

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 Gut-Arthritis Connection

Evidence suggests that autoimmune diseases may develop when microbes in the gut, mouth or skin – sometimes all three – send the wrong signals to the immune system.

Recently, Chinese researchers found that people with AS had much higher levels of an intestinal fungus called Ascomycota and lower levels of the fungus Basidiomycota than did those without AS. People with <u>inflammatory bowel disease</u> (IBD) - a group of disorders, including Crohn's disease and ulcerative colitis – have a similar pattern. About 10% of people with AS also have IBD, suggesting the two diseases may be linked to the same inflammatory process. In the United States, researchers found that women with lupus had five times as much of the gut bacteria Ruminococcus gnavus (RG) as healthy women did. Those with severe symptoms or the related kidney disease lupus nephritis had even more. The researchers suspect that RG actually causes lupus nephritis. People with IBD and AS also have too much of these bacteria, suggesting another link between the microbiome and autoimmune conditions.

The gut connection is also strong in RA. For example, studies of people with early RA show their microbiota composition is often less healthy than those without RA.



"One explanation for what might be happening is the 'leaky gut' hypothesis, in which the gut becomes more permeable, and fragments of these microbiota escape into the bloodstream," Buford says. "There, the immune system recognizes them as foreign and responds with inflammation that can invade joint tissues."

But what exactly is the link? Is dysbiosis a cause or an effect of disease? Veena Taneja, PhD, an

associate professor of immunology at Mayo Clinic in Rochester, Minnesota, echoes many other researchers: "It's clear that gut [microbes] play a significant role in immune regulations and that alterations in [microbiome] composition cause an abnormal immune response," she says. But an exact cause is still unknown.

Taneja thinks doctors will treat disease in the future using "microbes derived from the person's own gut."

How to Get Good Gut Health

Experts agree that the best way to cultivate the proper balance of gut microbiota is through food, managing stress and getting regular exercise and restorative sleep. Certain foods help feed microbes (prebiotics), while others contain healthy microorganisms (probiotics), so consuming a healthy, diverse diet that includes both will contribute to a healthy microbiome. Probiotic and prebiotic supplements may also help boost levels of healthy microorganisms, at least temporarily, but food sources are the best choices for the long-term.

What you eat can greatly encourage or inhibit the growth of certain types of gut bacteria, increase or decrease overall diversity and influence metabolites the microbes produce, which are key players in activating inflammation. The Mediterranean diet has been shown to have anti-inflammatory effects for arthritis and related conditions such as heart disease and diabetes. Scientists trace its benefits in part to its positive effect on the microbiome.

"We know the Mediterranean diet is good for patients with rheumatoid arthritis," says Monica Guma, MD, PhD, rheumatologist and researcher at the University of California, San Diego. "But there also might be something better." Something like the diet she and her colleagues designed.



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 longterm 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 polyunsaturated 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 a daily intake of omega-3 sources, like chia seed 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 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.	

Staples of the ITIS Diet

MAIN RECOMMENDATIONS

(WHAT/WHAT FOR)	BASED ON (WHY)	DIET STRATEGIES (HOW)	
Eliminate salt.	High salt intake has been related to autoimmunity.	Lower salt intake by eliminating precooked food.	
Substitute vegetables with potential anti- inflammatory properties for solanaceae (nightshade) vegetables.	Solanaceae vegetables contain glycoalkaloids. Glycoalkaloids have been reported to affect intestinal permeability. Vegetables with high content of phytochemicals were suggested to have anti-inflammatory properties.	Avoid the consumption of nightshade vegetables and increase consumption of phytochemical-rich vegetables.	
Decrease consumption of red meat.	It contains high levels of choline, which is the precursor of the inflammatory metabolite trimethylamine N-oxide (TMAO) and saturated FA.	Introduce healthy proteins like legumes, poultry and white fish, two to three days a week each. Avoid red meat.	
Reduce consumption of gluten.	Gluten has been associated with inflammatory states. Pseudocereals and whole grains reduce inflammation.	Replace refined wheat with whole grains.	
Avoid sugars, sugary foods and sugary beverages.	Sugary foods and beverages are linked to obesity, microbiome changes and low-grade inflammatory state.	Substitute honey for sugar. Avoid soda and juices.	
Substitute green tea for coffee.	Green tea contains polyphenols which decrease pro- inflammatory cytokines in animal and in vitro models of RA.	Drink green tea daily.	
Increase the intake of antioxidants, phytochemicals, vitamins and flavonoids.	Antioxidants, phytochemicals, flavonoids and vitamins were suggested to have anti-inflammatory properties.	Increase consumption of vegetables, fruits, whole grains and apple cider vinegar, and add a daily homemade green juice made of fruits and green vegetables.	

Shopping for Your Microbiome

Omega-3 polyunsat-	Probiotics	Phytochemical-rich	Sweetener
urated fats (Omega-3 PUFA)	 Plain yogurt (no sugar) with Lactobacillus Casei 	vegetables ☐ Garlic	□ Honey
□ Sardines	(such as Chobani brand)		Coffee replacement
□ Tuna	□ Miso	Pumpkin	☐ Green tea
□ Chia seeds		□ Zucchini	
☐ Flaxseed oil	Enzymatic fruits	□ Carrot	Antioxidant-rich foods
☐ Linseed oil	□ Pineapple□ Mango	□ Green leafy veggies	□ Vegetables (minus— nightshades)
Monounsaturated fatty	□ Papaya	Healthy proteins	☐ Fruits
acids (MUFA)		□ Red beans	Strawberries
□ Tree nuts (walnuts)	Spices	□ White beans	Apple cider vinegar
□ Avocado	☐ Turmeric	□ Lentils	□ Lemon
□ Olive oil	Black pepper	□ Garbanzos	□ Grapes
☐ Sesame seeds	☐ Ginger	□ Poultry	□ Lime
□ Tahini	☐ Cinnamon	☐ White fish	
		□ Tofu	Other
Prebiotics	Plant-based milks	□ Eggs	□ Vanilla extract
☐ Green leafy veg (arugula,	□ Almond		─ □ Celery
lettuce, spinach, broccoli,	□ Rice	Whole grains	□ Cucumber
zucchini, green beans,	□ Coconut	□ Rye	
parsley)	□ Oat	□ Corn	
□ Fruits (pear, apple,			Click <u>here</u> for a mobile-
banana)		□ Quinoa	friendly version of the

foods

microbiome shopping list.

□ Corn tortillas

Whole grains

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



It's GREAT To Meet You

We're so excited to have you in our community and can't wait to help you Live Your Yes!

Helpful Resources

To get started on your personal journey, we hope you'll take advantage of some of the many tools and resources designed for you. Here are a few to get you started.

- ▶ Join a Live Yes! Connect Group or the Online Community today to make connections and get information and resources to help you manage your pain.
- ▶ Have questions? Our licensed clinical staff is available to you to provide **one-on-one personal support**.
- A variety of tools are accessible online to help you reduce pain, promote your independence and live your best life.
- Ready to connect locally? Check out programs and events in your area.

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