, 1998.

The “Plate Method”



Quantitative Dietary Modifications

- Reduction in total calories. (as per BMI)
- Reduction in Carbohydrate content of diet (knock of roti and rice to minimum)
- Increase in protein content of diet, so reduce glycemic load and increase satiety. (Dals and Pulses)
- Increase consumption of veges. More than half plate.
- Decrease Fat content, choose right oil.

Joshi Shilpa RD,India,2010

Nuts….Advantages…

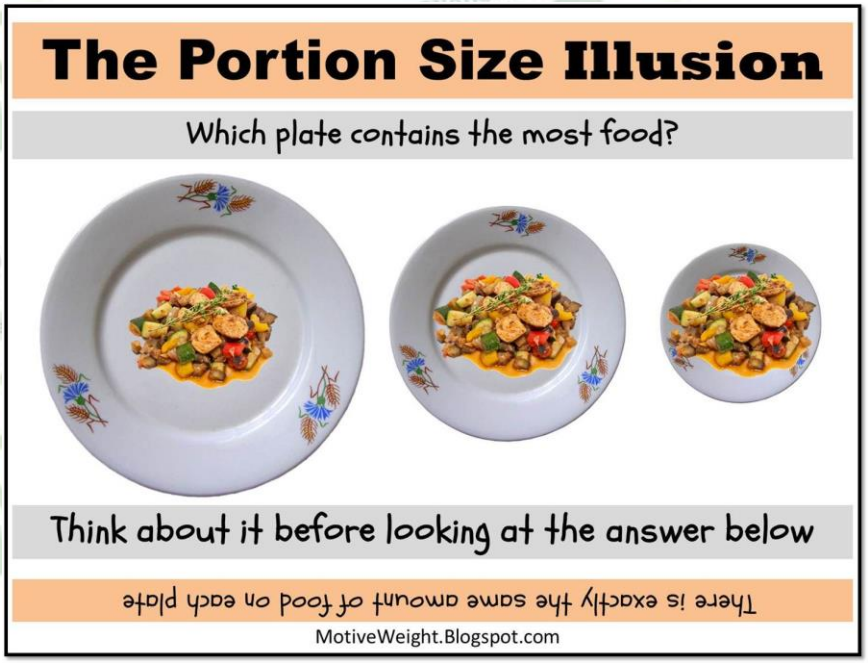
- When consuming nuts, which are high-energy foods rich in unsaturated fatty acids, there is a satiety effect that suppresses hunger and limits intake of other energy-dense foods.
- Intake of unsaturated fatty acids with nuts is intrinsically cardio protective.
- N-3 PUFA from nuts, mainly ALA in walnuts, protect from fatal coronary heart disease and sudden death due to their anti-arrhythmic properties.
- Nuts may contain other bioactive components capable of reducing blood cholesterol. The best candidate ,for these molecules are phytosterols.

Average Fatty Acid Composition of Nuts (grams per 100& g)

Nuts	Total fat	SFA	MUFA	PUFA	18& :& 2n-6	18& :& 3n-3
Almonds	50·6	3·9	32·2	12·2	12·2	0·00
Brazil nuts	66·4	15·1	24·5	20·6	20·5	0·05
Cashews	46·4	9·2	27·3	7·8	7·7	0·15
Hazelnuts	60·8	4·5	45·7	7·9	7·8	0·09
Macadamia nuts	75·8	12·1	58·9	1·5	1·3	0·21
Peanuts	49·2	6·8	24·4	15·6	15·6	0·00
Pecans	72·0	6·2	40·8	21·6	20·6	1·00
Pine nuts (dried)	68·4	4·9	18·8	34·1	33·2	0·16
Pistachios	44·4	5·4	23·3	13·5	13·2	0·25
Walnuts	65·2	6·1	8·9	47·2	38·1	9·08

Data for raw nuts, except when specified. SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; 18& :& 2n-6, linoleic acid; 18& :& 3n-3, α-linolenic acid.

Size of the plate /container matters!!



Teaching Aids Used

- Standardize Bowls, Spoons

- Standardize Food Models, Especially of Cereal Portion.
- Concept of size for “Eat out Foods”.

- Teaching to read labels.

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Spices in Anti Inflammatory Diet: Turmeric

- Bioactive component of turmeric is curcumin.
- It is medicinal and has anti-inflammatory properties.
- Anti inflammatory property is attributed to inhibition of prostaglandin synthesis.
- Turmeric also enhances detoxifying capacity of xenobiotics.It contains water soluble antioxidant “turmerin”which protects the membrane and DNA against oxidative injury.
- It also inhibits free radical induced damage to DNA

Additional Benefits of Anti Inflammatory Diet

- A significant increase in the consumption of polyphenols (found in vegetables and fruits), which are known to have anti-inflammatory benefits(via the inhibition of NF-kappa B) as well as activation of adenosinmonophosphate (AMP) kinase to increase the production of ATP.
- Once AMP kinase is activated, then a number of other metabolic processes that are important in blood sugar and blood lipid control are also set into motion.
- Another benefit of the proposed anti-inflammatory diet would be a decrease in the levels of endocannabinoids (derived from AA) in the brain, which play a significant role in hunger development.

- Yonsei Med J 46:585–596, 2005, Am J Clin Nutr 81:215S–217S, 2005
- Diabetes 55:2180–2191, 2006, Cell Biochem Biophys 47:332–347, 2007.

Dietary Inflammatory Index

- Diet has been shown to modulate inflammation.
- Large variety of foods available in an average diet results in a large number of nutrients that can interact with each other, producing synergistic or antagonistic effects.
- Overall dietary scores allow a better assessment of the dietary pattern.
- In this context, the Dietary Inflammatory Index (DII) was proposed to assess the inflammatory effect of an individual's diet .
- The DII represents a literature-derived, population-based dietary score summarizing the effect of dietary parameters on six inflammatory biomarkers according to a comprehensive review of the published literature.

Nutrients **2015**, *7*(6), 4124-4138; doi:10.3390/nu7064124

Dietary Inflammatory Index

- In addition to higher levels of inflammatory biomarkers, subjects consuming a pro-inflammatory diet, as represented by a higher DII, had increased indices of general and abdominal obesity.

- *Nutrients* **2015**, *7*(6), 4124-4138; doi:10.3390/nu7064124

Table 1. Scoring for each food parameter used for dietary inflammatory index calculation

Food parameter	Inflammatory effect score*
Energy	0·180
Carbohydrate	0·097
Fat	0·298
Alcohol	−0·278
Fibre	−0·663
Protein	0·021
Vitamin B_{12}	0·106
Vitamin B_6	−0·365
β Carotene	−0·584
n-3	−0·436
n-6	−0·159
MUFA	−0·009
SFA	0·373
Trans-fat	0·229
Fe	0·032
PUFA	−0·337
Riboflavin	−0·068
Thiamin	−0·098
Niacin	−0·246
Vitamin A	−0·401
Mg	−0·484
Zn	−0·313
Se	−0·191
Vitamin C	−0·424
Vitamin D	−0·446
Vitamin E	−0·419
Folate	−0·190
Caffeine	−0·110

* A negative value indicates anti-inflammatory effect and a positive score indicates pro-inflammatory effect.

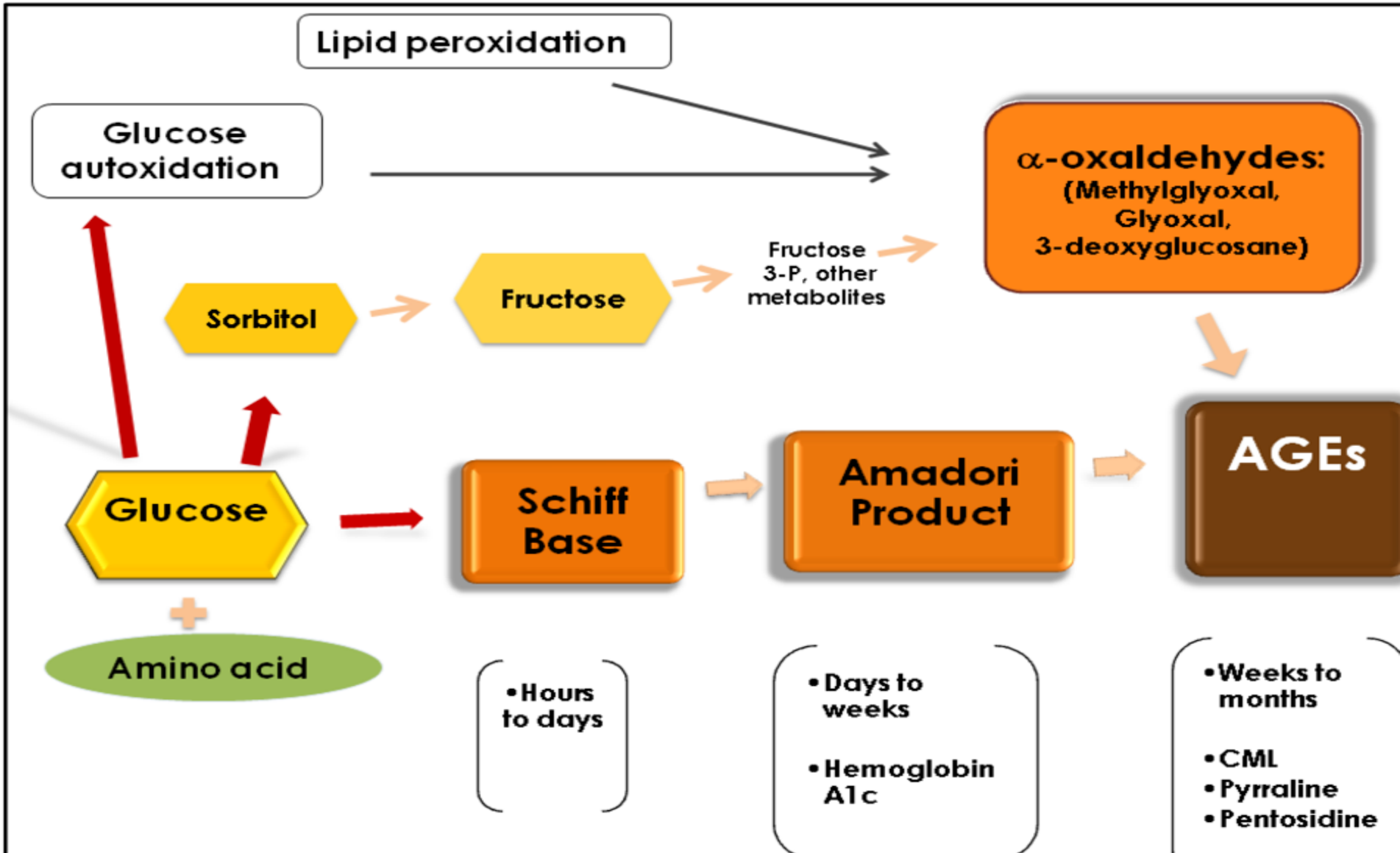
Changes in Indian Diets to Anti Inflammatory

- **Go from FARM TO FORK. Less Processed and more locally grown**.
- Less Emphasis on Carbs: Roti, Rice, Millets
- More Emphasis on Pulses and Dals.
- Inclusion of lots more locally grown non starchy vegetables like bottle gourd, ridge gourds, various green leafys, beans , Drumsticks etc
- Less Emphasis on refined N6 oils (corn, sunflower, safflower) and use of MUFA as preferred source of cooking fat like groundnut oil, rice bran oil and mustard oil.
- Inclusion of Nuts like walnuts and almonds in diet for ALA and MUFA content
- Inclusion of fish or fish oil supplements.
- Moderate use of less sweet locally grown fruits like jamun, guava, ber etc instead of high GI fruits like mangoes, lychees, sapota etc

Advance Glycation End products (AGE)

- Advanced glycation end products (AGEs) are a heterogeneous, complex group of compounds that are formed when reducing sugar reacts in a non-enzymatic way with amino acids in proteins and other macromolecules.
- This occurs both **exogenously (in food)** and **endogenously (in humans) .**
- Higher AGEs occur in those with chronic diseases.

Formation of Advance Glycation End Products. (AGE)



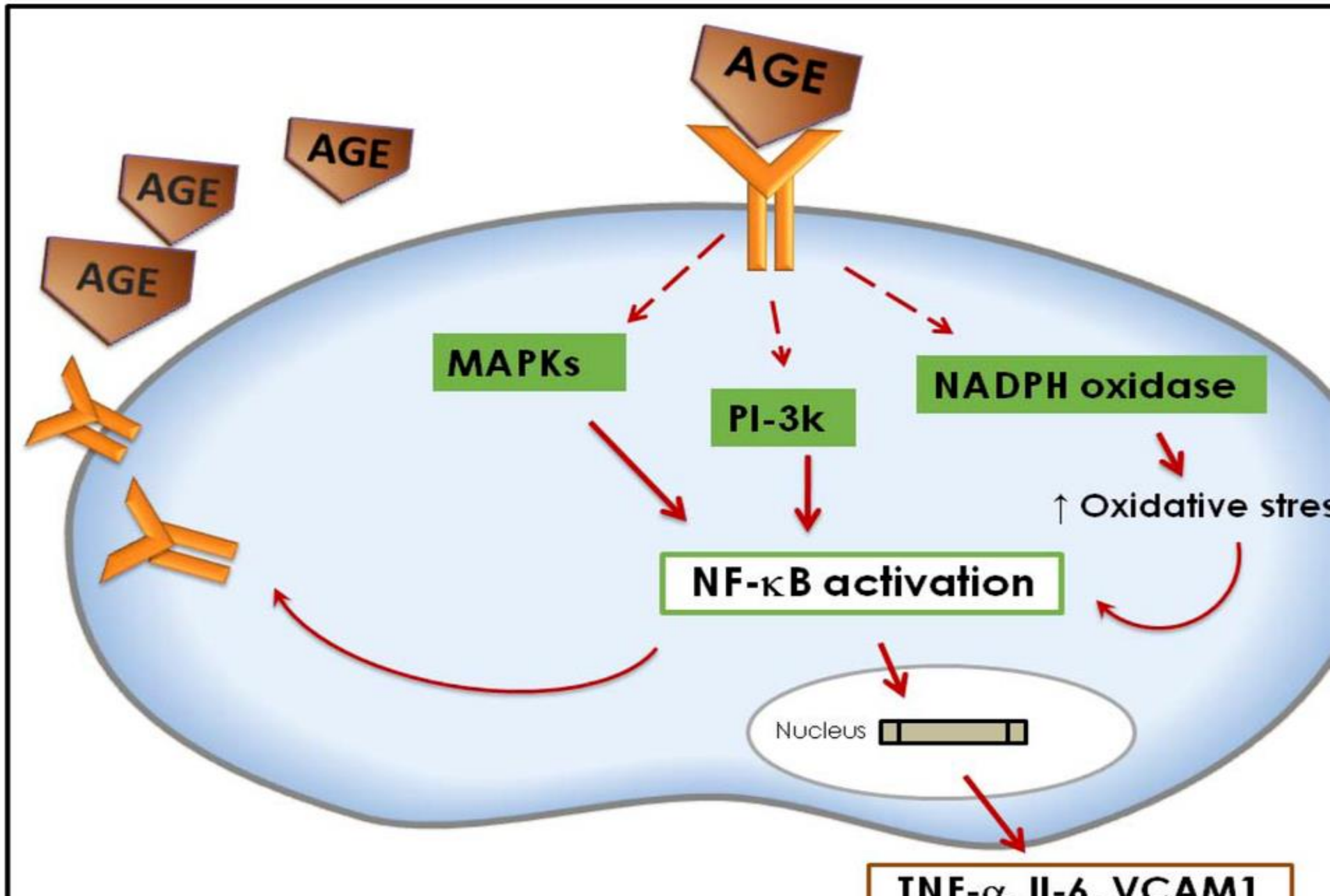
AGEs- Oxidative stress Relation

- The deleterious effects of AGEs in different tissues are attributed to their chemical, pro-oxidant, and inflammatory actions.
- The biological effects of AGEs are exerted by two different mechanisms:
- One independent of the receptor (damage of protein structure and extracellular matrix metabolism)
- Other involving the **receptor for advanced glycation end products (RAGE)** .
- The interaction of AGEs with the receptor RAGE triggers the activation of the mitogen-activated protein kinases (MAPKs) and the phosphatidylinositol-3 kinase (PI3-K) pathways that will lead to the activation of the transcription factor NF-κB.
- NF-κB activation increases RAGE expression, creating a positive feedback cycle that enhances the production of inflammation promoters.
- In addition, AGE-RAGE interaction activates NAD(P)H oxidase (a complex of enzymes which produces superoxide) and when this complex is upregulated, it increases intracellular oxidative stress.
- The sudden increase in oxidative stress by NAD(P)H oxidase in response to AGE-RAGE interaction will also activate NF-κB .

- Basta, G.; Lazzerini, G.; Del, T.S.; Ratto, G.M.; Schmidt, A.M.; De, C.R. At least 2 distinct pathways generating reactive oxygen species mediate vascular cell adhesion molecule-1 induction by advanced glycation end products. *Arterioscler. Thromb. Vasc. Biol.* **2005**, *25*, 1401–1407.

Wautier, M.P.; Chappey, O.; Corda, S.; Stern, D.M.; Schmidt, A.M.; Wautier, J.L. Activation of NADPH oxidase by AGE links oxidant stress to altered gene expression via RAGE. *Am. J. Physiol. Endocrinol. Metab.* **2001**, *280*, E685–E694

Mechanism of AGE action at cellular level



Exogenous Sources of AGEs

- AGEs can be found in cigarettes and in foods.
- Heat has been used for treatment of foods to improve their safety, bioavailability and taste.
- In addition to these positive effects, overheating of foods can also provoke protein degradation and other deteriorative reactions .
- Heat treatment in some foods results in promotion of the **Maillard reaction, which adds desirable flavor, color and aroma**.
- The Maillard reaction has been used for **caramel production, coffee roasting, and bread baking** among others. Some products of the Maillard reaction can be added to industrialized products such as **sodas and juices** among others

Dietary AGEs

- The AGEs content of a diet depends on the nutrient composition (foods rich in protein and fat have the highest content) and on the way food is processed.
- AGEs formation can be rapidly accelerated by increasing the time and degree of exposure to heat and can be introduced into the body in heat–processed foods.
- By AGE-specific, enzyme–linked immunosorbent assay (ELISA), and it was estimated **that ≈10% of ingested immunoreactive AGEs are transported into circulation, two-thirds of which remain in the body, and are incorporated covalently in tissues. Only one third is excreted via the kidneys .**

- Koschinsky, T.; He, C.J.; Mitsuhashi, T.; Bucala, R.; Liu, C.; Buenting, C.; Heitmann, K.; Vlassara, H. Orally absorbed reactive glycation products (glycotoxins): An environmental risk factor in diabetic nephropathy. *Proc. Natl. Acad. Sci. USA* **1997**, *94*, 6474–6479.

Dietary Restriction of AGEs

- Several intervention studies, both human subjects and animals, indicate that the high intake of dietary AGEs contributes to tissue damage that can be prevented by dietary AGEs restriction.
- These intervention studies reduced dietary AGEs by decreasing the heat during the preparation of foods.
- High long term consumption of AGEs has also been associated to higher levels of fasting glucose, insulin and serum AGEs, as well as increased AGEs localization and RAGE staining in ovarian tissue of rats.

- Diamanti-Kandarakis, E.; Piperi, C.; Korkolopoulou, P.; Kandaraki, E.; Levidou, G.; Papalois, A.; Patsouris, E.; Papavassiliou, A.G. Accumulation of dietary glycotoxins in the reproductive system of normal female rats. *J. Mol. Med.* **2007**, *85*, 1413–1420

Effects of Dietary Restriction of AGEs

- In human studies, Uribarri *et al*. demonstrated that intake of dietary AGEs by people with type 1 and 2 diabetes promotes the formation of pro-inflammatory mediators, leading to tissue injury.
- In another study in patients with type 2 diabetes mellitus, decreasing the intake of AGEs for six weeks contributed to decreased levels of circulating AGEs and inflammatory markers.
- The effects of reducing dietary AGEs have also been studied in nondiabetic peritoneal dialysis patients, a group that has very high AGE levels, and the results showed significant reduction in the levels of AGEs and C-reactive protein.

- Uribarri, J.; Stirban, A.; Sander, D.; Cai, W.; Negrean, M.; Buenting, C.E.; Koschinsky, T.; Vlassara, H. Single oral challenge by advanced glycation end products acutely impairs endothelial function in diabetic and nondiabetic subjects. *Diabetes Care* **2007**, *30*, 2579–2582
- Uribarri, J.; Peppa, M.; Cai, W.; Goldberg, T.; Lu, M.; He, C.; Vlassara, H. Restriction of dietary glycotoxins reduces excessive advanced glycation end products in renal failure patients. *J. Am. Soc. Nephrol.* **2003**, *14*, 728–731.
- Vlassara, H.; Cai, W.; Crandall, J.; Goldberg, T.; Oberstein, R.; Dardaine, V.; Peppa, M.; Rayfield, E.J. Inflammatory mediators are induced by dietary glycotoxins, a major risk factor for diabetic angiopathy. *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 15596–15601

Effect of Cooking Procedures on AGE Formation in Foods

- Preparation of common foods under varying conditions of water and heat had a different effect on AGE content.
- For example, scrambled eggs prepared in an open pan over medium-low heat had about one half the AGEs of eggs prepared in the same way but over high heat.
- Poached or steamed chicken had less than one fourth the AGEs of roasted or grilled chicken.
- In all food categories, exposure to **higher temperatures and lower moisture levels coincided with higher AGE levels for equal weight of food as compared to foods prepared at lower temperatures or with more moisture.**
- Thus, frying, broiling, grilling, and roasting yielded more AGEs compared to boiling, poaching, stewing, and steaming.
- Microwaving did not raise AGE content to the same extent as other dry heat cooking methods for the relatively short cooking times (**6 minutes or less**) that were tested.

J Am Diet Assoc. 2010 Jun; 110(6): 911–16.e12.

Pointers to help choose food

- When items in the meat category prepared by similar methods were compared, the highest dAGE levels were observed in beef and cheeses followed by poultry, pork, fish, and eggs.- **Cook on low Flame**
- It is noteworthy that even lean red meats and poultry contain high levels of dAGEs when cooked under dry heat.- **Curried meat better than tandoori**
- Higher-fat and aged cheeses, such as full-fat American and Parmesan, contained more dAGEs.- **Full fat Grilled Paneer tikkas or grilled cheese or fried paneer pakoras are not good food ideas**.
- High-fat spreads, including butter, cream cheese, margarine, and mayonnaise, were also among the foods highest in dAGEs.- **Avoid using fats on foods and then grilling them like grilled toast, parathas etc.**

Pointers to help choose food

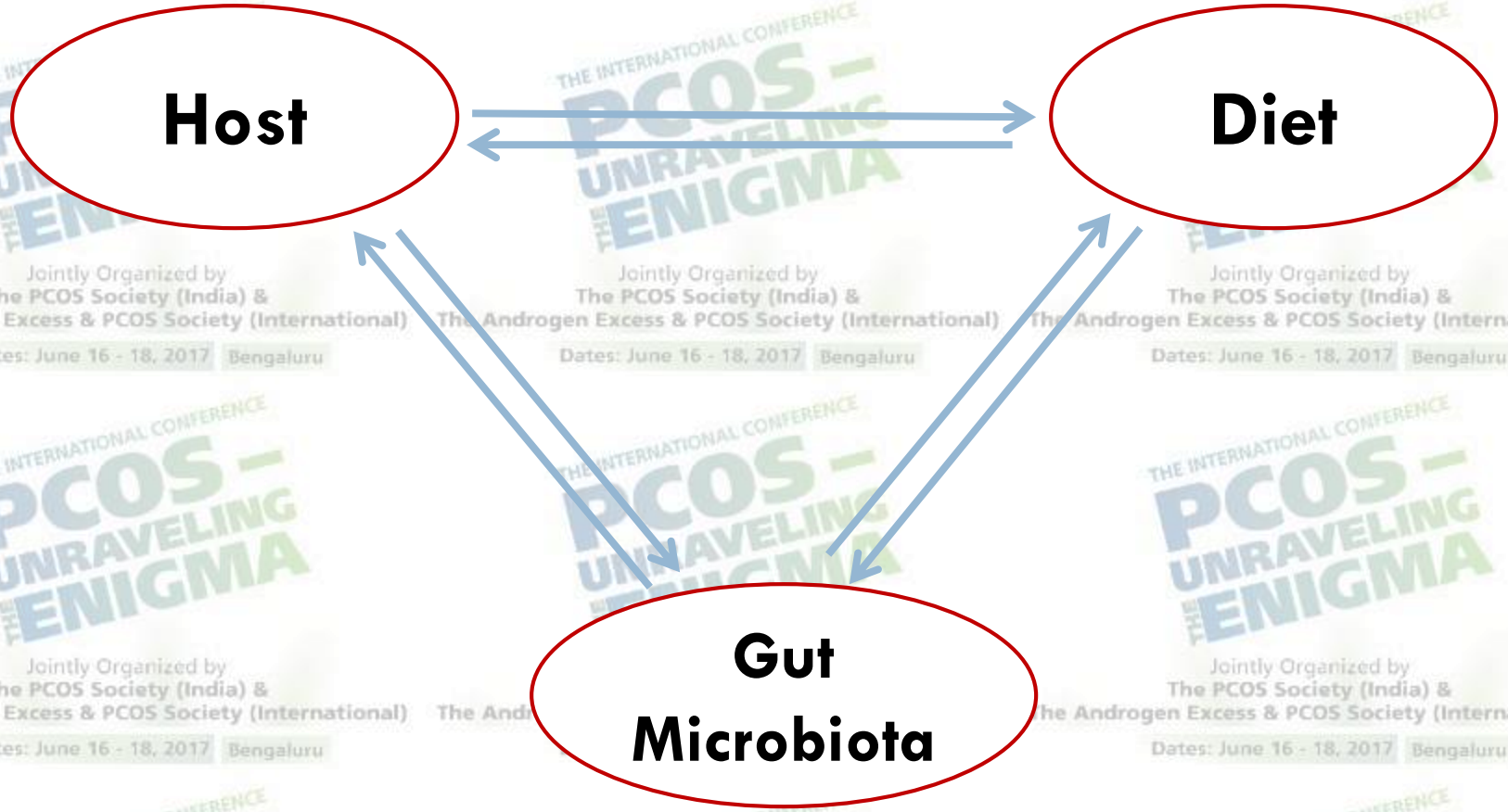
- The highest dAGE level per gram of food in this category was found in dry-heat processed foods such as crackers, chips, and cookies. **Avoid Indian processed foods like shhakar para, namak para, Khakara**
- Grains, legumes, breads, vegetables, fruits, and milk were among the lowest items in dAGE, unless prepared with added fats. For instance, biscuits had more than 10 times the amount of dAGEs found in roti, rolls, or bagels. **Use nuts and fruits as mid time snack rather than processed foods.**

Recent Aspects of Obesity Science

Gut Microbiota :

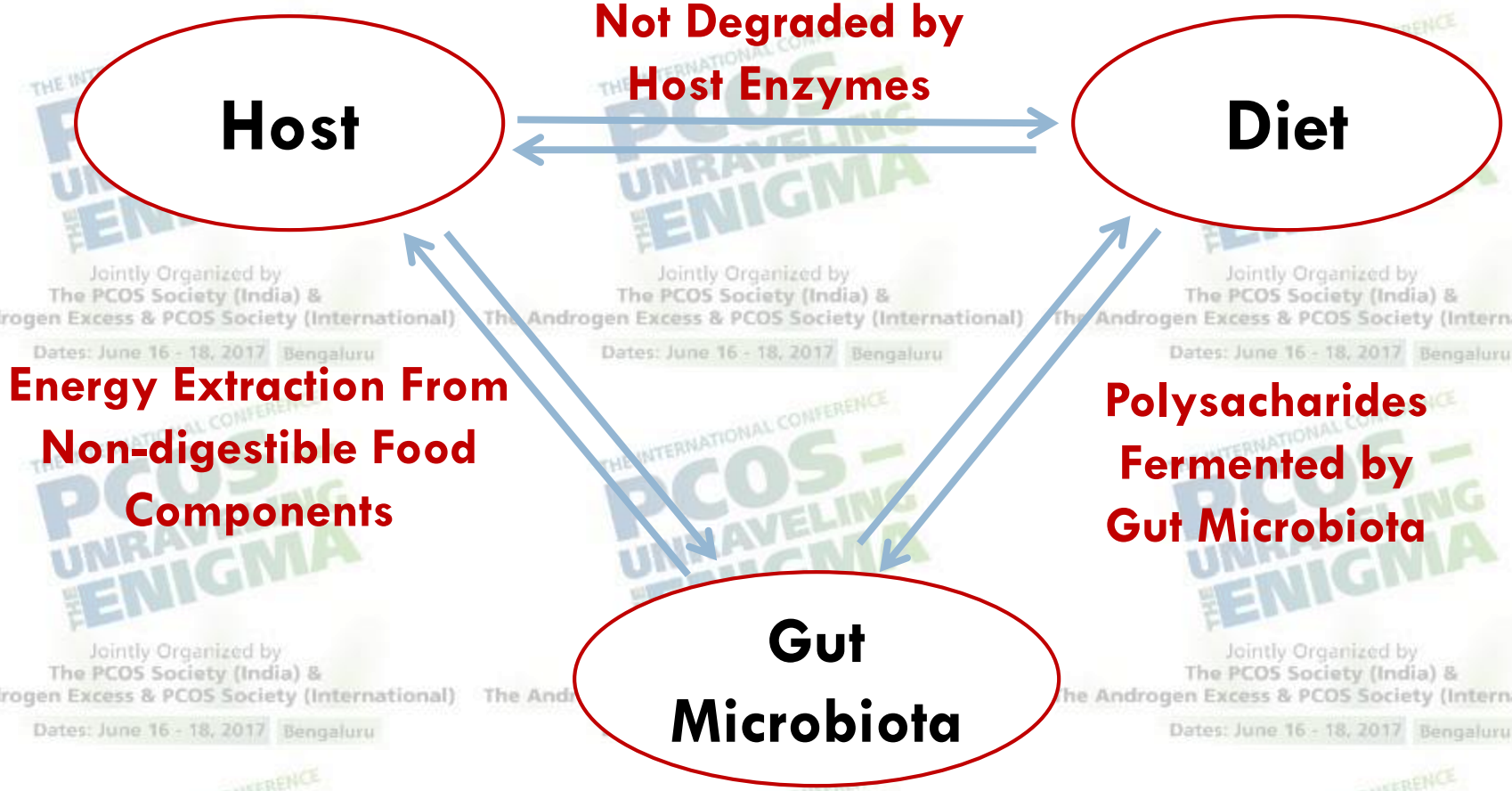
Controls Energy Homeostasis ...

Role of Gut Microbiota In Human ...



Chassard & Lacroix, **Curr Opin Clin Nutr Metab Care, 2013;** 16: 453-60

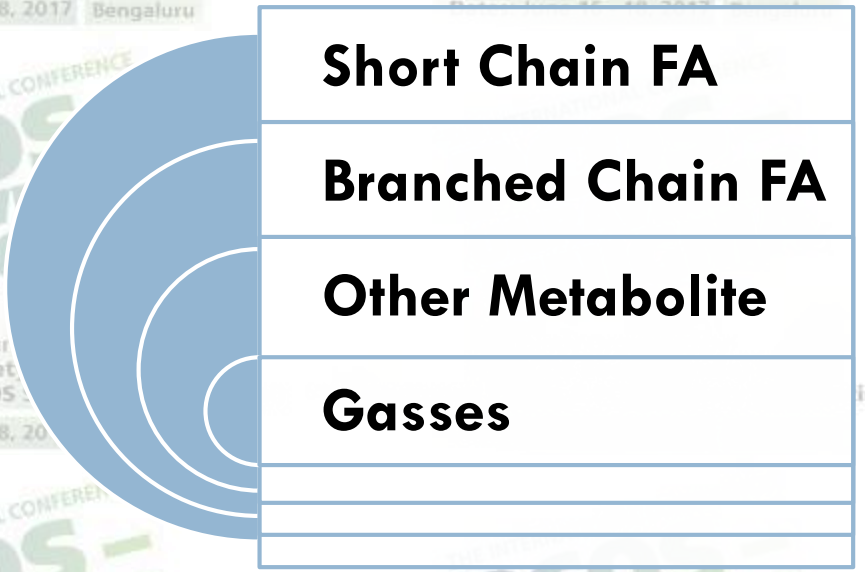
Role of Gut Microbiota In Human ...



Chassard & Lacroix, **Curr Opin Clin Nutr Metab Care, 2013**; 16: 453-60

Role of Gut Microbiota In Human ...

- Non Digestible CHO
- Resistant Starch
- Non-starch Polysacharide
- Residual Protein



Increased Energy harvest from Diet

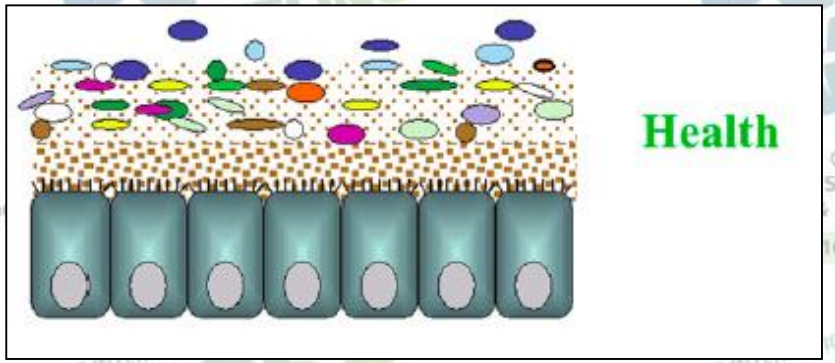
Gut Microbiota in Health & Disease ...

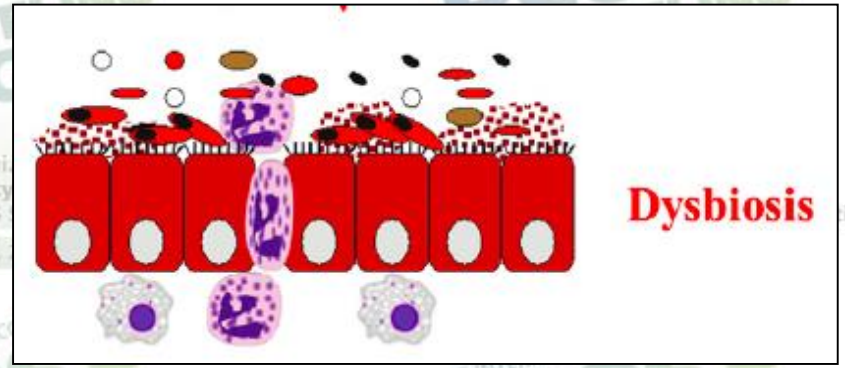
Normal Gut Microbiota

- **Symbiosis**
- Bile, Lipid, Glucose Metabolism
- Physiological Programming of Energy

Altered Gut Microbiota

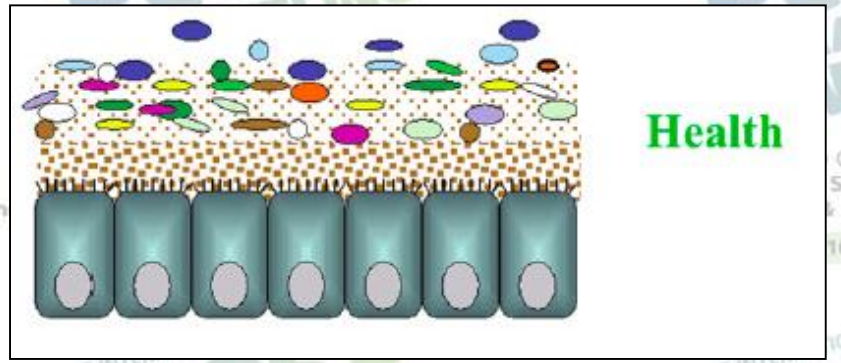
- **Dysbiosis**
- Inflammation
- Metabolic Diseases





Gut Microbiota – Role in Obesity …

- Gut Microbiota
  - ↑ LPL activity ⟶ ↑ FFA production & absorption
  - ↓ FFA oxidation
  - ↓ secretion of gut hormones PYY, GLP-1
  - Affecting gut transit time & energy harvest
  - Impairs satiety hormone signals from the gut



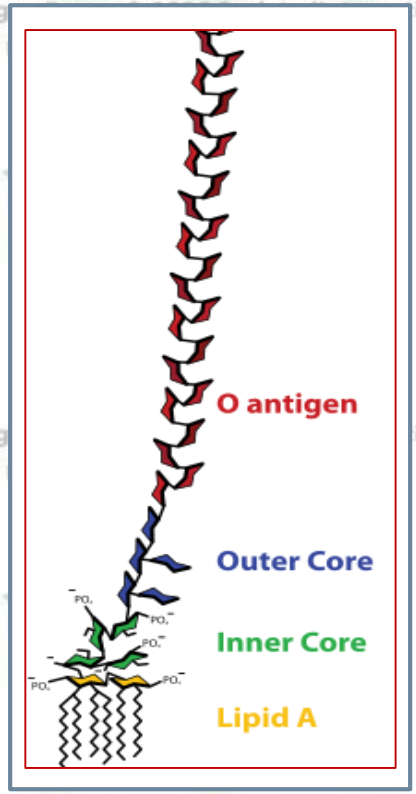
Recent Aspects of Obesity Science

Gut Microbiota :

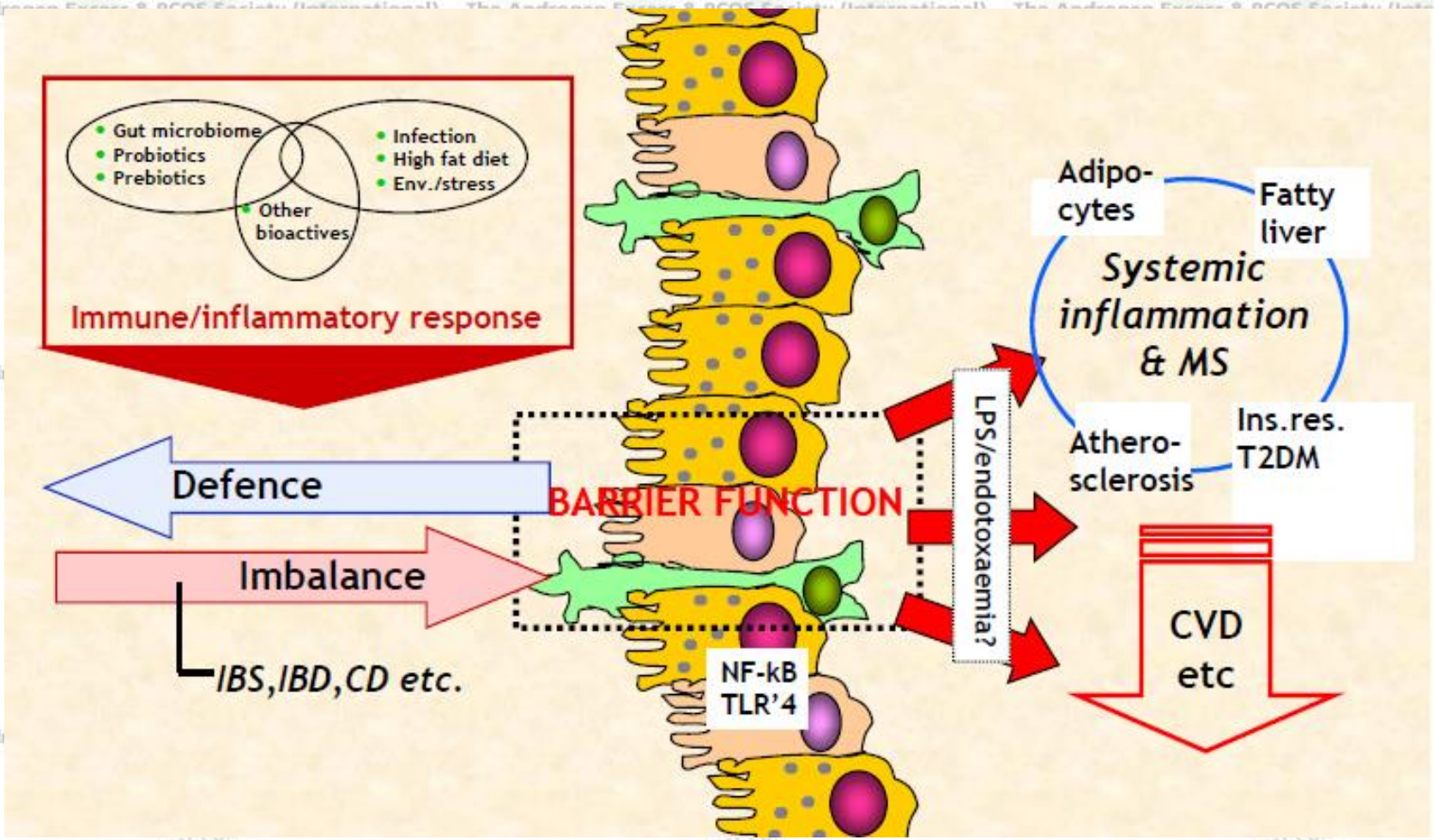
Dysbiosis Triggers Inflammation …

LPS - Endotoxins : Products of Dysbiosis ...

- **Lipopolysaccharides (LPS)**
- **Endotoxin**, consist of a lipid and a polysaccharide composed of O-antigen
- Found in the outer membrane of Gram-negative bacteria
- Leaks through Epithelial barrier
- Elicit strong inflammatory response



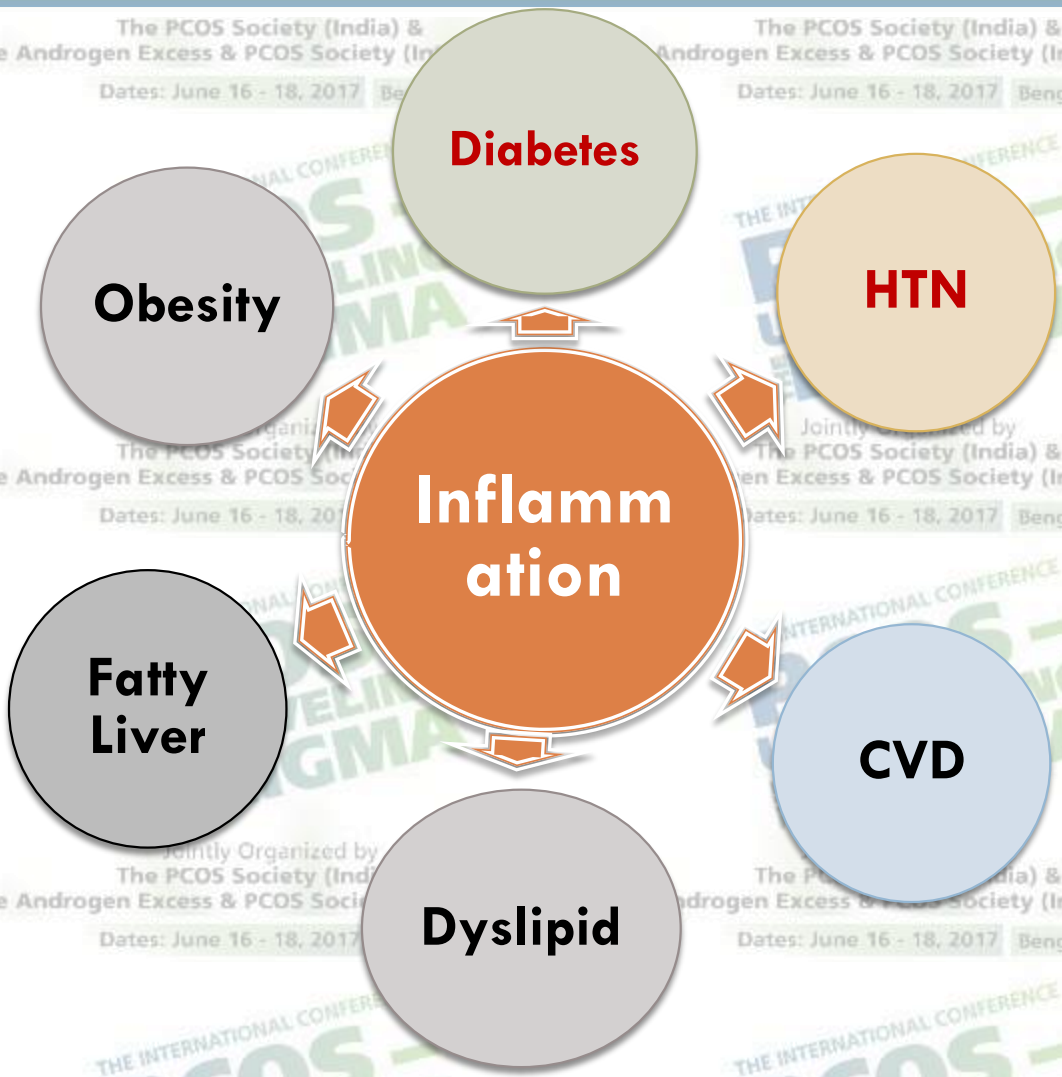
LPS Leaks Through Epithelial Barrier ...



Gut Microbiota – Role in Obesity …

- **High fat diet**
  - Changes microbiota character
  - **Damages intestinal microvilli**
  - **↑ absorption of LPS, food derived Antigens, TG**
    - Transported in chylomicron to visceral adipose tissue
    - **Inflammation**
- Lean individuals do not have VAT inflammation

Inflammation At The Centre of All ...



Dysbiosis Triggers Adipose Inflammation ...

Inflamed adipose tissue

- Causes **Leptin resistance** → weight gain
- Releases **inflammatory cytokines** → IR
- Decreases **adiponectin** → IR
- **Further weight gain & obesity complications**

Major Factors Behind Dysbiosis ...

Determinants of Obesogenic Gut Microbiota

1. **Rampant Use of Antibiotics**
2. **Dietary Nutrient Composition - Western diet**
3. Rampant **Cesarean Section Delivery**
4. Alternative **Baby Food**

Tips to improve Gut Microbiota

- Choose foods lower in fat and sugars.
- Choose plenty of Vegetables, Fibrous fruits, Dals with skins and whole grains . (Prebiotics Rich)
- Introduce probiotic rich foods in diet like dahi(curd), chaas (butter milk).
- Avoid maida products completely.

Conclusion

- PCOD is an inflammatory state.
- Use of anti inflammatory diets help reduce inflammations besides being lower in calories.
- AGE are also known to cause inflammation.
- To reduce AGE , right cooking methods should be adopted. Also prudent choice of ready to eat food must be made.
- Probiotics and Prebiotics help to maintain healthy colonic flora which help reduce inflammation.

Thank you

Glycemic Index: Mechanism

Consuming High GI food

Feed me

Food

Blood Glucose molecules

Faster gastric emptying

Quick release in the blood stream & higher insulin response

Blood

Feels hungry early

Consuming Low GI food

Low GI food

Blood Glucose molecules

Slows down gastric emptying

Slower release in blood stream & attenuated insulin response

Blood

Keeps you fuller for longer

Fiber content

- Prolong gastric emptying
- Increase small bowel transit time
- Delay absorption of carbohydrates & fat

E.g. Apples (28) – Low GI
Lychee (79) – High GI

Source: Foster Powell, Holt S and Brand-M[illegible]er JC. Am J Clin Nutr 2002

Relation between glucose and carbohydrate intakes and increased inflammation

- Glucose ingestion stimulated NAPDH oxidase in polymorphonuclear leukocytes and mononuclear cells and increased the generation of reactive oxygen species (ROS).
- Simultaneously, tocopherol concentrations decreased.
- Dietary carbohydrates stimulate triacylglycerol production in the liver and can cause hepatic steatosis .
- In patients with nonalcoholic fatty liver disease, carbohydrate intake correlates with the histologic evidence of inflammation which then may lead to increased serum concentrations of the inflammatory markers.
- *Am J Clin Nutr* 2006;83:774 –9.

Nut intake and PCOD

- Nut intake altered fatty acid composition of the diet.
- Almonds increased MUFA intake by 33% and decreased saturated fat by 25% without altering n-3 or n-6 PUFA.
- Walnuts increased n-3 PUFA and n-6 PUFA intakes by 11-fold and 5-fold, without affecting saturated fat or MUFA intakes.

Table 1. Scoring for each food parameter used for dietary inflammatory index calculation

Food parameter	Inflammatory effect score*
Energy	0·180
Carbohydrate	0·097
Fat	0·298
Alcohol	−0·278
Fibre	−0·663
Protein	0·021
Vitamin B_{12}	0·106
Vitamin B_6	−0·365
β Carotene	−0·584
n-3	−0·436
n-6	−0·159
MUFA	−0·009
SFA	0·373
Trans-fat	0·229
Fe	0·032
PUFA	−0·337
Riboflavin	−0·068
Thiamin	−0·098
Niacin	−0·246
Vitamin A	−0·401
Mg	−0·484
Zn	−0·313
Se	−0·191
Vitamin C	−0·424
Vitamin D	−0·446
Vitamin E	−0·419
Folate	−0·190
Caffeine	−0·110

* A negative value indicates anti-inflammatory effect and a positive score indicates pro-inflammatory effect.

The advanced glycation end product (AGE) content of 549 foods, based on carboxymethyllysine content

Grains/legumes	AGE ku/100g	Serving size (g)	AGEku/serving
Beans, red kidney, raw	116	100	116
Beans, red kidney, canned	191	100	191
Beans, red kidney, cooked 1 h	298	100	298
Pasta, cooked 8 min	112	100	112
Pasta, cooked 12 min	242	100	242
Pasta, spiral[b]	245	100	245
Rice, white, quick cooking, 10 min	9	100	9
Rice, Uncle Ben's white, cooked, 35 min (Mars, Inc, Houston, TX)	9	100	9
Rice, white, pan toasted 10 min, cooked 30 min	32	100	32

The advanced glycation end product (AGE) content of 549 foods, based on carboxymethyllysine content

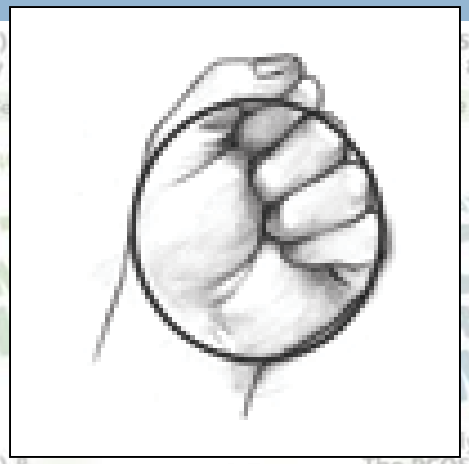
Vegetables (raw unless specified otherwise)	AGE ku/100g	Serving size (g)	AGEku/serving
Carrots, canned	10	100	10
Celery	43	100	43
Cucumber	31	100	31
Eggplant, grilled, marinated with balsamic vinegar[b]	256	100	256
Eggplant, raw, marinated with balsamic vinegar[b]	116	100	116
Green beans, canned	18	100	18
Portabella mushroom, raw, marinated with balsamic vinegar[b]	129	100	129
Onion	36	100	36
Tomato	23	100	23
Tomato sauce (Del Monte Foods, San Francisco, CA)	11	100	11
Vegetables, grilled (broccoli, carrots, celery)	226	100	226
Vegetables, grilled (pepper,	261	100	261

The advanced glycation end product (AGE) content of 549 foods, based on carboxymethyllysine content

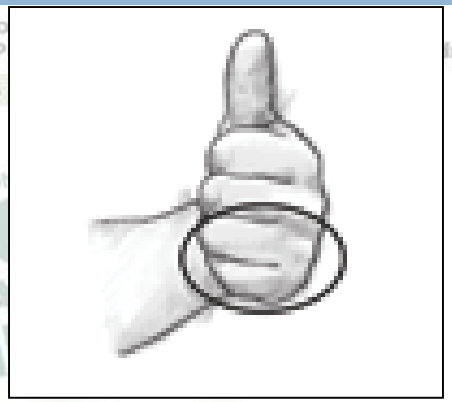
Fruits	AGE ku/100g	Serving size (g)	AGEku/serving
Apple, baked	45	100	45
Apple, Macintosh	13	100	13
Banana	9	100	9
Cantaloupe	20	100	20
Coconut cream, Coco Goya cream of coconut (Goya, Secaucus, NJ)	933	15	140
Coconut milk, leche de coco, (Goya)	307	15	46
Coconut, Baker's Angel Flake, sweetened (Kraft)	590	30	177
Dates, Sun-Maid California chopped (Sun-Maid, Kingsburg, CA)	60	30	18
Fig, dried	2,663	30	799
Plums, Sun-Maid dried pitted prunes (Sun-Maid)	167	30	50
Raisin, from Post Raisin Bran (Kellogg Co)	120	30	36

Hand Guide to Sensible Servings

3 oz –svg
meat, fish, poultry

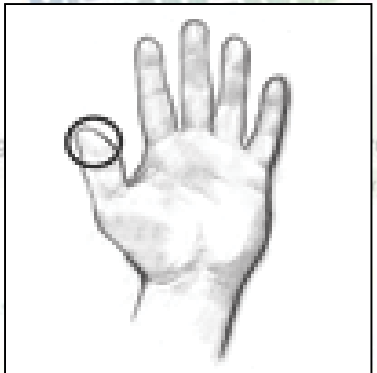


1 cup – svg
veggies, milk, salads, stews



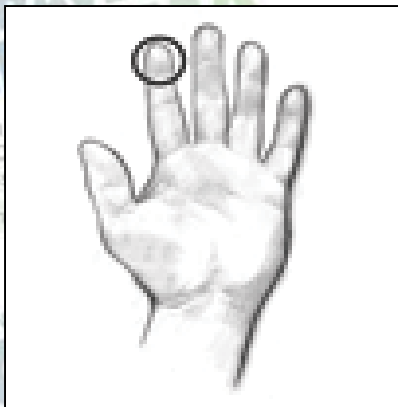
½ cup – svg
rice, cereal, fruit, beans

1 ounce – snack food, cheese



1 Tbsp – salad dressing, cream cheese, p-nut butter

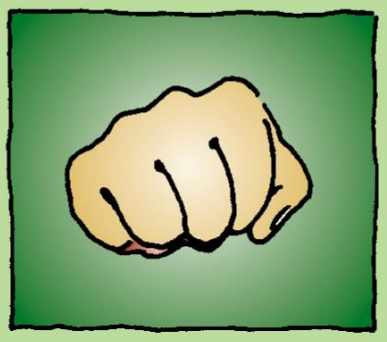
1 tsp – margarine, oil



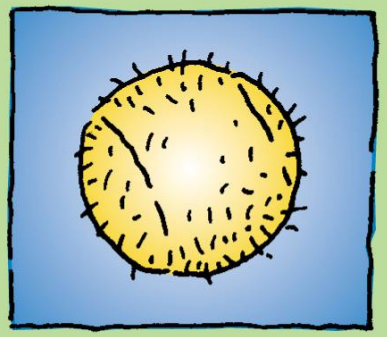
Tips for reducing portion sizes:

- Eat smaller portions
- Measure your servings
- Use smaller plates, bowls and glasses
- If eating out, share your entrée, or take half home

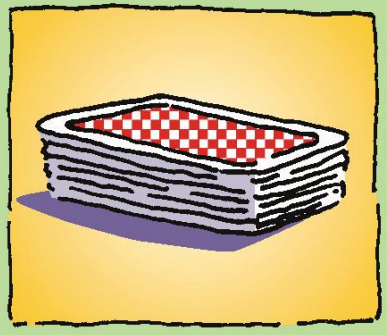
Use these images to remember serving sizes:



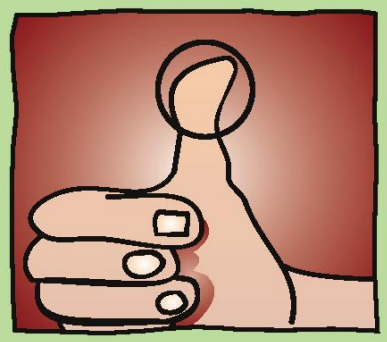
1 cup of rice, pasta, vegetables, cereal



A piece of fruit

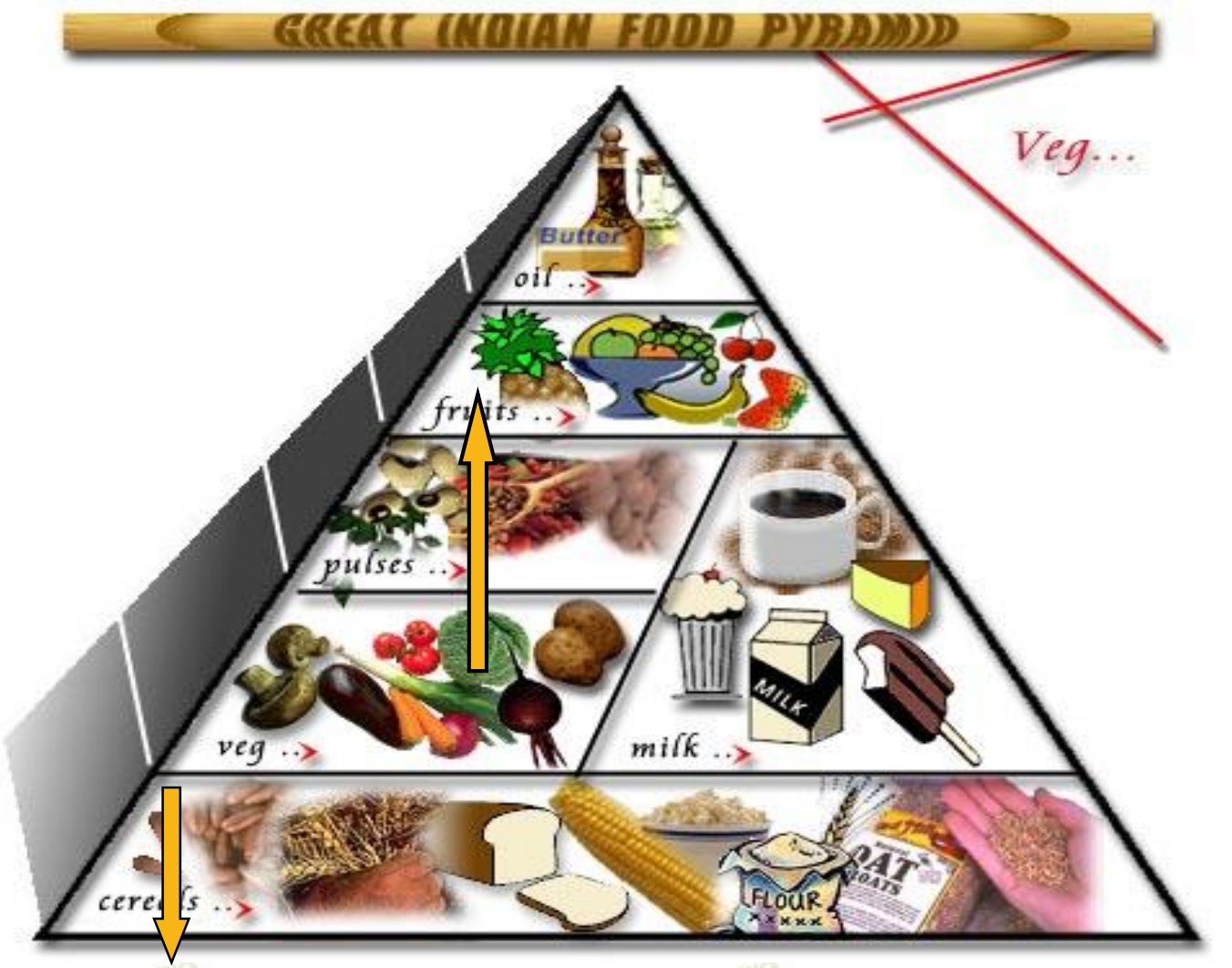


A single serving of meat (3–4 ounces)



Tablespoon of fat, salad dressing or peanut butter

Indian Food Pyramid



Indian Problems

- Portion sizes
- Cooking methods
- Left-over foods
- Fast foods/ snacking
- Eating out

- Myth….In which plate/bowl I eat it does not matter….

HOUSEHOLD MEASURES

Milk consumption and Inflammation

- Milk protein consumption induces postprandial hyperinsulinaemia and shifts the growth hormone/insulin-like growth factor-1 (IGF-1) axis to permanently increased IGF-1 serum levels.
- Insulin/IGF-1 signalling is involved in the regulation of fetal growth, T-cell maturation in the thymus, linear growth, pathogenesis of acne, atherosclerosis, diabetes mellitus, obesity, cancer and neurodegenerative diseases, thus affecting most chronic diseases of Western societies.
- Medical Hypotheses Volume 72, Issue 6, June 2009, Pages 631-639

N Acetyl Cysteine

- N-Acetylcysteine, or NAC, is an altered form of the amino acid cysteine used in supplements. The body converts NAC to cysteine, which is then converted to glutathione, an antioxidant. NAC is not found naturally in food sources; however cysteine is present in most high protein foods.
- NAC converts into cysteine. Cysteine is a nonessential amino acid produced by the body. However, it requires the essential amino acid methionine to do this, so some biologists consider cysteine an essential amino acid, as well.
- Besides non vegetarian foods ,vegetables like broccoli, red pepper and onion are significant sources of cysteine. Other plant sources include bananas, garlic, soy beans, linseed and wheat germ.

What happens during frying ?

Frying Conditions:

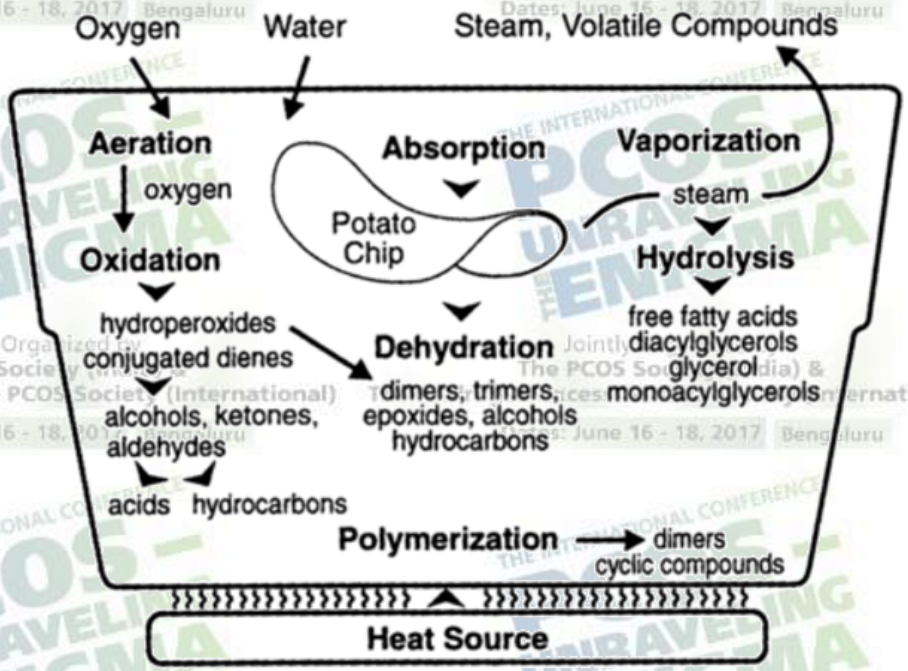
Food is subjected to high temperature with humid conditions and atmospheric oxygen

↓

Increased oxidation

↓

Increased free radical generation + Secondary products generation



Hence, Frying is not recommended !!

SECONDARY OXIDATION PRODUCTS - FRYING

ALTERATION	CAUSATIVE AGENT	NEW COMPOUNDS
Hydrolysis	Moisture	• Fatty acids • Diacylglycerols
Oxidation	Air	• Oxidized monomeric triacylglycerols • Oxidized dimeric and oligomeric triacylglycerols • Volatile compounds (aldehydes, ketones, alcohols, hydrocarbons, etc.)
Thermal alteration	Temperature	• Cyclic monomeric triacylglycerols • Isomeric monomeric triacylglycerols • Nonpolar dimeric and oligomeric triacylglycerols

HEALTH EFFECTS DUE TO SECONDARY OXIDATION PRODUCTS

- Increasing international concern about the toxic adversity of the formation of compounds in foods during cooking and processing.
- Long period as intermittent frying oil medium and fried foodstuffs contain:
  - High level of the oxidized fatty acids
  - Malonaldehyde
  - Trans fatty acids
  - Polar compounds

HEALTH EFFECTS DUE TO SECONDARY OXIDATION PRODUCTS

Impair of liver and renal functions

Rise of LDL

↓

Coronary heart disease

Carcinogenic

References:

1) Ganbi, H. H. A. (2011). Alteration in Fatty Acid Profiles and Formation of Some Harmful Compounds in Hammour Fish Fillets and Frying Oil Medium Throughout Intermittent Deep-Fat Frying Process. *World Applied Sciences Journal*, *12*(4), 536-544.2) Garrido-Polonio, C., García-Linares, M. C., García-Arias, M., López-Varela, S., García-Fernández, M. C., Terpstra, A. H., & Sánchez-Muniz, F. J. (2004). Thermally oxidized sunflower-seed oil increases liver and serum peroxidation and modifies lipoprotein composition in rats. *British Journal of Nutrition*, *92*(02), 257-265. 3) Ringseis, R., Gutgesell, A., Dathe, C., Brandsch, C., & Eder, K. (2007). Feeding oxidized fat during pregnancy up-regulates expression of PPARα-responsive genes in the liver of rat fetuses. *Lipids Health Dis*, *6*(6).4) Del Rio, D., Stewart, A. J., & Pellegrini, N. (2005). A review of recent studies on malondialdehyde as toxic molecule and biological marker of oxidative stress. *utrition, metabolism and cardiovascular diseases*, *15*(4), 316-328 (abstract).

HEALTH EFFECTS DUE TO SECONDARY OXIDATION PRODUCTS

- Increasing international concern about the toxic adversity of the formation of compounds in foods during cooking and processing
- Long period as intermittent frying oil medium and fried foodstuffs contain:
  - High level of the oxidized fatty acids
  - Malondialdehyde (MDA)
    - Principal and most studied product of PUFA peroxidation
    - Highly toxic molecule and should be considered as more than just a marker of lipid peroxidation
  - Trans fatty acids
  - Polar compounds

Approximate Fatty Acid Composition of Common Fats and Oils (g/100)

	Saturated	Mono-Unsaturated	Linoleic	Alpha Linolenic	Predominant Fatty Acids
Coconut*	90	7	2	<0.5	Saturated
Palm kernel	82	15	2	<0.5	Saturated
Ghee[a,b]	65	32	2	<1.0	Saturated
Vanaspati[b]	24	19	3	<0.5	Saturated
Red palm oil (raw)	50	40	9	<0.5	Saturated + Monounsaturated
Palm oil	45	44	10	<0.5	Saturated + Monounsaturated
Olive	13	76	10	<0.5	Monounsaturated
Groundnut	24	50	25	<0.5	Monounsaturated
Rape/mustard[c,d]	8	70	12	10	Monounsaturated
Sesame	15	42	42	1.0	Mono and poly-unsaturated

Approximate Fatty Acid Composition of Common Fats and Oils (g/100)

	Saturated	Mono-Unsaturated	Linoleic	Alpha Linolenic	Predominant Fatty Acids
Rice bran	22	41	35	1.5	Mono and poly-unsaturated
Cotton seed	22	25	52	1.0	Polyunsaturated
Corn	12	32	55	1.0	Polyunsaturated
Sunflower	13	27	60	<0.5	Polyunsaturated
Safflower	13	17	70	<0.5	Polyunsaturated
Soyabean[d]	15	27	53	5.0	Polyunsaturated

[a]: Mainly short and medium chain fatty acids (Coconut 77%, Ghee 25%)

[b]: Trans fatty acids (Ghee 2%, Vanaspati 53%)

[c]: Long chain monounsaturated fatty acids (50% eruric acid and 5% eicosenoic acid)

[d]: Good source of alpha-linolenic acid

Fatty Acid Composition and Cholesterol Content of Foods (g/100 g. Edible Portion)

Item	Fat (g/100 g)	Saturated Fatty Acids (g/100 g)	Cholesterol (mg/100 g)
Butter	80	50	250
Ghee	100	65	300
Milk (Cow)	4	2	14
Milk (Buffalo)	8	4	16
Milk (Skimmed)	0.1	-	2
Milk (Condensed)	10	6	40
Cream	13	8	40
Cheese	25	15	100
Egg (Whole)	11	4	400
Egg Yolk	30	9	1120
Chicken without Skin	18	6	60

Fatty Acid Content of Meat

Item	Fat (g/100 g)	Saturated Fatty Acids (g/100 g)	Cholesterol (mg/100 g)
Chicken with Skin	18	6	100
Beef	16	8	70
Mutton	13	7	65
Pork	35	13	90
Organ Meats			
Brain	6	2	2000
Heart	5	2	150
Kidney	2	1	370
Liver	9	3	300

Fatty Acid Composition and Cholesterol Content of Foods (g/100 g: Edible Portion)

Item	Fat (g/100 g)	Saturated Fatty Acids (g/100 g)	Cholesterol (mg/100 g)
Fresh Water & Sea Foods			
Prawns/Shrimps	2	0.3	150
Fish (Lean)	1.5	0.4	45
Fish (Fatty)	6	2.5	45

* Values vary depending on the feed of the animals.

[a] One whole egg or yolk of one egg contains 210 mg cholesterol

Gopalan et al., 1989; McCance and Widdowson, 1993

Metabolic Features of PCOS

- Insulin resistance is a common feature of PCOS affecting 50-70% of women.
- Android obesity is evident in ~52%-64% of women with PCOS.
- Abdominal adiposity in particular is present in ~30% of normal weight women with PCOS.

- Goodarzi MO, Korenman SG. The importance of insulin resistance in polycystic ovary syndrome. Fertil Steril. 2002; 77:255–58. 12. Carmina E, Bucchierri S, Esposito A, Del Puente A, Mansueto P, Orio F, et al.
- Abdominal fat quantity and distribution in women with polycystic ovary syndrome and extent of it relation to insulin resistance. J Clin Endocrinol Metab. 2007; 92:2500–5. [PubMed: 17405838]

Biochemistry of Inflammation.

- Circulating mononuclear cells utilize glucose during glycolysis for mitochondrial respiration.
- Some glucose is diverted to the hexose monophosphate shunt to generate nicotinamide adenine dinucleotide phosphate (NADPH) .
- Membrane-bound NADPH oxidase is activated by translocation of a cytosol component known as p47phox to the cell membrane .
- Oxidation of NADPH by NADPH oxidase generates superoxide, a reactive oxygen species (ROS) that induces oxidative stress.
- This in turn activates the transcription factor, nuclear factor κB (NFκB) by its dissociation from the inhibitory proteín, inhibitory κB (IκB).
- Activated NFκB translocates to the nucleus to promote TNFα and IL-6 gene transcription.

- Groemping Y, Lapouge K, Smerdon SJ, Rittenger K. Understanding activation of NADPH oxidase: a structural characterization of p47phox. Biophys J. 2003; 84:356A. [PubMed: 12524289]

The influence of adipose tissue on inflammation in PCOS

- **Obesity** is Pro inflammatory state.
- The pro inflammatory state of obesity contributes to the promotion of insulin resistance and atherogenesis when present in PCOS.
- The inflammatory load derived from adipose tissue in PCOS is in proportion to body mass, but is not uniquely greater compared to that of individuals without PCOS.

- Carmina E, Bucchierri S, Esposito A, Del Puente A, Mansueto P, Orio F, et al. Abdominal fat quantity and distribution in women with polycystic ovary syndrome and extent of it relation to insulin resistance. J Clin Endocrinol Metab. 2007; 92:2500–5. [PubMed: 17405838]