

Please repeat once before proceeding: **He Can Do It, She Can Do It, I Can Do It!**

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In Search of Best Probiotic: Part 4 *Lactobacillus plantarum*

In Search of Best Probiotics

Your Ticket to Exuberant Health for the Next 5 Years

Bacillus subtilis

Bacillus subtilis is a type of bacteria that has a rod-like shape and a positive reaction to a staining technique called Gram stain. It is found in the gut microflora, which are the communities of microbes that inhabit the digestive tract, of healthy children and adults. It belongs to a group of bacteria called Firmicutes and is also found in the soil and the roots of plants. It forms resistant spores, which are dormant forms of bacteria that can survive harsh conditions, to increase its shelf-

life and survival rate. Many studies have shown that *Bacillus subtilis* can improve



Ike Kim
Editor

health by producing substances that kill harmful microbes, enzymes that help digest food, and micronutrients that are essential for the body. It also enhances the structure and function of the intestines and prevents a disease called necrotic

enteritis, which causes inflammation and death of intestinal tissue, in animals. It is often used in animal farming. Clinical trials, which are studies that test the effects of a treatment in humans, have shown that *B. subtilis* is safe and beneficial when taken as a dietary supplement. The FDA, which is the agency that regulates food and drugs in the US, considers *B. subtilis* and other *Bacillus* species to be “generally regarded as safe”. *B. subtilis* is widely used in biotechnology and produces up to

60% of commercial enzymes, which are molecules that speed up chemical reactions. *B. subtilis* is also a source of chemicals, enzymes, and antimicrobial



materials that can be used for various purposes. This remarkable bacterium produces seven different antibiotics and is replacing virginiamycin, which is a standard antibiotic that is similar to pristinamycin and quinupristin/dalfopristin and is used in about 70% of poultry production. Virginiamycin is being banned or restricted in South Korea, the US, and the European Union because of the increasing concern about antimicrobial resistance and food safety. Antimicrobial resistance is when microbes become resistant to antibiotics and cause infections that are hard to treat.

Furthermore, Rhayat et al. reported the effect of *Bacillus subtilis* strains on the intestinal barrier function and inflammatory response, which are the

processes that protect the gut from harmful substances and infections, in a scientific journal called *Frontiers in Immunology* in 2019. One of their findings was that a specific *Bacillus subtilis* strain, called *Bs 29784*, improved the intestinal barrier function under normal conditions by increasing the expression of tight junction proteins in chickens. Tight junction proteins are molecules that help the cells in the intestine stick together and prevent leaks.

Immunomodulatory Effects

Ali S et al studied the effect of *Bacillus subtilis*-fermented soybean extract, which is a product made by using a type of bacteria to ferment soybeans, on the inflammation and immune responses of mouse cells. They exposed the cells to the extract for 21 days and then stimulated them with LPS, which is a substance that causes inflammation. They measured the expression of proinflammatory cytokines, which are molecules that promote inflammation, and found that the extract reduced their expression. They also measured the expression of CD18+, CD4+, and CD8+ T cells, which are types of immune cells that fight infections, and the expression of IL-2, IL-4, and IFN- γ , which are molecules that regulate immune responses. They found that the extract increased their expression. The results were published online in *Food Technology*, a scientific journal, on November 23rd, 2022.

Risk of Bacteremia with *Bacillus subtilis* in Children Undergoing Chemotherapy

In a study published in the electronic edition of the Journal of Infection and Chemotherapy in March 2023, Ayagi R et al reported that eating natto, which is a fermented soybean product, is a risk factor for *Bacillus subtilis* bacteremia, which is a blood infection caused by a type of bacteria, among children who are receiving chemotherapy for childhood cancer. The authors identified 23 patients who had *B. subtilis* bacteremia and compared them to 92 controls who did not have the infection but matched for age and disease in a ratio of 1:4. They found that the chance of having natto intake for *B. subtilis* bacteremia was 3.6 times higher (95% confidence interval [CI]: 1.2-10.5) when they analyzed the data with one variable at a time. They excluded patients who had neutropenia, which is low levels of white blood cells from the study. The finding is not very surprising because alpha-streptococci infections, which are infections caused by another type of bacteria, have been known to occur with high-dose chemotherapy for the past 50 years.

Actionable Recommendation:

- ✓ **Patients who are receiving chemotherapy, which is a treatment that uses drugs to kill cancer cells, may have bacteria from their own intestines enter**

their blood. This can cause infections and complications. Therefore, patients who are undergoing chemotherapy should avoid taking probiotics, which are living bacteria or yeast that can improve health. Probiotics may be harmful for these patients because they may interfere with the chemotherapy or cause more infections.

- ✓ **Chemotherapy can damage the intestines and make them more leaky, which means that substances that should stay in the intestines can pass through to the blood. This can also affect the balance of microbes in the gut, which are important for digestion and immunity.**
- ✓ **Consult with your oncologist prior to any probiotic therapy while undergoing chemotherapy.**

PQQ (pyrroloquinoline quinone, methoxatin) and Human Memory

Pyrroloquinoline quinone (PQQ), also called methoxatin, was discovered in 1964 by J.G. Hauge, and its structure was determined in 1979 by Salisbury et al. In 2003, Japanese researchers published a paper in the scientific journal *Nature* that PQQ met the definitions of a vitamin. However, subsequent studies found PQQ to be essential for long-term health but not for immediate survival. Mammals do not

synthesize PQQ; its deficiency from the diet leads to growth impairment, compromised immune status, and abnormal reproductive function, therefore, dietary inclusion is essential for maintaining human health. It is widely present in vegetables such as parsley, green peppers, kiwi fruit, papaya, and tofu. These foods contain about 2-3 mcg per 100 grams. Green tea provides about the same amount per 120 mL serving. The nutritional requirements of PQQ are probably in line with folic acid and biotin in terms of micrograms per day versus milligrams per day.

Published on 15th February 2023 in *Food & Function*, Ikemoto et al showed that supplementing with 20 mg of oral PQQ per day for 12 weeks resulted in mild improvements in composite memory and



verbal memory in both younger and older adults. Specifically, PQQ improved cognitive flexibility, processing speed, and

execution speed) after 8 weeks in younger adults aged 20-40. Only older adults aged 41-65 years showed improvements in complex and verbal memory after 12 weeks. In general, PQQ decreases blood glucose but there are reports of paradoxical increases in glucose levels in diabetic patients. So, careful monitoring is warranted for its use in diabetes.

Actionable Recommendation:

- ✓ **For patients having mild memory loss, PQQ 10 mg daily is recommended to gauge any side effects, gradually increasing to 20 mg daily.**
- ✓ **Careful blood glucose monitoring is recommended when starting on PQQ, especially in diabetic patients.**

Probiotic Therapeutics in Respiratory Tract Infections and Diseases in Upcoming Issues!

Natalini J et al published a review article on the dynamic lung microbiome in health and disease in *Nature Reviews* on November 16, 2022. The authors discuss the microbiota that exists in the upper respiratory tract which consists of the nasal cavity, paranasal sinuses, nasopharynx, oropharynx, and the supraglottic portion of the larynx and microbiota that exists in the lower respiratory tract, comprised of the infra-glottic portion of the larynx, trachea, and lungs. It appears recolonizing the respiratory tract as a therapeutic concept

has gained momentum in the research arena. Fonseca W et al showed that oral supplementation with *Lactobacillus johnsonii* in pregnant mice can reduce Th2 type cytokines and lung inflammation in Respiratory Syncytial Virus (RSV)-infected newborn mice in 2021 in the Journal of Experimental Medicine. Tomosada Y et al was able to show nasal administration of live *Lactobacillus rhamnosus* CRL1506 can provide complete protection against RSV infection in mice as reported in the August 15, 2013 edition of BMC Immunology. More recently, Chen C et al showed that intranasal administration of *Lactobacillus johnsonii* reduced hyperoxia-induced lung injury by modulating gut microbiota in neonatal mice and published their observations on July 31, 2023, in the Journal of Biomedical Science. As a continuing series, the microbiome in the respiratory tract will be discussed extensively with potential respiratory probiotic therapeutics. Personalized translational medicine cases will be presented in the Safe Health Report.

Actionable Recommendation:

- ✓ **Do not miss personalized translational medicine from pre-clinical trials if you believe you are a guinea pig!**

FDA Recalls Eye Drops

Dr. Berne's MSM drops 5% solution is recalled by the FDA due to both bacterial

(*Bacillus species*) and fungal contamination (*Exophiala, sp.*). The second eye drop, LightEyez MSM Eye Drops – Eye Repair is recalled due to multiple bacterial contamination (*Pseudomonas, Mycobacterium, Mycolicibacterium, Methylobacterium* species). Both could cause vision loss or even death.

COVID 19 Update (August 29, 2023):

The US Centers for Disease Control reported that there were 12,613 hospital admissions related to COVID-19, which is a disease caused by a new coronavirus with



its numerous variants, in the US in the last 7 days. This is a 21.6% increase from the previous week. As of August 24th, 2023, the COVID-19 Omicron subvariant EG.5, also known as 'Eris', makes up 20.6% of the cases, and the FL.1.5.1 variant, also known as 'Fornax', makes up 13.3%. Both Eris and Fornax variants are derived from

XBB, which is another variant of the coronavirus, as well as the next seven smallest variants listed in the table. This means that the new COVID-19 vaccine and booster shots that are being developed will work for EG.5 and FL.1.5.1 because

✓ **With so many different viral infections in addition to COVID-19 variants, it still makes sense to wear N-95 masks to protect yourself from others if you are older and immune-compromised.**

<i>lineage Number</i>	<i>Percent Total</i>
<i>EG.5</i>	<i>20.6 %</i>
<i>FL.1.5.1</i>	<i>13.3 %</i>
<i>XBB.1.16</i>	<i>10.7%</i>
<i>XBB.2.3</i>	<i>10.6%</i>
<i>XBB.1.16.6</i>	<i>8%</i>
<i>XBB.1.16.1</i>	<i>5.9%</i>
<i>XBB</i>	<i>5.1%</i>
<i>XBB.1.5</i>	<i>4.7%</i>
<i>XBB.1.9.1</i>	<i>4.1%</i>

they are closely related to the XBB.1.5 variant that is targeted by the revised shots approved by the US FDA, which is the agency that regulates food and drugs in the US. However, this also means that Covid-19 caused by BA.2.86 variant will not be prevented by the new vaccines in the coming months. Symptoms of Covid-19 range from mild to severe and include cough, congestion to more severe shortness of breath, and low oxygen levels. These symptoms may require urgent medical care, especially for older people and people with weak immune systems.

Recommendations:

9HEALTH RECIPE #7 SHE CAN DO IT, HE CAN DO IT, I CAN DO IT!

[Low Carb Icaria Soufiko]

Servings: [6-8 Servings]

Prep time: [60 min]

Total time: [105 min]



Ingredients

[1/4 extra virgin olive oil]

[2 large onions, chopped]

[4 cloves of garlic, minced]

[2-pound ripe tomatoes,
peeled and sliced]

[2 pounds of potatoes, peeled
and sliced]

[2-pound eggplants, sliced]

[1 teaspoon dried oregano]

[2 bell peppers roasted,
peeled, sliced]

[1/4 cup chopped fresh
parsley]

[salt and pepper to taste]

Directions

1. Preheat the oven to 375°F (190°C) and lightly grease a baking dish.
2. In a large skillet over medium-high heat, heat 2 tablespoons of olive oil and sauté the onions and garlic until soft, about 15 minutes. Add the tomatoes, salt, pepper, and oregano and simmer until thickened, about 20 minutes.
3. In a small saucepan over high heat, bring some water to a boil and add some salt. Cook the potatoes for 10 minutes, then drain and set aside.
4. In another large skillet over high heat, heat the remaining olive oil and fry the eggplant slices in batches until golden on both sides, about 5 minutes per batch.
5. To assemble the dish, spread half of the tomato-onion mixture on the bottom of the prepared baking dish. Strew a layer of potatoes and sprinkle

1

with some salt, pepper, and oregano. Next, add some more tomato-onion mixture and a layer of eggplant. Press down lightly with a large spoon. Sprinkle with some salt, pepper, and oregano, then scatter some of the roasted peppers on top.

6. Bake for 40 minutes or until bubbly and golden on top.
7. Season with salt and pepper to taste with sprinkled parsley on top.

Special Cooking Information

[Max Cooking Heat for Olive Oil:
Extra Virgin – 350°F, Virgin – 420°F,
Olive oil – 390°F-470°F, once boiling
point is reached, olive oil becomes
toxic! Baking, boiling, and steaming
are preferred over frying]

Recent FDA Medication/Food December Recall

Recall Date	Brand Name	Product Description	Recall Reason Description	Company Name
7/31//2024	Lupin Pharmaceuticals, Inc.	Birth Control Pills:	May not be effective; Lot: L200183-Exp 1/24;Lot: L201560-Exp 9/24	Lupin Pharmaceuticals, Inc.
8/1/2023	Ozona, Go Healthy	Liquid Probiotics for adults and toddlers; Probiotics for cats, dogs, swine, and equine	Foodborne Illness	Ozona Organics, LLC
8/4/2023	Dräger	Carina Sub-Acute Care Ventilators	Product Safety/Potential Foreign Material	Drägerwerk AG & Co. KGaA
8/8/2023	Zespri	Organic green kiwifruit	Possible Listeria monocytogenes contamination	David Oppenheimer and Company I LLC
8/9/2023	Soft serve on the go	Soft serve ice cream and sorbet cups	Possible Listeria monocytogenes contamination	Real Kosher Ice Cream
8/11/2023	NESTLÉ® TOLL HOUSE®	Chocolate Chip Cookie Dough	Potential presence of wood fragments	Nestle USA
8/23/2023	Numerous Brand Names	Numerous human food, animal (pet) food, medical devices, and drug products	Potential Salmonella contamination and presence of rodent activity at the distribution center & temperature abuse	Inmar Supply Chain Solutions
8/23/2023	Food Lion, Kroger and more	Frozen sweet corn and mixed vegetables	Potential Foodborne Illness	Twin City Foods, Inc.

Case Number 10: Relapsing polychondritis

What's the probability of 5-year survival for this 52-year-old male with newly diagnosed relapsing polychondritis?

*The following real-life case examples are hypothetical stories in the palliative or hospice care settings, imagined by the author with the help of artificial intelligence. Frailty scores are commonly used not only to decide if a patient should be placed in palliative or hospice care but also to assess whether the patient is a suitable candidate for major surgery in the case of surgical intervention. Unfortunately, patients with low frailty scores often do not survive five years after a major health crisis. No one is an exception since everybody eventually succumbs to the law of gravity. Case examples may contain personalized **Translational Medicine** from pre-clinical trials.*

Robert Patton, a 52-year-old male, suffers from newly diagnosed relapsing polychondritis.

Assessment and plans on the morning of 08/08/2023 include: The patient is a 52-year-old man with a newly diagnosed relapsing polychondritis 6 months ago. He had been treated with prednisone for 3 months and now transitioned to weekly methotrexate. While prednisone is now completely tapered off by his immunologist, he now has iatrogenic diabetes secondary to intense prednisone therapy. He states his left ear has a complete recovery of feelings, but he still has a tingling sensation on his upper right ear lobe. His rheumatologist is considering the dose of methotrexate. He seeks counseling if there is additional things he can do for his primary disease and type 2 diabetes. Pt states that the disease is currently localized to both of his ears. He has no feelings in either ear due to damage to the ear cartilage.

Current Medications:

Methotrexate 20 mg weekly

Metformin 500 mg BID

Possible Interventions:

Reduction or avoidance of collagen source

Reduction or avoidance of propionate

Reduction or avoidance of excess sugar

Akkermansia to increase intestinal tight junction

Synopsis:

Robert Patton

*All patient data is fictional and imagined by the author with AI assistance. Safe Health Report complies fully with US HIPPA regulations.

Age:52
Sex:male
Weight:160 pounds
Height:5 feet 8 inches

Activities of Daily Living (ADL) components: transfer, bed mobility, toileting, and eating

- **0 – Independent:** If the resident completed the activity with no help or oversight every time during the 7-day prior period.
- **1 – Supervision:** If oversight, encouragement, or cueing was provided three or more times during prior 7 days.
- **2 – Limited Assistance:** If resident was highly involved in the activity and received physical help in guided maneuvering of limb(s) or other non-weight-bearing assistance three or more times during the last seven days.
- **3 – Extensive Assistance:** If resident performed part of the activity over the prior 7 days, help of the following type(s) was provided three or more times: ▪ Weight-bearing support provided three or more times. ▪ Full staff performance of activity during part, but not all, of the prior 7 days.
- **4 – Total Dependence:** If there was full staff performance of an activity with no participation by the resident for any aspect of the ADL activity. The resident must be unwilling or unable to perform any part of the activity over the entire prior 7-day period.
- **7 – Activity occurred only once or twice:** If the activity occurred but not 3 times or more. ▪
- **8 – Activity did not occur:** If, over the prior 7-day period, the ADL (or any part of the ADL) was not performed by the resident or staff at all. ADL support measures the most support provided by staff over the prior 7 days.

*Adapted from Minnesota Department of Health Guideline

Robert's ADL Score 0

First, his five-year survival appears excellent based on his overall health and

disease remission. The etiology of relapsing polychondritis is unknown. Yet, some immune biomarkers are described in pre-clinical studies as follows. Current treatment of RP with methotrexate along with prior prednisone is what worked for the patient's relapsing polychondritis putting him into remission. We definitely recommend following the physician's directions closely.

Second, we recommend the above recommendations after getting approval from his rheumatologist. One thing to remember for our readers is that **most pre-clinical studies covered in this newsletter deal with associations only,**

Eye of the Tiger Test for Robert Patton
*All patient data is fictional. Safe Health Report complies fully with US HIPPA regulations.

Clinical Frailty Score

- 1 – Very Fit: Very fit for their age with no disease symptoms, very active, and exercise regularly- 5 days a week
- 2 – Fit: Still no active disease as in 1 but exercise only occasionally – three times a week or only seasonally
- 3 – Managing Ok: Disease symptoms are well managed. Not able to exercise at all other than walking.
- 4 – Very Mild Frailty: Symptomatic disease. Not dependent on others for daily activities but disease symptoms slow down their activities. May need a cane for walking occasionally for example
- 5 – Mild Frailty: Symptomatic disease limits daily activities. Needs walkers. Needs help with walking and shopping.
- 6 – Moderate Frailty: Needs help with walking, shopping, climbing stairs, and bathing with disease progression.
- 7 – Severe Frailty: Completely dependent for personal care and daily activities but seem stable and at risk of death within the next 6 months.
- 8 – Very Severe Frailty: Same as 7 but unstable and even mild illness is likely to cause death.
- 9 – Terminally Ill: As in 8 but not likely to live next 3-6 month.

*Adapted from [Rockwood & Theou 2020](#)

Robert's Frailty Score 1

which means that a cause-and-effect relationship has not been established. Again, it is important to note that human clinical studies on this topic are lacking in relapsing polychondritis and more research is needed to fully understand the disease and its treatments.

We appreciate the drug information request on this topic regardless.

Background of Immune Cells

CD4⁺ cells, otherwise known as helper T cells or T cells, are subsets of white blood cells within your immune system. CD4 cells are further divided into T helper type 1 (Th1), T helper type 2 (Th2), regulatory T cell (Treg), and pro-inflammatory T helper cell type 17 (Th17). Cross-regulation and mutual inhibition exist between Th1 and Th2 cells through the secretion of cytokines. Th1 cells secrete, interleukin (IL)-2 and interferon (IFN)- γ and lead to cell-mediated responses, whereas Th2 cells secreting IL-4, IL-5, and IL-13) lead to humoral immune responses. Imbalance in favor of the Th2 response results in allergy. Treg expressing CD4 and CD25 (CD4⁺ CD25⁺ Treg) plays a critical role in maintaining auto-tolerance and inhibiting the occurrence and development of autoimmune diseases.

Relapsing Polychondritis

Relapsing polychondritis (RP) is a rare disease that causes inflammation of cartilage, particularly in the ears, nose, eyes, throat, and joints. Although relapsing polychondritis is an immune-mediated systemic disease, the exact cause or mechanism of the disease has not been elucidated. Symptoms range from inflamed cartilage, particularly ears

and nose with redness, swelling, and pain to any cartilaginous tissue damage in the rib cage, large and small joints, eyes, heart, lungs, blood vessels, and even kidneys. Unfortunately, the cause of relapsing polychondritis is currently unknown;



however, the pathogenesis is autoimmune. The evidence of an autoimmune etiology includes findings of infiltrating T-cells, antigen-antibody complexes in the cartilage, both cellular and humoral response to endogenous and exogenous against collagen type II, and the fact that immunosuppressive medications suppress the disease progression. Although there is currently no cure for relapsing polychondritis, it is often effectively treated with medications such as prednisone, methotrexate, and other immunosuppressives.

Gut microbiome alterations in RP

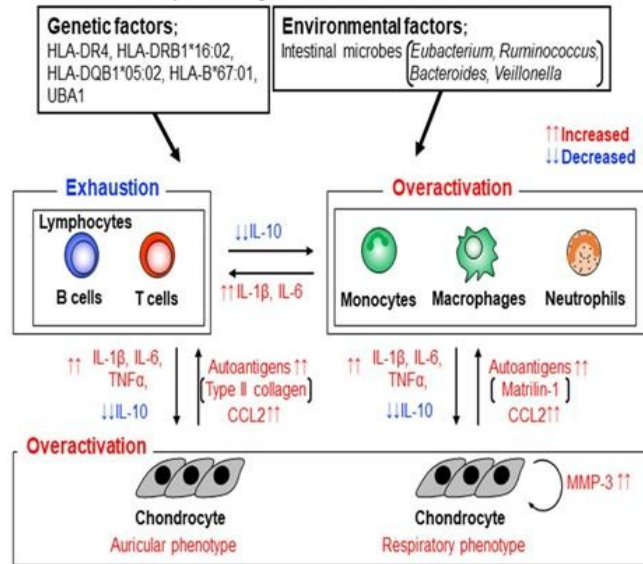
Shimizu et al proposed that the immunopathogenesis of relapsing polychondritis may involve the alteration of gut microbiota. Specifically, the authors observed that *Veillonella*

parvula, *Bacteroides eggerthii*, *Bacteroides fragilis*, *Ruminococcus bromii*, and *Eubacterium dolichum* were predominantly found in relapsing polychondritis patients compared with normal individuals. All of these species are reported to be associated with propionate production in the human intestine, which may affect interleukin-10 production by various immune cells, particularly by Th2 cells. The gene expression level of IL-10, a potent anti-inflammatory cytokine of Treg cells that plays a crucial, and often essential, role in preventing inflammatory and autoimmune pathologies, was significantly higher in freshly isolated peripheral blood mononuclear cells (PBMC) from patients with RP than in those from healthy controls. After the initiation of cell culture with mitogen stimulation, the authors found that the IL-10 gene expression level was significantly decreased in patients with RP compared to that in healthy controls. The researchers suggested that the decreased production of IL10 by Treg cells and increased production of TNF α by PBMC may lead to chondritis in relapsing polychondritis patients. In summary, the gene expression analysis of PBMCs revealed Treg cell exhaustion or anergy in patients with RP. The results were published online in the September 20, 2018, issue of PLOS One by Shimizu and his colleagues.

Immunopathology

Figure 1. Relapsing Polychondritis

Stratification of human autoinflammatory and autoimmune diseases by evaluating immune conditions [14, McGonagle and McDermotte. PLoS Med. 2006; 3:e297.



HLA-DR4 appears to be a susceptibility allele for relapsing polychondritis. A genetic study by Terao et al demonstrated that HLA-DRB1*16:02, HLA-DQB1*05:02, and HLA-B*67:01 are associated with relapsing polychondritis as published online on May 30, 2016, *Rheumatology* (Oxford) issue.

In the initial stages, neutrophils infiltrate into cartilage, which suggests neutrophil activation plays a critical role in the initiation of relapsing polychondritis. Inflammatory CD4⁺ Th cells and CD68⁺ monocytes/macrophages are predominant in granulation tissues. Then the damaged chondrocytes produce MMP-3 and cathepsins. MMP-3 was observed in the cartilage and perichondrium, whereas MMP-8 and MMP-9 were detected only in perichondrium granulation tissues. Cartilage tissues are progressively destroyed and finally replaced by fibrous connective tissues.

As previously mentioned, IL-10 level, a major effector cytokine of regulatory T (Treg) cells, was significantly higher in freshly isolated peripheral blood mononuclear cells (PBMC) from patients with relapsing polychondritis but much lower after mitogen stimulation when compared to normal controls. Such observation led Shimizu et al to suggest Treg cell exhaustion or Treg cell undergo apoptosis in patients with relapsing polychondritis and the skewed T cell function associated with innate cell overactivation based on the gene expression analysis of PBMC.

Humoral Response

Foidart et al in 1978 described in the *New England Journal of Medicine* several cartilage elements that were identified as potential autoantigens and reported 33% of patients had autoantibodies against type 2 collagen. Further, Cremer et al described type 2 collagen-immunized rats developing auricular chondritis in the presence of type 2 collagen-reactive antibodies. Their findings were published in 1981 in the *Journal of Experimental Medicine*. Such specificity of autoimmune injury to cartilaginous tissues has led investigators to test the hypothesis of whether a cartilage-specific autoantibody is central to the pathogenesis of relapsing polychondritis. Various studies find circulating antibodies to cartilage-specific collagen types II, IX, and XI to be present in 30%-70% of patients with relapsing polychondritis. Specifically, researchers have found that antibodies to

type II collagen are present during acute relapsing polychondritis episodes with such antibody levels correlating with the severity of the episode. Shimizu J and Murayama M et al presented a nice summary review of “Innate immune responses: Behçet disease and relapsing polychondritis” on June 26, 2023, issue of *Frontiers of Medicine* (Sec. Rheumatology).

Potential Areas of Intervention

While genetic risk factors are not modifiable, potential environmental risk factors may potentially be altered through lifestyle.

Reduction of Collagen Containing Foods

Since studies have found that 30%-70% of patients with relapsing polychondritis have auto-antibodies to cartilage-specific collagen types II, IX, and XI, it seems reasonable to avoid meat and fish that are rich in connective tissue. When these collagen types are introduced to already circulating autoantibodies, one can reasonably expect acute episodes of RP. This entails avoiding any type of collagen supplementation including hyaluronic acid. This does not mean you should turn into a vegan since vegans are also known to contract relapsing polychondritis.

Propionate

Next to avoid would be an exogenous source of propionic acid. Just like anything else in life, too much or too little propionic acid appears to change gut-induced immune response. If the work of Shimizu and his

colleagues is to be believed, i.e., too much propionic acid as the main byproduct of the gut microbiome, then avoidance of exogenous source propionic acid seems reasonable. Propionic acid is one of the most abundant short-chain fatty acids made by the gut microbiome. It exists in molar ratios of 20:20:60 along with butyric acid and acetic acid respectively. It is also liberally used as a **preservative and food stabilizer in the food industry**. The foods most likely to contain propionate are commercially prepared bread, tortillas, pizza dough, pastries, breakfast cereals, pasta and noodles, dried and condensed milk, flavored milk, dairy-based spreads, cheese, some processed meats, certain processed fruit and vegetable products, and dairy, egg, and fat-based desserts such as puddings, frosting, and confections. It would be ok to consume baked goods as long as they are prepared by oneself. While it is generally recognized as safe by the FDA as a preservative, it appears to contribute to both insulin resistance and high blood sugar in recent studies.

Minimizing Sugar Intake

Propionic acid fermentation is carried out by several bacteria that belong to the genus *Propionibacterium* and to the species *Clostridium propionicum*. When sugar is available, these bacteria use the glycolysis pathway to make pyruvate which is carboxylated to oxalacetate by methyl malonyl coenzyme-A. Oxalacetate is subsequently reduced to

propionate via malate, fumarate, and succinate. Since Mr. Patton is diabetic with RP, I would recommend 9Health Blue Zone diet and minimize sugar and sucrose intake.

Endotoxin

Endotoxin, also called lipopolysaccharide (LPS), is a phospholipid that makes up the outer cell wall of Gram-negative bacteria. LPS is a major component of the outer membrane that plays a role in host-pathogen interactions with the human innate system. As little as 1 to 2 mg of LPS given intravenously is lethal due to serologic reactions. For this reason, LPS levels in pharmaceutical products and medical devices must be strictly monitored using the Limulus amoebocyte lysate (LAL) assay. While the effects of acute LPS exposure have been well-documented, evidence has started to emerge suggesting that chronic low-level LPS exposure (0.5 to 2 ng/kg body weight) may be related to certain types of autoimmune diseases and allergies.

As reported by Dillingham M et al in the September 18th edition of the Journal of Inflammation, in vivo intravenous LPS administration dose-dependently increased circulating cytokine levels of TNF- α , IL-6, and IL-8 in human subjects. As expected, LPS administration also dose-dependently increased body temperature by 1.5°C and heart rate by 28 ± 13.2 bpm. At this time, we can do is do minimize the systemic absorption of LPS by perhaps taking *Akkermansia* as discussed in the August issue.

Proof of Concept for Disease Modification with Microbiome Change

Hu FY et al reported all 17 relapsing polychondritis (RP) patients had significantly both lower absolute number and proportion of Treg cells vs healthy controls (absolute number, 45.10/ μ l vs. 22.48/ μ l, $p < 0.001$; proportion, 5.19% vs. 3.78%, $p < 0.001$) regardless of whether patients had received immunosuppressive treatment or not. Similarly, the authors found absolute number of Th2 cells in all RP patients was decreased (10.19/ μ l vs. 7.44/ μ l, $p = 0.030$). The authors also reported no significant differences in percentages and absolute numbers of Th1 and Th17 cells between RP patients and healthy controls. The results were published in the May 21, 2021, Clinical and Experimental Rheumatology issue. It is hard to know if probiotics such *Lactobacillus johnsonii* will restore Treg cells in RP. At this time, we cannot recommend Lactobacillus probiotics due to a lack of scientific evidence.

Avoiding IL-10 producers such as *Bacillus subtilis* is also recommended in relapsing polychondritis where IL-10 is already elevated. Uesugi et al found that chaperone protein, GroEL, found in the supernatant of 23 types of *B. subtilis* natto causes anti-inflammatory IL-10 and pro-inflammatory IL-12 in THP-1 dendritic cells (THP-1 DC) after co-incubation. Authors' study was

published on May 14th, 2023, edition of Microorganisms. While a cause-and-effect relationship has not been established, it is prudent to avoid *B. subtilis* in RP.

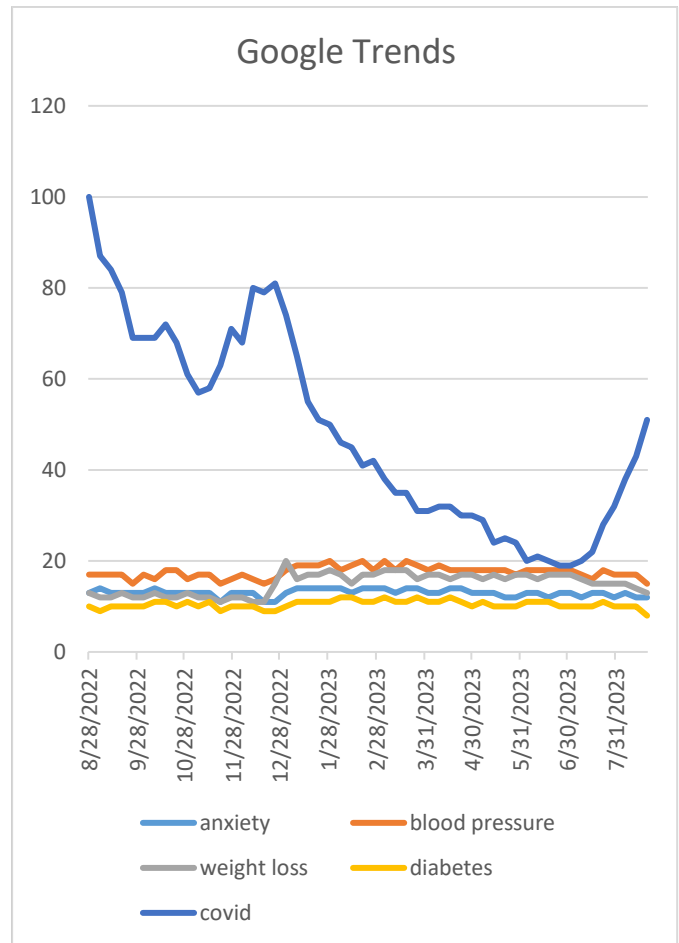
Take Home Lesson:

- ✓ **Coordinate closely with a rheumatologist on medical therapy for RP since untreated or relapsed RP can be quite dangerous, i.e. shortened lifespan.**
- ✓ **After getting approval from the rheumatologist, consider instituting possible interventions discussed if not contra-indicated for RP.**

Google Topic Trends

Google search words were compared to see which were the top 5 from the following: ADHD, allergies, anxiety, blood pressure, calorie consumption, concussions, depression, diabetes, flu, heart attacks, kidney stones, RSV, UTI, and drug addiction. It turns out covid was the top search term followed by blood pressure, weight loss, anxiety, and diabetes. Weight gain, blood pressure, and diabetes are interrelated to food intake as it changes human gut microbiome balance.

Diabetes, weight gain and blood pressure stem from the same etiology, namely excess carbohydrate intake. In the case of weight gain, fructose intake which constitutes between 15-20% of total calorie intake



is the main reason for weight gain. It puts us into hibernation mode and causes disruption in mitochondrial biogenesis. Specifically, fructose intake causes de novo lipogenesis in the liver, in which precursors of acetyl-CoA are converted into fatty acids without triggering insulin or leptin (satiety hormone) secretion. To make matters worse, additional fructose is generated from one's own body when there is a high blood sugar level from excessive consumption of glycemic index carbohydrates. So then you have triglycerides being stored in the adipose cells (fat cells) in addition to their role in atherosclerosis (narrowing of blood

vessels). So, there you have it. This would be the number one cause of obesity. The other causes of obesity are discussed in detail on 9Health Blue Zone Diet, basically free of charge at \$0.99 on Amazon. If you want to take matters into your own hands regarding these favorable conditions for obesity, please read the book for your own sake!

Take Home Lesson:

- ✓ **Avoid all fructose sources including minimizing table sugar. If you can avoid any sweet-tasting bakery goods, candies, drinks, or fruits, you are one step ahead of the game.**
- ✓ **Stick with two meals during active periods in a day. For example, breakfast should be around 8 am or 9 am, and lunch should be eaten around 1-2 pm, and only a light salad for dinner.**
- ✓ **Try to include a soup of your preference, and try to avoid fried foods in general.**
- ✓ **Avoid heavy dinner. All of the calories will end up in the fat battery!**
- ✓ **Walk 30 minutes twice a day.**
- ✓ **If you have not lost significant weight in 3 months, your money will be refunded!**

MrGineaPig's Core Long-Term Trial

LONG-TERM TRIAL	SUPPLEMENT	START DATE	
Muscle Weakness	Hyaluronic Acid	07/01/2019	50 mg-1 capsule daily
Back Pain	Pantothenic acid	09/1/202	500 mg 1 capsule daily
	Pantethine	09/01/2022	450 mg 1 capsule daily
BPH/ prostatitis Prevention	Cranberry Extract 600 mg	12/20/2022	1 capsule three times a day
Memory Loss Prevention	PQQ 10 mg	08/24/2023	1 capsule daily
	*the day I don't remember Occam's razor, cavernous transformation, Bondo, I will know I have issues.		
Mealtimes	Breakfast 09:00 -Lunner (13:00)	01/07/2023	+Salad with Balsamic Vinegar Lunner = Lunch + Dinner
Disclaimer			
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March Risk Factors for Premature or Unexpected Death

Immediate Risks	Internal Threat	External Threat	Other Topics
1. Covid 19 - EG.5	1. Poor diet	1. War	1. Shortness of breath
2. Covid 19- FL.1.5.1	2. Smoking	2. Earthquake	2. Back pain
3. Fentanyl-laced pills	3. High blood pressure	3. FDA recalls	3. Hemorrhoids
4. Gun violence	4. Obesity	4. Meat preservatives	4. Incontinence
5. Drug shortage	5. Sedentary Lifestyle	5. Trans fatty acid	5. Joint swelling
6. RSV	6. Suicide	6. Pesticides	6. Fibromyalgia
7. HMPV		7. Heavy metals	7. Health Insurance

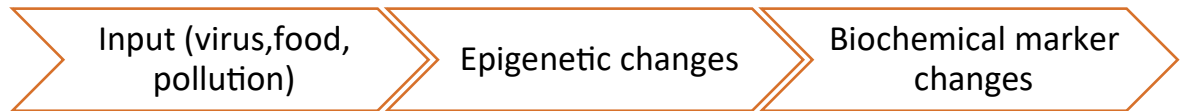
Topics Chosen: Covid-19 update, Clostridium difficile, Search of Best Diet Series

Format of Safe Health Report

Section 1: Conditions or internal environment that increases the risk of premature death or pose an immediate danger to your health (both mental and physical) as in an avalanche.

Section 2: External environment that increases premature death, FDA recalls.

Section 3: Case examples of premature death. If you are in a similar situation, remove yourself out of harm's way! Can we extend **our expiration dates** when in the eye of the storm before disease strikes at a tissue level. Remember epigenome is what activates a specific set of genes.



Purpose of Safe Health Report

If you feel you are being used by someone or somebody or institution or institutionalized philosophy or even by your parents or siblings or your coworkers or even your boss, you are a GineaPig. This newsletter is designed to empower GineaPigs in the area of human health and possibly decrease the risk of **premature death**.

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