Under the Spotlight: Anti-Inflammatory Diet

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Disclosure

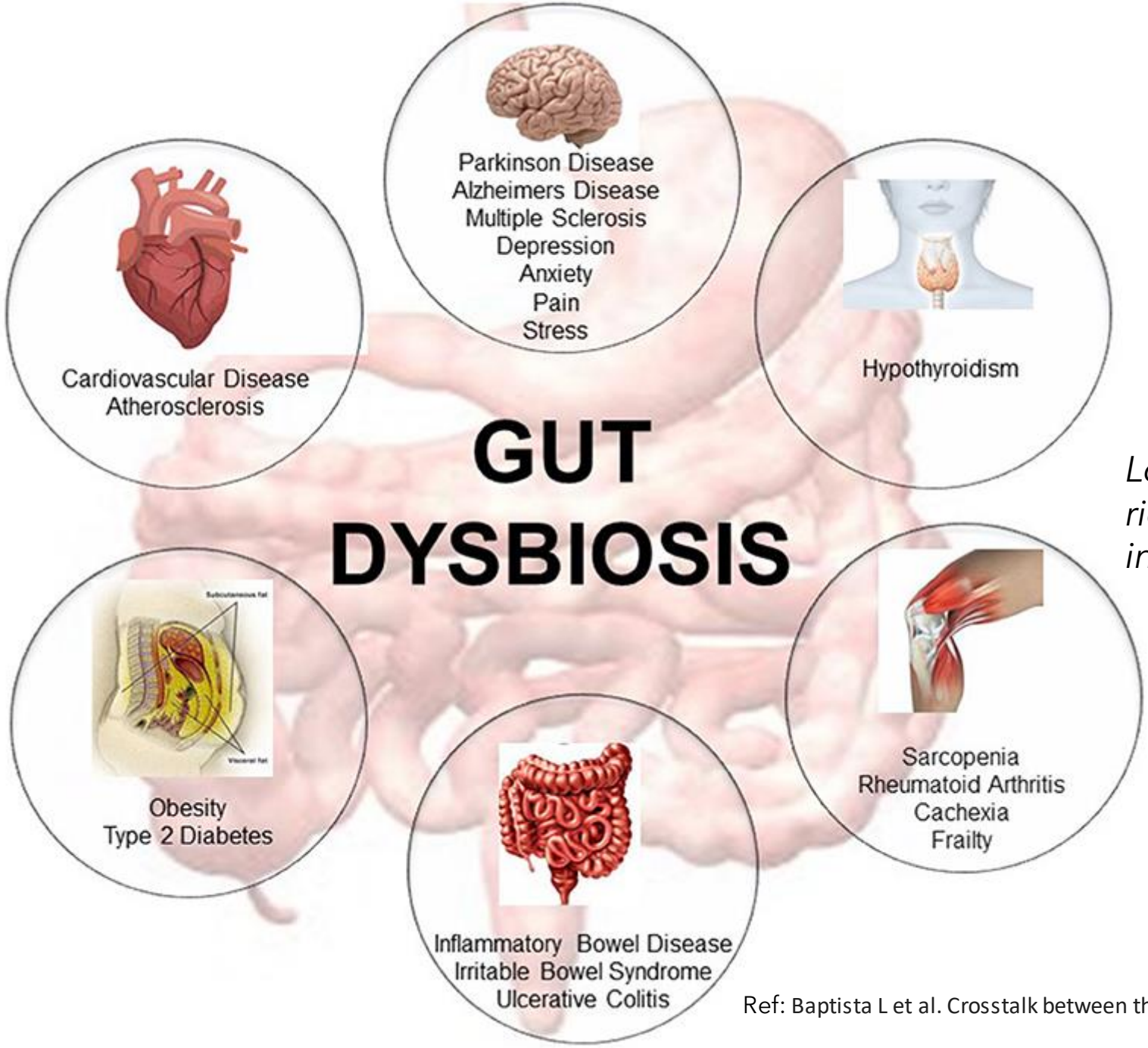
- No conflict of interest.

Gut-Brain Axis and the Gut Microbiome

- The gut–brain axis (CNS, autonomic, enteric nervous system, and peripheral nerves) , establishes an interdependent relationship between **host-microbe** and **environment**.

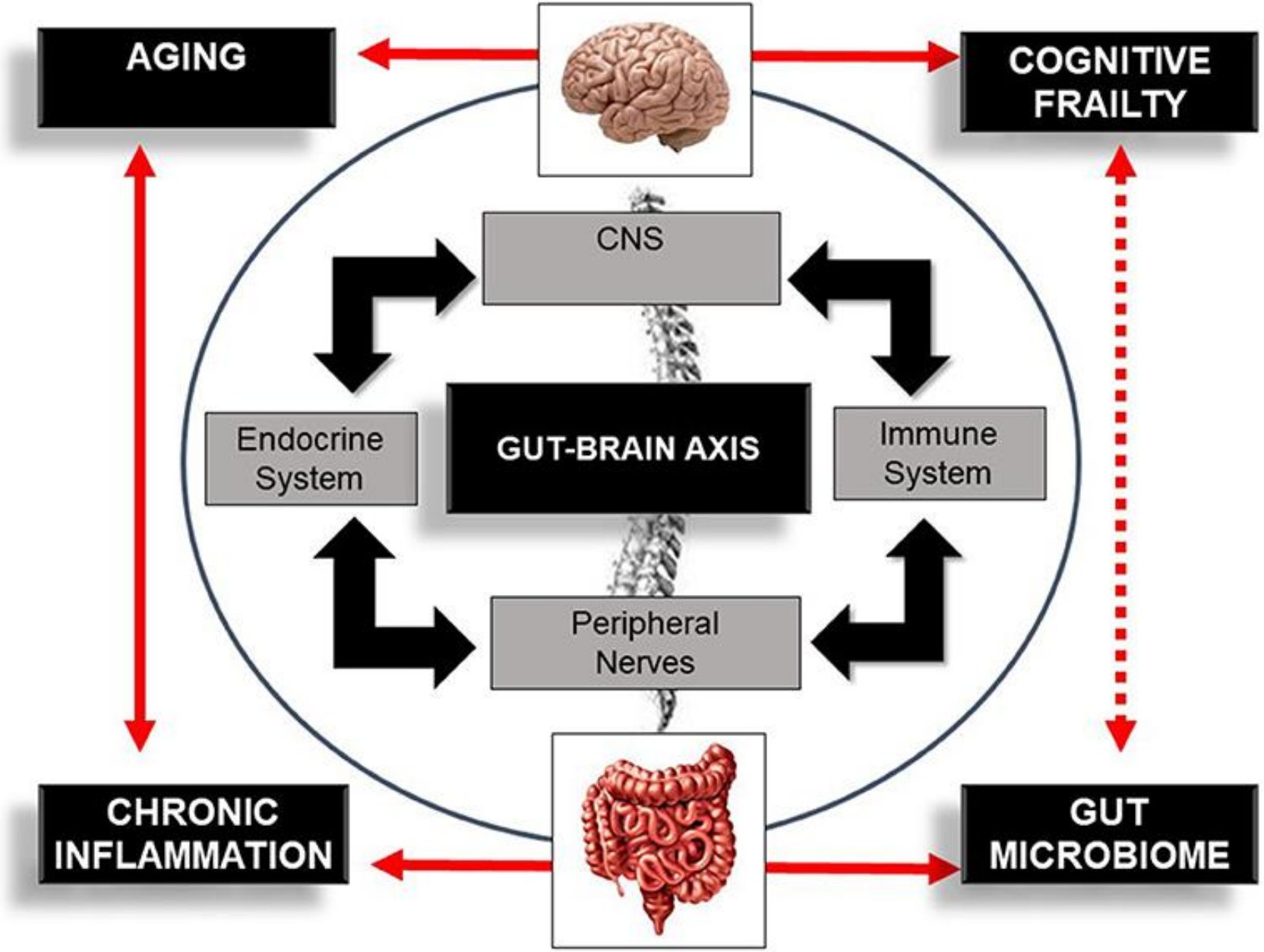
- Modulates host immune function, metabolic balance, and resilience to infection.

Ref: Baptista L et al. Crosstalk between the gut microbiome. Frontiers in Nutrition 2020



Loss of microbe species richness and interindividual variability

Ref: Baptista L et al. Crosstalk between the gut microbiome. Frontiers in Nutrition 2020



Ref: Baptista L et al. Crosstalk between the gut microbiome. Frontiers in Nutrition 2020

- Lipids- affect gut permeability as major constituents of cell membranes and influence the gut microbiome.

- Lipids also regulate multiple cell functions through intercellular and intracellular signaling mediators in the brain and the enteric system.

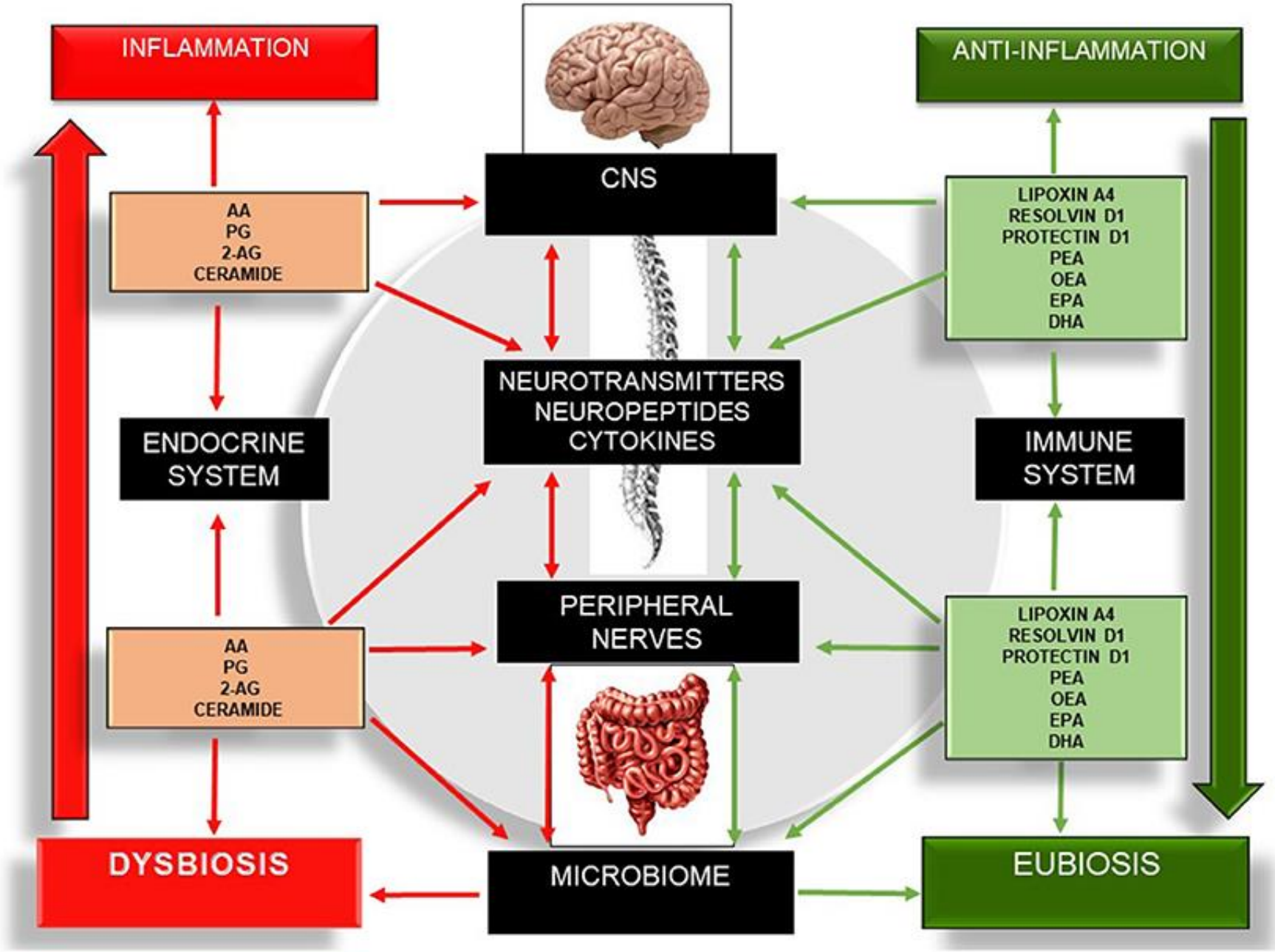
Ref: Baptista L et al. Crosstalk between the gut microbiome. Frontiers in Nutrition 2020

- These lipid signaling mediators a.k.a bioactive lipids -> bloodstream-> distant organs.

- Exert either pro or anti-inflammatory actions on the microbiome, immune system and CNS.

- Diet influences formation & function of bioactive lipids via availability of ω-6 and ω-3 PUFA precursors.

Ref: Baptista L et al. Crosstalk between the gut microbiome. Frontiers in Nutrition 2020



2-AG, 2-Arachidonoylglycerol;
DHA, Docosahexaenoic Acid;
EPA, Eicosapentaenoid Acid;
OEA, Oleoilethanolamide;
PEA, Palmitoylethanolamine;
PG, Prostaglandins.

Ref: Baptista L et al. Crosstalk between the gut microbiome. Frontiers in Nutrition 2020

Environment dominates over host genetics in shaping human gut microbiota

- Genotype and microbiome data from 1,046 healthy individuals with several distinct ancestral origins who share a relatively common environment.

Ref: Rothschild et al. *Nature* March 2018

- Significant similarities in the compositions of the microbiomes of genetically unrelated individuals who share a household.

- >20% of the inter-person microbiome variability is related to diet, drugs and anthropometric measurements.

Ref: Rothschild et al. *Nature* 2018 March

- Microbiome data significantly improve the prediction accuracy for many traits, eg. glucose and obesity measures.

- Microbiome alterations -> better clinical outcomes in genetically diverse patient populations.

Ref: Rothschild et al. *Nature* 2018 March

"Good news.
Your cholesterol has stayed the same,
but the research findings have changed."

https://www.rd.com/list/medical-cartoons

Anti-Inflammatory Diet in Rheumatoid Arthritis (ADIRA) – RCCT indicating effects on disease activity.

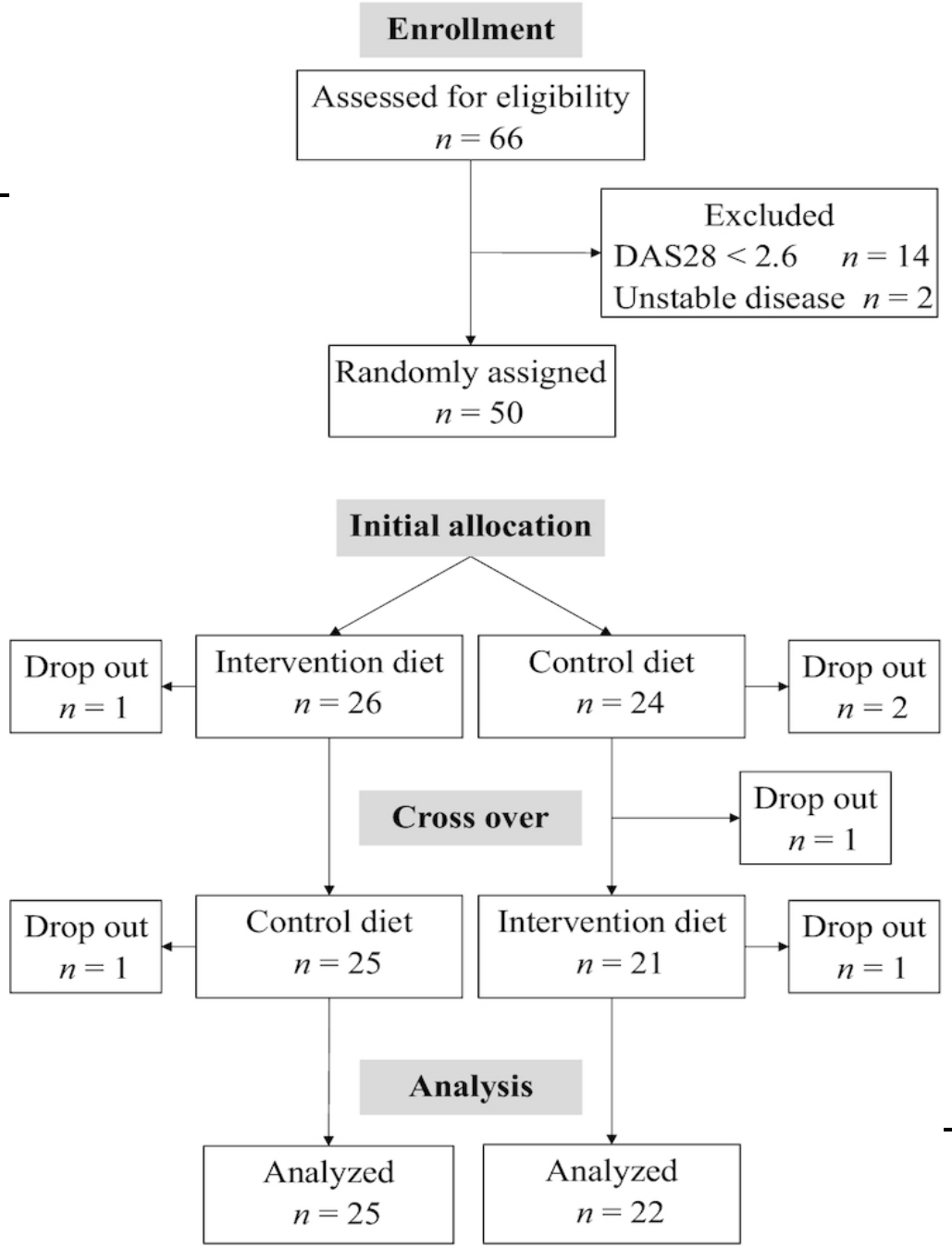
- 50 patients with RA were randomly assigned to an intervention diet with suggested anti-inflammatory foods

Ref: Vadell et al (ADIRA)-a RCCT indicating effects on disease activity. Am J Clin Nutr. 2020 Jun

- *v/s* control diet - similar to the general dietary intake in Sweden x 10 weeks.

- After a 4-mo washout period participants switched diets.

Ref: Vadell et al (ADIRA)-a randomized, controlled crossover trial indicating effects on disease activity. Am J Clin Nutr. 2020 Jun



Ref: Vadell et al (ADIRA)-a randomized, controlled crossover trial indicating effects on disease activity. Am J Clin Nutr. 2020 Jun

- **Primary outcome** –change in DAS28-ESR in pts completing >=1 diet period - no sig difference (n=47; *p0.16*).

- Pts completing both diet periods, DAS28-ESR sig decreased (n=44; *p 0.04*).

Ref: Vadell et al (ADIRA)-a randomized, controlled crossover trial indicating effects on disease activity. Am J Clin Nutr. 2020 Jun

Design of an Anti-Inflammatory Diet (ITIS diet) for Patients with RA

- Designed a diet that includes a high intake of anti-inflammatory ingredients.

- Feedback from highly motivated patients

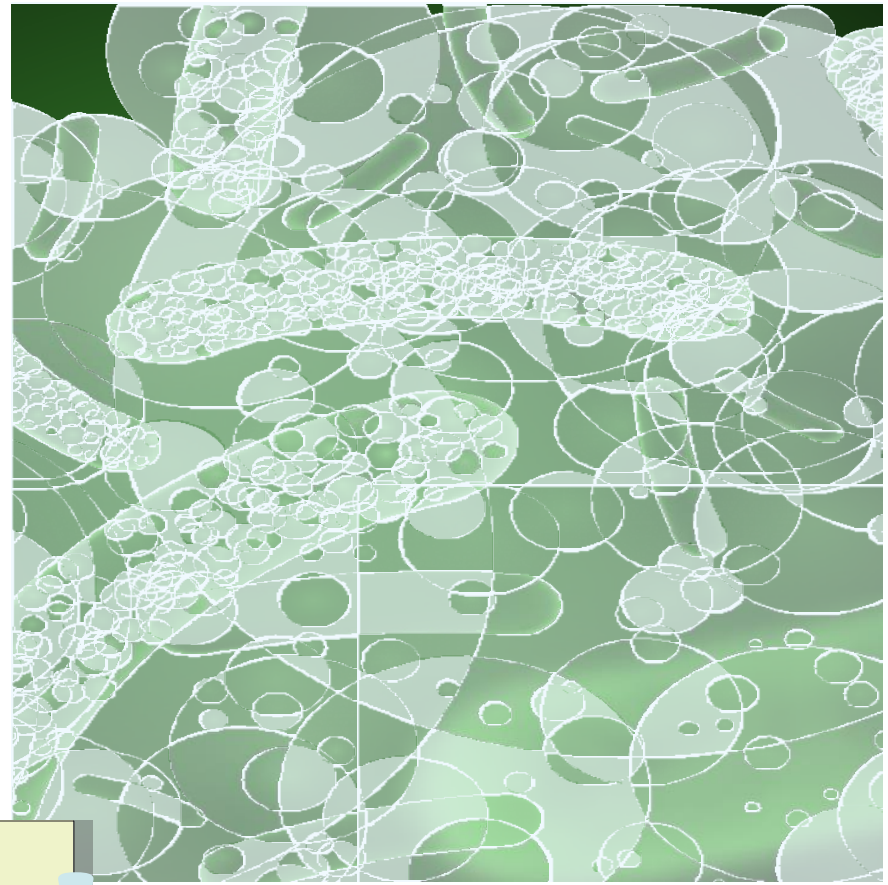
Ref: Contemp Clin Trials Commun. 2020 Mar

https://www.arthritis.org/liveyes/premium/good-gut-health

Ref: Contemp Clin Trials Commun. 2020 Mar

The Microbiome and Why It Matters

The gut microbiome plays an integral part in the well-being of people with arthritis. Learn how you can benefit from good gut health.



Balance is often the key to a happy, healthy life, and when it comes to your gut, that old adage couldn't be more accurate. Like a garden that requires the right balance of nutrients to produce the healthiest plants, a healthy, balanced gut microbiome – the ecosystem of trillions of microorganisms inhabiting the digestive tract – may help stabilize the immune system. The gut microbiome is associated with many health and disease impacts in the body, including overall health and inflammatory forms of arthritis.

In addition to the gut, microbes inhabit every part of the body, creating different ecosystems in various areas, such as the nasal microbiome and the skin microbiome. Each one interacts with the immune system and greatly affects how it responds. When it is out of balance – generally from illness, poor diet, antibiotics, smoking, stress or obesity – the immune system can also get out of whack. This "dysbiosis" is an imbalance in the types and numbers of microbes with less microbial diversity overall, which may let the balance of harmful versus helpful microbes tip in the unhealthy direction. When this happens, chronic low-grade inflammation and disease may follow, according to Thomas W. Buford, PhD, associate professor and endowed scholar in the Department of Medicine at the University of Alabama at Birmingham. Dysbiosis has been linked to autoimmune diseases including rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS) and systemic lupus erythematosus.

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To learn more about the benefits of the gut microbiome from top experts in the field, tune in to the Arthritis Foundation's Live Yes! With Arthritis podcast episode: Microbiome, Gut Health & Arthritis.

The ITIS Diet

They spent a year designing what she calls the ITIS diet*, a plant-based diet supercharged with anti-inflammatory foods and herbs that may improve gut health and arthritis symptoms.

There is no evidence that this diet changes the microbiome, which is very difficult to do, Dr. Guma says. "It might need months of diet to actually make a meaningful change." It may help reduce inflammation and symptoms, though.

The diet includes many things the standard Mediterranean doesn't, including a daily homemade green drink (green vegetables and fruit); a high daily intake of monounsaturated fatty acids (MUFA); daily green tea and more. It also excludes some things the Mediterranean diet allows, such as gluten and nightshade vegetables, which may worsen arthritis symptoms in some people.

In her study, 22 highly motivated RA patients followed the ITIS diet for two weeks while continuing their prescribed medications. Half experienced a 50% improvement in pain and swelling as well as in subjective measures such as fatigue, often in three or four days. A few patients went into complete remission. Even the 50% who did not show improvements felt better and had more energy and less fatigue, Dr. Guma says, but it's not clear why some didn't have less pain and swelling, too.

Dr. Guma emphasizes that she's not suggesting the diet can replace arthritis drugs. It had several important limitations: There was no control group for comparison. And it's unknown if ITIS has long-term benefits. (In studies of the Mediterranean diet, the benefits disappeared when people stopped following it.) Dr. Guma plans to conduct longer trials with more participants.

**Funded by the Center for Integrative Health at University of California, San Diego*

Staples of the ITIS Diet

MAIN RECOMMENDATIONS (WHAT/WHAT FOR)	BASED ON (WHY)	DIET STRATEGIES (HOW)
Lower the omega-6/omega-3 polyunsatu- rated fatty acids (PUFA) ratio to 2:1.	A low omega-6/omega-3 PUFA ratio reduces inflamma- tion and improves autoimmunity symptoms.	The diet must contain fatty fish twice per week and daily intake of omega-3 sources, like chia seeds and flaxseed oil.
Increase intake of monounsaturated fatty acids (MUFA).	MUFA have a beneficial effect in rheumatoid arthritis (RA).	Daily intake of MUFA-rich nuts, seeds and vegetables
Decrease intake of pro-inflammatory fatty acids (FA) such as trans-FA and saturated FA (present in dairy products, red meat and processed foods).	Industrially produced trans-FA increase inflammatory markers and saturated FA increase inflammation.	Avoid pre-cooked food, red meat and processed meat. Cook by baking, boiling or vapor. Avoid frying for long periods because it modifies PUFA to trans-FA.
High intake of prebiotics	Dietary fiber, whole-grain complex carbohydrates and sugar alcohols present in fruits are prebiotics that support healthy microbiome and increase short-chain fatty acid production, improving immunity.	Daily green leafy vegetables, fruits and homemade green juice (prebiotic source). Promote whole grains (prebiotic source) and avoid refined flours.
Daily intake of probiotics	Probiotics reduce levels of pro-inflammatory cytokines and improve disease activity in RA.	Daily yogurt (a brand that contains *Lactobacillus Casei* among other species) and miso (probiotic source)
Help digestion of large proteins in the gut	Fiber consumption and enzymatic fruits will help protein digestion. Bromelain and papain were shown to have an anti-inflammatory effect as well. Large proteins in dairy products are not completely digested and can feed proteolytic bacteria, resulting in the production of pro-inflammatory metabolites.	Daily enzymatic fruit (pineapple, mango and papaya are sources of bromelain, papain and other proteolytic enzymes). Increase fiber intake. Substitute plant-based milks (almond, rice, coconut) for dairy.
Condiment with anti-inflammatory spices	Turmeric, black pepper and ginger have antioxidant and anti-inflammatory actions. Black pepper increases bioavailability of curcuma in turmeric.	Turmeric and black pepper should be used at the same time.

Shopping for Your Microbiome

Omega-3 polyunsaturated fats (Omega-3 PUFA)
- ☐ Sardines
- ☐ Tuna
- ☐ Chia seeds
- ☐ Flaxseed oil
- ☐ Linseed oil

Monounsaturated fatty acids (MUFA)
- ☐ Tree nuts (walnuts)
- ☐ Avocado
- ☐ Olive oil
- ☐ Sesame seeds
- ☐ Tahini

Prebiotics
- ☐ Green leafy veg (arugula, lettuce, spinach, broccoli, zucchini, green beans, parsley)
- ☐ Fruits (pear, apple, banana)
- ☐ Whole grains

Probiotics
- ☐ Plain yogurt (no sugar) with *Lactobacillus Casei* (such as Chobani brand)
- ☐ Miso

Enzymatic fruits
- ☐ Pineapple
- ☐ Mango
- ☐ Papaya

Spices
- ☐ Turmeric
- ☐ Black pepper
- ☐ Ginger
- ☐ Cinnamon

Plant-based milks
- ☐ Almond
- ☐ Rice
- ☐ Coconut
- ☐ Oat

Phytochemical-rich vegetables
- ☐ Garlic
- ☐ Onion
- ☐ Pumpkin
- ☐ Zucchini
- ☐ Carrot
- ☐ Green leafy veggies

Healthy proteins
- ☐ Red beans
- ☐ White beans
- ☐ Lentils
- ☐ Garbanzos
- ☐ Poultry
- ☐ White fish
- ☐ Tofu
- ☐ Eggs

Whole grains
- ☐ Rye
- ☐ Corn
- ☐ Oats
- ☐ Quinoa
- ☐ Corn tortillas

Sweetener
- ☐ Honey

Coffee replacement
- ☐ Green tea

Antioxidant-rich foods
- ☐ Vegetables (minus nightshades)
- ☐ Fruits
- ☐ Strawberries
- ☐ Apple cider vinegar
- ☐ Lemon
- ☐ Grapes
- ☐ Lime

Other
- ☐ Vanilla extract
- ☐ Celery
- ☐ Cucumber

Click here for a mobile-friendly version of the microbiome shopping list.

A Day's Menu From the ITIS Diet

7-8 A.M. SMOOTHIE

Grapes, celery, spinach, cucumber, lime and water

7-8 A.M. BREAKFAST

1-2 tablespoons of oats with oat, almond, rice or other plant-based milk. Add berries (optional).
Green tea infusion.

10-11 A.M. SNACK

Plain yogurt (Chobani, no sugar added)

12-1 P.M. LUNCH

OPTION 1: Salad (generous plate)
OPTION 2: Grains with vegetables
OPTION 3: Legumes with vegetables

4 P.M. SNACK

Mango, papaya, pineapple, apple, pear or banana + 4 walnuts

6-7 P.M. DINNER

OPTION 1: Vegetable soup + protein (eggs, poultry, fish, tofu)
OPTION 2: Miso soup + baked/steamed/grilled vegetables + protein
OPTION 3: Salad + protein

Baseline microbiome and metabolome are assoc. with response to ITIS diet in an exploratory trial in patients with RA

- Interventional study – 20 RA pts
- Inclusion criteria- RA pts w/ no changes in Rx in the last 3 months.

Ref: Coras R et al . Clin Transl Med . 2022 Jul

- Pain improved from 3.89 ± 1.9 before v/s 2.45 ± 2.4 after diet ($p < .01$)

- No significant change in BMI. Although pts w/ BMI ≥ 30 had higher disease activity, scores decreased in all patients.

- Pts that reached remission had lower DAS28CRP.

Ref: Coras R et al . Clin Transl Med . 2022 Jul

Controlled trial of fasting and one-year vegetarian diet in RA

- The effect of fasting followed by one year of a vegetarian diet was assessed in a single blind RCT.

Ref: Kjeldsen-Kragh J et al Controlled trial of fasting and one-year vegetarian diet in RA *Lancet 1991*

- 27 patients - 4 week stay at a health farm.
- Initial 7–10-day subtotal fast foll by individually adjusted gluten-free vegan diet x3.5 months.
- Control group of 26 patients - 4 weeks at a convalescent home but ate an ordinary diet.

Ref: Kjeldsen-Kragh J et al Controlled trial of fasting and one-year vegetarian diet in RA *Lancet 1991*

- After 4 weeks at the health farm the diet group showed a sig. improvement in # of tender joints, # of swollen joints, pain score, duration of morning stiffness, grip strength, ESR, CRP, WBC count, and a HAQ score.

- *Benefits in the diet group were still present after 1 year*

Ref: Kjeldsen-Kragh J et al Controlled trial of fasting and one-year vegetarian diet in RA *Lancet 1991*

Key Points

- A *balanced* approach is key.
- *Increase* PUFA and MUFA intake.
- *Daily intake* of pre and probiotics.

https://www.rd.com/list/daily-life-cartoons

- *Decrease* pro-inflammatory FAs- trans fats and saturated fats (dairy products, red meat and processed foods.

- *Add* condiments with anti-inflammatory properties.

https://www.rd.com/list/diet-cartoons/

Thank you

https://www.rd.com/list/daily-life-cartoons