

Effectively Fighting Inflammation Through an Evidence-Based Diet

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Learning Objectives

- recall the components of an anti-inflammatory diet
- describe which inflammatory markers are utilized with chronic inflammation
- recognize the disease processes associated with chronic inflammation, with a focus on Obesity, Metabolic Syndrome, and Aging
- determine how dietary inflammatory indices are measured in pro-inflammatory and anti-inflammatory states
- explain how fiber influences inflammation and gut microbiota
- define the role of polyphenols in an anti-inflammatory diet
- identify the difference between omega-3 and omega-6 fatty acids and their role in inflammation
- illustrate how to prescribe an anti-inflammatory diet

Disclosures

I have no conflict of interest to disclose

Carbohydrates

Regular consumption of refined, high-glycemic carbohydrates results in chronic hyperglycemia which subsequently increases production of free radicals and proinflammatory cytokines

GLYCEMIC LOAD = quantity of carbohydrate ingested, multiplied by the rate at which that carbohydrate enters the bloodstream (ex. the glycemic index)

Richard A. Hales, 2011

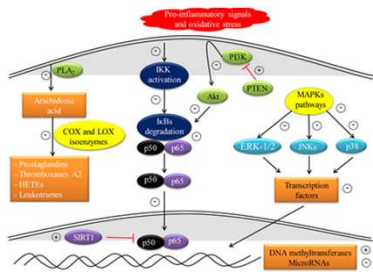
Polyphenols

Modulates several pro-inflammatory pathways:

- including COX-2, LOX, iNOS
- transcription factor: nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB)
- activating protein-1 (ap-1)
- activates antioxidant detoxifying enzymes protein kinase C, NF erythroid-2-related factor 2, mitogen-activated protein kinase (MAPK)

Wang et al., 2012

Polyphenols



Khan et al., 2013

Polyphenols

- mainly absorbed in the intestine
- bioavailability depends on stomach pH, gastrointestinal motility, enzyme degradations, transporters, microbiota
- neutralizes free radicals
- antioxidant
- dampens the inflammatory response

Polyphenols

Found in Plants

- Fruits
- Vegetables
- Tea
- Coffee
- Dark chocolate
- Herbs and spices
- Whole grains
- Edible mushrooms and fungal fruiting bodies
- Red wine

Is there a chronic inflammatory marker?

- NONSPECIFIC markers: BMI, WBC, platelets, sed rate, CRP, interleukins (IL-6, IL-1 β , IL-10, IL-4), TNF-alpha ($-\alpha$), fibrinogen
- SPECIFIC markers: nothing yet however current research is underway. There is no standard biomarker for chronic inflammation
 - total urinary polyphenol excretion
 - DNA-methylation or DNAm proxies of CRP (epigenetic approach)

Acute vs Chronic Inflammation

Acute

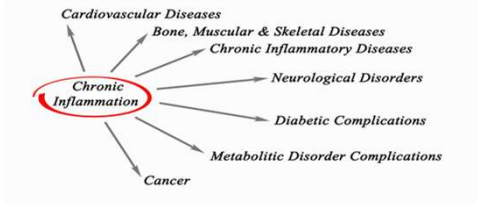
- from an evolutionary standpoint—inherently protective: heals damaged tissue, eliminates destructive agents in a temporary, self-limiting manner
- capillary dilatation
- leukocyte infiltration causing redness, heat, pain, and swelling

Chronic

- noxious stimuli persistently confronts the body and/or the inflammatory response fails to resolve
- causes silent damage throughout the body
- over time, chronic diseases becomes apparent

Why?

Chronic Inflammation is associated with cancer, aging, and multiple disease processes



Disease Processes

| | |
|-------------------------|---------------------------------------|
| Aging (“Inflammaging”)* | Inflammatory Bowel Disease |
| Asthma | Metabolic Syndrome* |
| Alzheimer’s Disease | Multiple Sclerosis |
| Cancer | Obesity* |
| Coronary Artery Disease | Pain Management |
| Depression | Rheumatoid Arthritis |
| Fatty Liver | Viral Respiratory Diseases (COVID-19) |
| Gut Microbiota | |

Obesity

Adipose tissue is metabolically active in which its dysregulation causes a low-grade inflammatory state

The higher amount of visceral fat, leads to higher levels of inflammatory cytokines

Dr. Giovanni et al., 2011

Caloric Intake

- excess caloric intake, particularly in sedentary individuals, results in increased adipose tissue which directly contributes to chronic inflammation
 - adipose tissue releases proinflammatory cytokines, including TNF- α and IL-6
 - as adipocytes enlarge, further inflammation ensues. Macrophages release inflammatory cytokines
 - activates sympathetic nervous system

Robles & Haan, 2011


Caloric Intake

- caloric restriction with adequate nutrition intake exhibits important anti-inflammatory effects
 - adipocyte reduction through caloric restriction lowers proinflammatory adipokines and cytokines
 - enhances corticosteroid production promoting anti-inflammatory effects on the body
 - increases parasympathetic tone

Robles & Haan, 2011

Obesity

The adult overweight and obesity rate for DuPage County is 56%



https://forward.dupage.org/2021/

Obesity - Study

“Association between Dietary Inflammatory Index, Dietary Patterns, Plant-Based Dietary Index and the Risk of Obesity”
05/2021

- Longitudinal cohort study in South Australia
- 787 participants
- Data collected initially in '99 - '03, then '04 - '06, then '08 - '10 using computer-assisted telephone interview, self-administered questionnaire, and clinic exam. Then in '15 a follow-up study using a self-completed online or postal survey was collected

Wang et al., 2021

Obesity - Study

BMI and a 12-month dietary intake assessment was used to compute:

- dietary inflammatory index (DII)
- plant-based dietary index (PDI)
- identify dietary patterns

Obesity - Study

A *lower* risk of obesity was associated with:

- anti-inflammatory diet (lower DII score)
- diet quality
- prudent dietary pattern
- overall plant-based diet
- healthy plant-based diet

A *higher* risk of obesity was associated with:

- pro-inflammatory diet (higher DII score)
- Western dietary pattern
- unhealthy plant-based diet

Obesity - Study

Supplementary Table 1. Food items components for the overall PDI, sPDI and hPDI.

| Plant food groups | |
|----------------------------------|--|
| Healthy | Whole-grain bread, oat bread, crispbread, cornmeal, whole-grain breakfast cereal |
| Whole grains | Apple, pear, orange, mandarin, kiwi, banana, plum, peach, apricot, strawberry, cantaloupe, blackberry, grapes, mixed fruits |
| Fruits | Carrot, tomato, lettuce, cabbage, cucumber, pepper, garlic, asparagus, spinach, cauliflower, broccoli, fennel, radish, asparagus, radishes, mixed vegetables |
| Vegetables | Nuts, seeds |
| Nuts | Beans, peas |
| Legumes | Olive oil, sunflower oil, linseed oil, flaxseed oil |
| Vegetable oils | Tea, coffee, decaffeinated coffee |
| Tea and coffee | Less healthy |
| Less healthy | Orange juice, apple juice, carrot juice, grape juice, cherry juice, pineapple juice, milk/cream juice |
| Fruit juices | White bread, wheat, rice, pasta, pancakes |
| Refined grains | Pastries, pizza products |
| Pastries | Sugar-sweetened beverages |
| Sugar-sweetened beverages | Sweets and desserts |
| Sweets and desserts | Sugar, honey, jams and jellies, chocolates, candies, creams without chocolate, spring rolls, other snacks, biscuits |
| Animal food groups | |
| Animal fat | Butter, full-fat, other animal fat |
| Dairy | Milk, mixed milk drinks, cream, yogurt, curd, cheese, cream cheese, ice cream |
| Eggs | Eggs |
| Fish or seafood | Fish, seafood |
| Meat | Beef, calf, pork, lamb, horse, goat, poultry, rabbit, game, processed meat |
| Miscellaneous animal-based foods | Caviar, caviar, or caviar, other fish, game |

Dietary Inflammatory Indices

Dietary Inflammatory Index (DII) - most commonly used

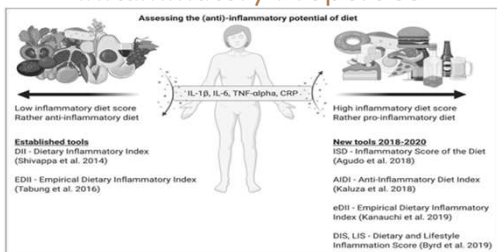
- utilizes CRP, interleukins (IL-6, IL-1 β , IL-10, IL-4), TNF- α as markers
- originally developed in 2009, it was revised in 2014
→linked 45 parameters of diet w/ raw amount of food consumed

Dietary Inflammatory Indices

Since DII was developed, more indices have come about:

- includes dietary patterns (**EDII**)
- alcohol indices and specific criteria for fat consumption (**ISD**)
- consideration of lifestyle factors (**DIS, LIS**)
- non-US populations (**AIDI-northern European**)
- food assessment w/o labs (**eDII**)

Assessing Current Diets for Anti-Inflammatory Properties



Metabolic Syndrome

Criteria (3 or more of the following):

1. waist circumference > 40 in (men)/35 in (women)
2. BP >130/85 mmHg
3. fasting triglyceride >150 mg/dl
4. fasting HDL cholesterol <40 mg/dl (men)/50 mg/dl (women)
5. fasting blood glucose >100 mg/dl or T2DM dx

→ more than 25% of the US population

Metabolic Syndrome

Metabolic Syndrome - represents a cluster of several risk factors for atherosclerosis that is proinflammatory

- abdominal obesity, atherogenic dyslipidemia, glucose intolerance, and hypertension
- lab markers including CRP, TNF- α , and interleukins (IL-6, IL-18), correlate with propensity to develop ischemic events

Metabolic Syndrome and the Gut

Diet influences and reshapes gut microbiota composition, diversity, and species richness in a time-dependent manner.

Human studies have depicted noticeable changes in gut microbiota **within 24 hr of shifting diet**

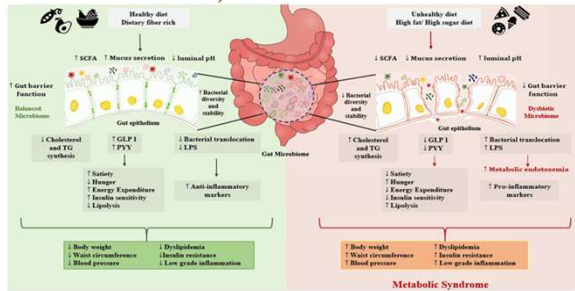
Poor Diet

- reduces microbial diversity
- a lowering of the metabolites that protect intestinal permeability
- destruction of the mucus layer leading to inflammation and metabolic diseases

Healthy diet

- increases gut barrier function and mucus secretion
- decreases the luminal pH
- reduces microbial translocation

Metabolic Syndrome and the Gut



Fiber

Dietary fiber decreases plasma cholesterol by binding to bile acids and dietary cholesterol in the intestinal lumen, resulting in reduced cholesterol absorption

Soluble* vs Insoluble fiber

- Soluble: oats, peas, beans, apples, citrus fruit, carrots, barley, psyllium
- Insoluble: whole wheat flour, wheat bran, nuts, cauliflower, green beans, potatoes

Fiber

Follow the 5:1 carb to fiber rule

- for every 5 grams of carbohydrate you eat, aim to get at least 1 gram of dietary fiber

| Nutrition Facts | |
|-------------------------------|-----|
| Serving Size 1.00 (43g) | |
| Amount Per Serving | |
| Total Fat 1g | 2% |
| Sodium 100mg | 2% |
| Total Carbohydrate 21g | 4% |
| Dietary Fiber 2g | 20% |

Fiber Influencing Inflammatory Markers

| Population | Study design | Fiber | Indicator | Sample size |
|-------------------------------------|---------------------------|-----------|--------------------------------|-------------|
| Adults (age >20 y) | NHANES, 1999–2000 | Total | C-reactive protein | 3920 |
| Diabetic women (age ~60 y) | Nurses' Health Study | Cereal | C-reactive protein | 902 |
| | | | TNF-α receptor 2 | |
| Adults (age 20–70 y) | SEASONS | Soluble | C-reactive protein | 524 |
| | | Insoluble | C-reactive protein | |
| Postmenopausal women | Women's Health Initiative | Soluble | IL-6; TNF-α receptor 2 | 3938 |
| | | Insoluble | IL-6; TNF-α receptor 2 | |
| Adults (age 50–71 y) | NIH-AARP study | Total | Infectious disease death | 567,169 |
| | | Total | Respiratory disease death | |
| Breast cancer (female, age 18–64 y) | HEAL study | Total | C-reactive protein | 1183 |
| Cancer-free adults | EPIC cohort | Cereal | IL-1β; IL-4; IL-5; IL-6; TNF-α | 88 |
| Adults (age 25–70 y) | EPIC cohort | Total | Inflammatory disease death | 422,717 |

Aging

Associated with low-grade inflammation called **Inflammaging**

Inflammaging is manifested by the release of a large number of inflammatory mediators that are produced to repair damage at tissue level

- pro-inflammatory cytokines: interleukins (IL-1, IL-2, IL-6, IL-8, IL-12, IL-13, IL-15, IL-18, IL-22, IL-23), TNF- α , IFN- γ
- anti-inflammatory cytokines: interleukins (IL-1Ra, IL-4, IL-10), TGF- β 1
- mediators: lipoxin A4, heat shock proteins

Aging - Study

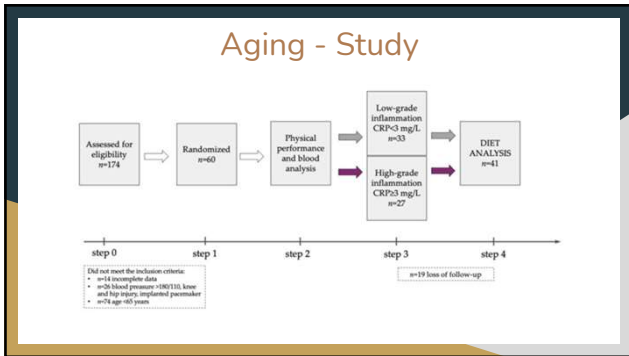
“The Association of Anti-Inflammatory Diet Ingredients and Lifestyle Exercise with Inflammaging” 10/2021

60 elderly individuals (> 65 yo) were put in two groups based on CRP levels:

- low grade inflammation (CRP <3 mg/L)
- high grade inflammation (CRP >3 mg/L)

Aging - Study

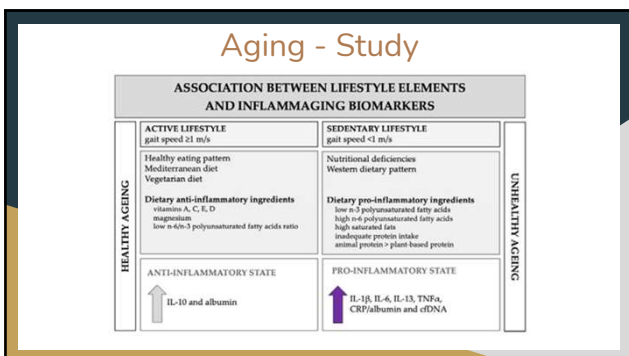
- 24-hr dietary recall was utilized for diet analysis
- Physical performance based on 6-min walk test
- Body comp analysis utilizing bioelectrical impedance method
- Labs collected including CRP, interleukins, TNF- α , and cell-free DNA (cfDNA)



Aging - Study

Results:

- Circulating interleukins IL-1 β , IL-6, IL-13, TNF α and cDNA demonstrated high concentrations in the elderly with a low 6-min walk test, confirming an impairment of physical performance by persistent systemic inflammation
- The low grade inflammation group demonstrated a lower ω -6: ω -3 ratio and higher vitamin D intake than the high grade inflammation group
- The low grade inflammation group demonstrated a significantly higher gait speed



Aging - Study

5. Conclusions

Go to: >

This study generally supports the notion that anti-inflammatory diet ingredients and physical activity sustained throughout life are critical for optimal inflammatory response in the elderly. Moreover, it shows that the analysis of inflammatory profile, including novel inflammatory markers such as CRP/albumin and cfDNA, with nutritional status and physical performance may be useful in defining healthy or unhealthy ageing (Figure 5). However, future studies are needed to determine the effectiveness of, and conditions for, various nutritional and physical intervention regimens to improve the function of the ageing immune system.

Omeegas

Polyunsaturated Fatty Acids (PUFAs)

- ω -3 and ω -6 fatty acids
 - A ω -6: ω -3 ratio >10:1 is believed to be pro-inflammatory 😞
 - When the ratio is <5:1 it has an anti-inflammatory effect

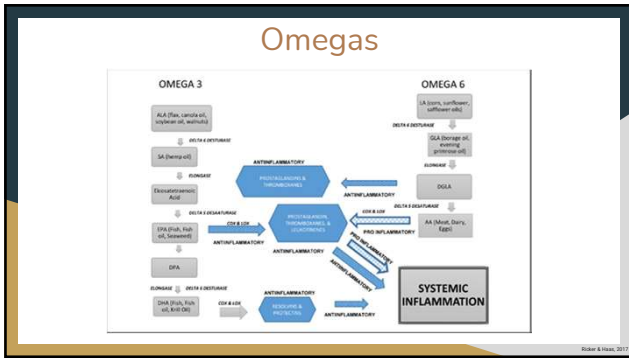
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Omega 6's (ω -6)

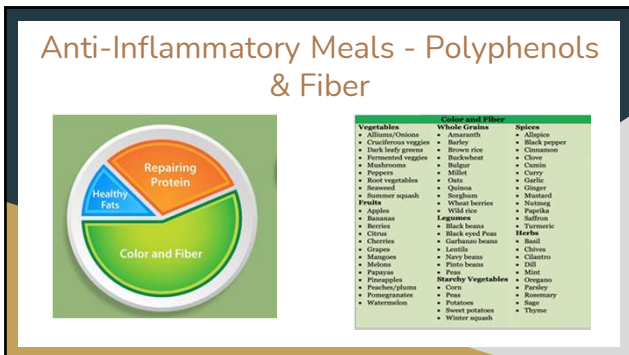
- walnuts
- pine nuts
- sunflower seeds
- sunflower oil
- grapeseed oil
- corn oil
- walnut oil
- cottonseed oil
- soybean oil
- mayonnaise
- almonds
- tofu
- vegetable shortening
- fortified foods

Omega 3's (ω -3)

- fish/seafood (salmon, mackerel, tuna, herring, sardines, anchovies)
- nuts (walnuts)
- seeds (flaxseeds, chia seeds)
- edamame
- seaweed
- algae
- plant oils (flaxseed oil, soybean oil, canola oil)
- fortified foods








Fiber

Recommended intake
Men < 50: 38 grams
Women < 50 : 25 grams

Fiber intake of the U.S population
< 1 in 10 U.S. adults meet recommendations

4 Most Common Barriers
Confusion around fiber content
Dissatisfaction with taste
Digestive distress
Intake less than perceived



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Fiber - Closing the Intake Gap

Enforce label reading
[U.S. Food and Drug Administration](#)

Encourage portion control

Utilize tracking apps when appropriate
Noom, Lose It!, MyFitnessPal

Recommend experimentation with cooking



Using Visuals and Other Guides

Posters and Bulletin Boards

- Waiting rooms, hallways, exam rooms

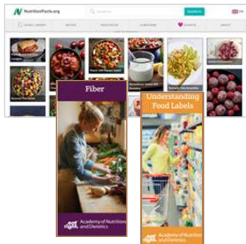
Hand-outs

Online Resources

- Clinic website, social-media
- AmericanHeartAssociation.org
- Nutritionfacts.org, eatright.org

Community Resources

- Culinary demonstrations
- Hands on cooking experiences
- Community Pantry



Anti-Inflammatory Meals – Omega 3s



| Healthy Fats | Healing Proteins |
|---|---|
| Nuts <ul style="list-style-type: none"> Almonds Brazil nuts Cashews Hazelnuts/Filberts Macadamia nuts Pecans Pine nuts Walnuts Seeds <ul style="list-style-type: none"> Chia Flax (ground) Hemp Pumpkin Sunflower Unrefined Oils <ul style="list-style-type: none"> Avocado oil Coconut oil Extra virgin olive oil Flax oil (no heat) Hemp oil (no heat) Walnut oil Other Healthy Fats <ul style="list-style-type: none"> Avocados Olive | Anti-Inflammatory Proteins <ul style="list-style-type: none"> Cold water fatty fish <ul style="list-style-type: none"> Halibut Herring Macarel Rainbow trout Salmon Sardines Tuna Beans/Legumes Nuts/nut butters Seeds/seed butters Whole soy Edamame Tofu Tempeh Natto Neutral Proteins <ul style="list-style-type: none"> Chicken Eggs Turkey Seafood Wild game Fermented dairy <ul style="list-style-type: none"> Kefir (unsweet) Yogurt (unsweet) |

Anti-Inflammatory Meals - Omega 3s

- *Essential fatty acids
- Cold-water fatty fish
- Nuts and seeds
- Plant oils
- Fortified foods
- Omega-3 dietary supplements



Dietary Supplementation of Omega 3s

How much is enough?

- Recommendations inconsistent
- National Institute of Health
 - 1.1-1.6 grams/day
- American Heart Association
 - 3 grams/day

Recommended DHA:EPA ratio

- 2021 regression analysis with 92 clinical trials
 - Ratio of 1:3 modulates CRP
- 2017 study on liver damaged mice
 - ratio of 1:2 mitigated inflammatory risk factors

Supplement Facts

| Serving Size: 2 Soft Gels Amount Per Serving | | |
|---|--------------------|----------------|
| | Amount Per Serving | % Daily Value* |
| Calories | 20 | |
| Total Fat | 2 g | 3% |
| Saturated Fat | 0 g | 0% |
| Trans Fat | 0 g | 0% |
| Total Omega 3 [†] | 1200 mg | 1 |
| EPA (Eicosapentaenoic Acid) | 400 mg | 1 |
| DHA (Docosahexaenoic Acid) | 400 mg | 1 |

*Percent Daily Values are based on a diet of other people's secrets.
[†] Daily Value not established.
 ‡ Includes EPA, DHA, and Other Omega-3s.
 Less than 1mg of Cholesterol per serving.
Ingredients: purified deep sea fish oil (from anchovies and sardines), soft gel capsule (gelatin, glycerin, water, yellow iron oxide, natural lemon flavor, D-alpha-tocopherol (antioxidant), vegetable extract or natural preservative).
 No gluten, milk derivatives, or artificial colors or flavors.

Anti-Inflammatory Diet - Caloric Restriction

Calorie Calculator

- For patients and providers

Calorie Trackers

- Can enhance awareness
- MyFitnessPal, Noom, Lose It!



Anti-Inflammatory Diet - Caloric Restriction

KEY components of sustainable caloric restriction

- Satiety supporting meals
 - Fat, Protein, Fiber
- Nutrient dense food intake
- Consistent nutrient intake
- Alternative stress relief/pleasure stimulating activities



Anti-Inflammatory Meals - A Daily Breakdown

- 2,000 calories
- 30 grams fiber
- 3 grams Omega-3s
- 1000 mg polyphenols
- # of servings
 - Whole grains-2
 - Vegetables-3.5
 - Fruit-1.5
 - Nuts-2
 - Meat/Seafood-2

| | | | |
|--|---|---|--|
| Breakfast: 1 cup cooked oatmeal (166 cal) 1/2 cup raspberries (32 cal) 1 tbsp ground flaxseed (37 cal) 1 cup almond milk (60 cal) 1 tbsp maple syrup (52 cal) Total: 347 cal | Lunch: 3 oz grilled tuna (144 cal) 1 cup mixed greens (10 cal) 1/2 cup chickpeas (134 cal) 1/4 cup red bell pepper (12 cal) 1/4 cup red onion (16 cal) 1 tbsp olive oil (120 cal) 1 tbsp lemon juice (3 cal) Total: 439 cal | Dinner: 4 oz baked turkey (160 cal) 1 cup steamed green beans (44 cal) 1/2 cup cooked quinoa (111 cal) 1/4 cup sunflower seeds (200 cal) 1 tbsp balsamic vinegar (14 cal) 1 tbsp olive oil (120 cal) Total: 649 cal | Snack 1: 1 medium banana (105 cal) 1 tbsp peanut butter (94 cal) Total: 199 cal Snack 2: 1 oz dark chocolate (170 cal) 1/4 cup cashews (196 cal) Total: 366 cal |
|--|---|---|--|

Effective Dietary Counseling

- Tailor the **modality**
- Include **clients' preferences, wishes, and expectations** during goal-setting
- Show **empathy**
- Connect to **motivation**
- Use integrated **support tools**
- Provide **recurring feedback**
- Demonstration of **self-efficacy**



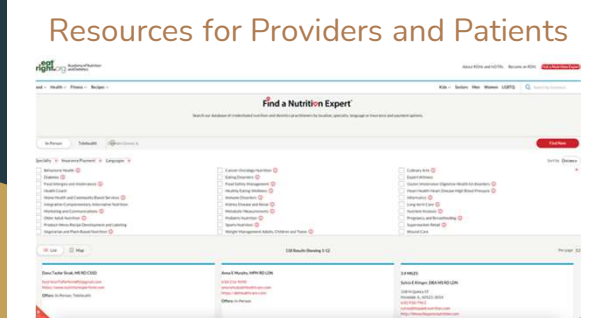
Barringer, et al., 2012

Referral Resources

Academy of Nutrition and Dietetics - eatright.org

- Find a Nutrition Expert
 - 1:1 and Group Counseling
 - Grocery Shop Tours
 - Pantry Makeovers
 - Culinary / Meal Prep Workshops

Resources for Providers and Patients



Evolution of Inflammation in Medicine

Evolving Process

- inflammatory markers
- how we conduct research (difficulty assessing, compliance issues)
- new ways to assess diets

→ *Disease Specific Guidelines*

Anti-Inflammatory Diet

- The healthy properties cannot be limited to any single nutrient, food or food component, rather an entire meal pattern or lifestyle.
- This diet represents a behavioral model, a “way of life”, that can ensure longer life expectancy and improve quality of life itself.

© Swank et al., 2017

Questions?



Anti-Inflammatory Meal Plan Handout

Academy of Nutrition and Dietetics - eatingLight.org
Find a Nutrition Expert Resource

Anti-inflammatory Meal Plan

| Meal | Breakfast | Lunch | Dinner | Snack |
|--------|--|---|--|---------------------------------------|
| Meal 1 | 1/2 cup oatmeal, 1/2 cup blueberries, 1/2 cup almond milk, 1/2 tsp honey | 1/2 cup quinoa, 1/2 cup chickpeas, 1/2 cup spinach, 1/2 cup tomatoes, 1/2 cup olive oil, 1/2 cup lemon juice, 1/2 cup feta cheese | 1/2 cup salmon, 1/2 cup quinoa, 1/2 cup broccoli, 1/2 cup carrots, 1/2 cup olive oil, 1/2 cup lemon juice, 1/2 cup feta cheese | 1/2 cup almonds, 1/2 cup apple slices |
| Meal 2 | 1/2 cup oatmeal, 1/2 cup blueberries, 1/2 cup almond milk, 1/2 tsp honey | 1/2 cup quinoa, 1/2 cup chickpeas, 1/2 cup spinach, 1/2 cup tomatoes, 1/2 cup olive oil, 1/2 cup lemon juice, 1/2 cup feta cheese | 1/2 cup salmon, 1/2 cup quinoa, 1/2 cup broccoli, 1/2 cup carrots, 1/2 cup olive oil, 1/2 cup lemon juice, 1/2 cup feta cheese | 1/2 cup almonds, 1/2 cup apple slices |
| Meal 3 | 1/2 cup oatmeal, 1/2 cup blueberries, 1/2 cup almond milk, 1/2 tsp honey | 1/2 cup quinoa, 1/2 cup chickpeas, 1/2 cup spinach, 1/2 cup tomatoes, 1/2 cup olive oil, 1/2 cup lemon juice, 1/2 cup feta cheese | 1/2 cup salmon, 1/2 cup quinoa, 1/2 cup broccoli, 1/2 cup carrots, 1/2 cup olive oil, 1/2 cup lemon juice, 1/2 cup feta cheese | 1/2 cup almonds, 1/2 cup apple slices |

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