Low-Fat, Whole-foods, Plant-based “Paddison Program” Diet And Lifestyle Approach For Rheumatoid Arthritis: A Guide For Rheumatologists

ABSTRACT

There is an ever-increasing body of evidence that supports the health advantages of plant-based nutrition. Working with a modified 'Paddison Program' version of this dietary framework, along with a strong daily exercise plan, enabled the author of this report to recover from crippling RA and become symptom free and drug free long term[1] and help many others achieve life-changing results rarely witnessed with this condition[2] The objective of this report is to provide published evidence of the impact of lifestyle choices on RA disease progression, highlighting the link between gut health and disease activity, and to encourage medical practitioners to encourage safe, healthy lifestyle habits for their patients to minimise their disease perpetuation.

SUMMARY

Every patient needs to eat, and eat they will. So why not encourage them to eat in a way that supports their overall health? Despite popular belief that diet plays little role in RA outcome, the truth is that diet plays a dominant role, and changes to diet create rapid changes in patient symptoms. The table below explores the interaction between the BLAAME (bacteria, leaky gut, acidosis, acid levels in the stomach, mucosal lining integrity and enzymes) with disease severity.

Issues: BLAAME	Description	Cause	Natural Solution (Effective)	Supplement Solution (Mildly Effective)
Bacteria	Autoimmune disease are dramatically influenced by gut bacteria [3] In cases of Rheumatoid Arthritis (RA), newly diagnosed patients have much higher presence of certain gut bacteria[4], more pathogenic gut bacteria[5], and lower levels of healthy bifodobacteria [6] than controls. Established RA patients commonly have small intestinal bacterial overgrowth, and the severity of RA symptoms are proportional to the bacterial overgrowth [7 8] Likewise, in other autoimmune conditions, correlation has been validated between the altered intestinal microbiota composition with the onset of Type 1 Diabetes [9] While bacterial diversity is associated with health, [10] Psoriatic Arthritis (PsA) patients have less gut bacteria, and both PsA [11] and Crohns patients [12] have less diversity than controls.	Diet has a huge impact on gut bacteria and therefore immune function [13 14 15] Antibiotics can permanently change the gut flora [16] and even a single use can set a platform for pathogenic bacteria [17] and rapidly reduce bacterial diversity [18]	Prebiotics (bacteria-friendly foods) such as leafy greens and all plant foods [19 20 21] Fermented foods (bacteria-rich foods) such as miso paste, sauerkraut, kefir. [22 23 24] Exercise [not endurance ex.[25]] improves microbiome [26 27 28 29 30 31 32] Brain and gut microbiome are linked in a functional axis; [33] improving either improves immune control	Probiotic Supplements have been shown to reduce RA symptoms via restoration of the gut microbiome [34 35 36 37 38 39]
Leaky Gut	Intestinal permeability or 'leaky gut' is associated with Rheumatoid Arthritis [40] This process involves undigested food particles or bacteria leaking into the bloodstream, creating a cross reactivity to the body's own tissues.[41] The presence of joint inflammation means more gut inflammation	NSAID’s are a major cause [48 49 50 51 52 53] Prednisone causes leaky gut in just five low dosages, either	Avoidance of aggravators, heals naturally, cabbage juice and other NRF2 promoters [60 61 62 63 64 65] Prebiotic fructans [66 67] Exercise [68 69 70 71]	L-Glutamine supplementation can improve gut permeability [72 73 74 75 76 77 78 79] Curcumin [80 81 82] Arginine [83 84]

	[42] [43] [44] Gut inflammation creates gut lesions, furthering more joint inflammation [45] Biopsies of intestinal tissue of RA sufferers show a partial or complete loss of the epithelium. [46] If the leaky gut can be reversed by re-establishing the intestinal barrier then autoimmune diseases can be arrested [47]	IV or tablet form [54] Methotrexate[55] [56] Stress [57] [58] [59]		Probiotics [85] [86]
Acid Secretion Deficiency (Stomach)	RA sufferers have a high frequency of low gastric acid secretion[87] [88] Low HCL equates to poor protein digestion. Undigested proteins leaking into the blood can trigger self-attack on the joint lining through molecular mimicry [89] Low HCL contributes to the small intestinal bacterial overgrowth [90] [91] (as described above) Low HCL means decreased absorption of ferric iron [92] possibly perpetuating anaemia, along with other minerals and trace elements [93] exacerbating malnutrition (see Mucosal lining below).	Stress [94] [95] [96] and Autonomic imbalance [97] [98] [99] [100]	Celery juice [101] [102] oatmeal (later), Apple Cider Vinegar Meditation [103] Alternate nostril breathing [104] to improve vagus, which can help improve gastric acidity Yoga [105] [106]	Betaine Hydrochloride [107] [108] [109]
Acidosis	The Western diet develops a diet-induced low-grade systemic metabolic acidosis [110] We become more acidic as we age due to declined renal function (kidneys) [111] The synovial fluid in RA patients is too acidic, associated with more inflammation [112] [113] The most influencing factors on acid/alkaline balance are protein (acid forming) and potassium (alkaline forming) [114]	Western diet, stress, all medications, poor respiration [115] [116] [117] [118] [119] [120] and age[121] [122]	Plant-based “Phase 3” foods in the Paddison Program are all alkaline forming, to arrest acidosis: Buckwheat, Quinoa, Sweet potato, greens, seaweed Celery and & Cucumber juice [123] [124] [125] [126] Polyphenol-rich foods such as olives, citrus, grapes, green tea that also target TNF [127] [128] [129]	RA symptoms improved from alkalizing minerals supplementation [130] and potassium supplementation [131] [132]
Mucosal Lining	Nutrients are absorbed in the mucosal lining which also acts as protective gut barrier. A depleted mucosal lining leads to a state of malnutrition in RA patients [133] and the nutritional status/gut health and RA severity are inversely related. [134]	Prednisone, NSAIDs [135] [136] [137] [138] Stress, causing autonomic imbalance and fight-or-flight system dominance [139]	Counteract malnutrition with leafy green vegetables which are rich in macro/micro nutrients [140] [141] [142] Okra, Oatmeal, Brown Rice may help restore mucosal lining via microbiome benefits [143]	Curcumin [144] [145] [146] Glutamine [147] [148]

Enzymes	Enzymes are required for all digestive and metabolic activity in the body [149] Digestive enzymes are depleted with age, but can be accessed through foods	Western Diet	Sprouted nuts and seeds, raw honey, green juices, all raw foods, pineapple, papaya, Miso [150]	Bromelain, papain, nattokinase [151]

FAQ's

HAS LEAKY GUT EVER BEEN PROVEN?

The term “leaky gut” has become increasingly common in medical research, frequently appearing in the most prestigious publications. A review of the available articles reveals that there is growing consensus that the shift in microbiome demographics and intestinal permeability play a causative role in immune alteration towards an inflamed or autoimmune disease state.

Here's what some leading researchers are publishing in the leading medical journals:

International Journal of Clinical and Experimental Pathology: “Autoimmune hepatitis is associated with leaky gut and intestinal microbiome dysbiosis. The impaired intestinal barrier may play an important role in the pathogenesis of autoimmune hepatitis”[152]

Therapeutic Advances in Gastroenterology: “In health, homeostasis exists between the intestinal microbiome, mucosal barrier, and immune system. In irritable bowel disease, this homeostasis is disrupted leading to durable alterations in the intestinal microbiome (dysbiosis), disrupted barrier function (leaky gut), and immune system activation (inflammation)”[153]

FEBS Letters: “these studies suggest that the intestine may be a critical organ in triggering disease through altered immune homeostasis and a leaky gut with proinflammatory conditions may be an event that begins before the actual onset of clinical phenotype”[154]

Journal of Internal Medicine: “In addition, a leaky gut mucosa can trigger systemic inflammation mediating peripheral insulin resistance that together with a blunted incretin response aggravates the hyperglycaemic state”[155]

American Journal of Clinical Nutrition: “The data suggest that a leaky gut barrier is linked with liver steatosis and could be a new target for future steatosis therapies.”[156]

Pediatric Diabetes: “Increasing evidence, both functional and morphological, supports the concept of increased intestinal permeability as an intrinsic characteristic of type 1 diabetes (T1D) in both humans and animal models of the disease.”[157]

WHAT ABOUT NUTRITIONAL DEFICIENCIES?

Although nutrient deficiency is a primary concern for many people when considering plant-based eating, the Academy of Nutrition and Dietetics states[158] that “vegetarian diets, including total vegetarian or vegan diets, are healthful, nutritionally adequate, and may provide health benefits in the prevention and treatment of certain diseases.” The Academy’s position paper goes on to conclude that “well-planned vegetarian diets are appropriate for individuals during all stages of the life cycle, including pregnancy, lactation, infancy, childhood, and adolescence, and for athletes.” Plant-based diets, including calorie-restricted, weight-loss diets, have been found to be more nutritionally sound than typical dietary patterns. [159]

ARE THERE OTHER BENEFITS?

It is now well established that RA is associated with increases in both morbidity and mortality compared with the general population. RA increases the risk of cardiovascular (CV) mortality by up to 50% compared with the general population[160]

[161] [162] Plant-based diets have been associated with lowering overall and ischemic heart disease mortality[163] Furthermore, a plant based diet have also been associated with sustainable weight management[164] reducing medication needs [165] [166] [167]; lowering the risk for most chronic diseases [168] [169]; decreasing the incidence and severity of high-risk conditions, including obesity[170], hypertension [171], hyperlipidemia and hyperglycemia[172], and even possibly reversing advanced coronary artery disease [173] [174]and type 2 diabetes [175].

ARE THERE ANY DANGERS, RISKS OR CONTRAINDICATIONS?

- The first two days of the Paddison Program is a 2 day cleanse. If patients are taking medications that require food, these two days should be skipped.
- High blood pressure can usually resolve itself within a few days to a few weeks. Patients on high blood pressure medications should be made aware of this, so as to be monitored closely and avoid potential overmedication and be given guidelines about their medication dosages should their blood pressure comes back to normal.
- Patients eating an all-plant diet should consume a B12 supplement to avoid potential deficiency.

SUMMARY

A whole-foods, low-fat, plant based (vegan) diet is the ideal approach for a patient with Rheumatoid Arthritis. Succinctly stated by authors of this British Journal of Rhueumatology study “We conclude that a vegan diet changes the faecal microbial flora in RA patients, and changes in the faecal flora are associated with improvement in RA activity”. [176] The Paddison Program for Rheumatoid Arthritis builds on the successful vegan dietary framework and adds evidence-based modifications to enhance these improvements to gastrointestinal health and intestinal barrier repair. For more information visit www.paddisonprogram.com

References:

1 Clint Paddison TEDx Presentation
2 www.paddisonprogram.com/testiomonials
3 "The gut microbiota shapes intestinal immune responses during health and disease" Nature Reviews Immunology 9, 313–323 (1 May 2009)

4 Arthritis Rheumatol. 2016 Nov 18. "Evidence for Immune Relevance of Prevotella copri, a Gut Microbe, in Patients with Rheumatoid Arthritis". Pianta A et al

5 "Intestinal flora in early rheumatoid arthritis" Br J Rheumatology, 1994 Nov, 33(11):1030-8

6 "Fecal Microbiota in Early Rheumatoid Arthritis" Rheumatology, Vol 35 no. 8 1500 – 1505]

7 "Small intestinal bacterial overgrowth in patients with rheumatoid arthritis" Ann Rheum Dis. 1993 Jul;52(7):503-10]

8 Henriksson AE, Blomquist L, Nord CE, Midtvedt T, Uribe A. Small intestinal bacterial overgrowth in patients with rheumatoid arthritis. Ann Rheum Dis. 1993 Jul;52(7):503-10

9 Ann N Y Acad Sci. 2011 Dec;1243:103-18. "Type 1 diabetes: role of intestinal microbiome in humans and mice". Boerner BP, Sarvetnick NE.

10 Nat Rev Microbiol. 2009 Dec;7(12):887-94. "What are the consequences of the disappearing human microbiota?" Blaser MJ, Falkow S.

11 Scher J.U. et al, Arthritis Rheumatol. 2015 Jan;67(1):128-39. doi: 10.1002/art.38892. "Decreased bacterial diversity characterizes the altered gut microbiota in patients with psoriatic arthritis, resembling dysbiosis in inflammatory bowel disease".

12 Gut. 2006 Feb; 55(2): 205–211. "Reduced diversity of faecal microbiota in Crohn's disease revealed by a metagenomic approach" C Manichanh et al

13 Mackos AR, Varaljay VA, Maltz R, Gur TL, Bailey MT. Role of the Intestinal Microbiota in Host Responses to Stressor Exposure. Int Rev Neurobiol. 2016;131:1-19

14 Abhari K, Shekarforoush SS, Hosseinzadeh S, Nazifi S, Sajedianfard J, Eskandari MH. The effects of orally administered Bacillus coagulans and inulin on prevention and progression of rheumatoid arthritis in rats. Food Nutr Res. 2016 Jul 15;60:30876

15 DeChristopher LR, Uribarri J, Tucker KL. Intake of high-fructose corn syrup sweetened soft drinks, fruit drinks and apple juice is associated with prevalent arthritis in US adults, aged 20-30 years. Nutr Diabetes. 2016 Mar 7;6:e199

16 Nature 476, 393–394 (25 August 2011) doi:10.1038/476393a. Published online 24 August 2011

17 "The influence of single dose intravenous antibiotics on faecal flora and emergence of Clostridium difficile" N. S. Ambrose, Margaret Johnson, D. W. Burdon and M. R.B. Keighley

18 The pervasive effects of an antibiotic on the human gut microbiota, as revealed by deep 16S rRNA sequencing. PLoS Biol. 2008 Nov 18;6(11):e280. doi: 10.1371/journal.pbio.0060280. Dethlefsen L1, Huse S, Sogin ML, Relman DA

19 Vitetta L, Coulson S, Linnane AW, Butt H. The gastrointestinal microbiome and musculoskeletal diseases: a beneficial role for probiotics and prebiotics. Pathogens. 2013 Nov 14;2(4):606-26

References:

20 Collins B, Hoffman J, Martinez K, Grace M, Lila MA, Cockrell C, Nadimpalli A, Chang E, Chuang CC, Zhong W, Mackert J, Shen W, Cooney P, Hopkins R, McIntosh M. A polyphenol-rich fraction obtained from table grapes decreases adiposity, insulin resistance and markers of inflammation and impacts gut microbiota in high-fat-fed mice. J Nutr Biochem. 2016 May;31:150-65.

21 Peltonen R1, Nenonen M, HelveT, Hänninen O, ToivanenP, Eerola E. Br J Rheumatol. 1997 Jan;36(1):64-8.Faecal microbial flora and disease activity in rheumatoid arthritis during a vegan diet.

22 Kawaguchi K, Matsumoto T, Kumazawa Y. Effects of antioxidant polyphenols on TNF-alpha-related diseases. Curr Top Med Chem. 2011;11(14):1767-79

23 Beaulieu J, Girard D, Dupont C, Lemieux P. Inhibition of neutrophil infiltration by a malleable protein matrix of lactic acid bacteria-fermented whey proteins in vivo. Inflamm Res. 2009 Mar;58(3):133-8.

24 Bálint G, Apáthy A, Gaál M, Telekes A, Resetár A, Blazsó G, Falkay G, Szende B, Paksy A, Ehrenfeld M, Shoenfeld Y, Hidvégi M. Effect of Avemar--a fermented wheat germ extract--on rheumatoid arthritis. Preliminary data. Clin Exp Rheumatol. 2006 May-Jun;24(3):325-8.

25 JanssenDuijghuijsen LM, Mensink M, Lenaerts K, Fiedorowicz E; Protégé study group., van Dartel DA, Mes JJ, Luiking YC, Keijer J, Wichers HJ, Witkamp RF, van Norren K. The effect of endurance exercise on intestinal integrity in well-trained healthy men. Physiol Rep. 2016 Oct;4(20)

26 Campbell SC, Wisniewski PJ 2nd. Exercise is a Novel Promoter of Intestinal Health and Microbial Diversity. Exerc Sport Sci Rev. 2017 Jan;45(1):41-47.

27 Estaki M, Pither J, Baumeister P, Little JP, Gill SK, Ghosh S, Ahmadi-Vand Z, Marsden KR, Gibson DL. Cardiorespiratory fitness as a predictor of intestinal microbial diversity and distinct metagenomic functions. Microbiome. 2016 Aug 8;4(1):42

28 Yano H, Uchida M, Oyanagi E, Iemitsu M, Onodera S, Kremenik MJ, Miyachi M. Voluntary Exercise Attenuates Obesity and Systemic Inflammation by Alteration of Gut Microbiota in TLR5-Deficient Mice: 2658 Board #181 June 3, 9: 30 AM - 11: 00 AM. Med Sci Sports Exerc. 2016 May;48(5 Suppl 1):742.

29 Denou E, Marcinko K, Surette MG, Steinberg GR, Schertzer JD. High-intensity exercise training increases the diversity and metabolic capacity of the mouse distal gut microbiota during diet-induced obesity. Am J Physiol Endocrinol Metab. 2016 Jun 1;310(11):E982-93.

30 Cerdá B, Pérez M, Pérez-Santiago JD, Tornero-Aguilera JF, González-Soltero R, Larrosa M. Gut Microbiota Modification: Another Piece in the Puzzle of the Benefits of Physical Exercise in Health? Front Physiol. 2016 Feb 18;7:51

31 Holland AM, Hyatt HW, Smuder AJ, Sollanek KJ, Morton AB, Roberts MD, Kavazis AN. Influence of endurance exercise training on antioxidant enzymes, tight junction proteins, and inflammatory markers in the rat ileum. BMC Res Notes. 2015 Sep 30;8:514

32 Van Houten JM, Wessells RJ, Lujan HL, DiCarlo SE. My gut feeling says rest: Increased intestinal permeability contributes to chronic diseases in high-intensity exercisers. Med Hypotheses. 2015 Dec;85(6):882-6

33 Wang HX, Wang YP. Gut Microbiota-brain Axis. Chin Med J (Engl). 2016 5th Oct;129(19):2373-80

34 Wang P, Tao JH, Pan HF. Probiotic bacteria: a viable adjuvant therapy for relieving symptoms of rheumatoid arthritis. Inflammopharmacology. 2016 Oct;24(5):189-196

References:

35 Alipour B, Homayouni-Rad A, Vaghef-Mehrabany E, Sharif SK, Vaghef-Mehrabany L, Asghari-Jafarabadi M, Nakhjavani MR, Mohtadi-Nia J. Int J Rheum Dis. 2014 Jun;17(5):519-27 Effects of Lactobacillus casei supplementation on disease activity and inflammatory cytokines in rheumatoid arthritis patients: a randomized double-blind clinical trial.

36 Zamani B, Golkar HR, Farshbaf S, Emadi-Baygi M, Tajabadi-Ebrahimi M, Jafari P, Akhavan R, Taghizadeh M, Memarzadeh MR, Asemi Z. Clinical and metabolic response to probiotic supplementation in patients with rheumatoid arthritis: a randomized, double-blind, placebo-controlled trial. Int J Rheum Dis. 2016 Sep;19(9):869-79

37 Vaghef-Mehrabany E, Alipour B, Homayouni-Rad A, Sharif SK, Asghari-Jafarabadi M, Zavvari S. Probiotic supplementation improves inflammatory status in patients with rheumatoid arthritis. Nutrition. 2014 Apr;30(4):430-5

38 Round JL, Mazmanian SK. The gut microbiota shapes intestinal immune responses during health and disease. Nat Rev Immunol. 2009 May;9(5):313-23

39 Vaahtovuo J, Munukka E, Korkeamäki M, Luukkainen R, Toivanen P. Fecal microbiota in early rheumatoid arthritis. J Rheumatol. 2008 Aug;35(8):1500-5

40 Int Rev Neurobiol. 2016;131:127-141, 2016 Sep 15. "Intestinal Barrier and Behavior". Julio-Pieper M

41 Altern Ther Health Med. 2015;21 Suppl 1:34-45. “Molecular mimicry as a mechanism for food immune reactivities and autoimmunity”. Vojdani A.

42 “Course of gut inflammation in spondylarthropathies and therapeutic consequences”, Bailliere’s Clinical Rheumatology, Vol. 10, Issue 1, Feb 1996, 147-164

43 Fasano A. Leaky gut and autoimmune diseases. Clin Rev Allergy Immunol. 2012 Feb;42(1):71-8. doi: 10.1007/s12016-011-8291-x. Review. PubMed PMID: 22109896

44 Mielants H, De Keyser F, Baeten D, Van den Bosch F. Gut inflammation in the spondyloarthropathies. Curr Rheumatol Rep. 2005 Jun;7(3):188-94. Review

45 “Gut inflammation in the spondyloarthropathies” Current Rheumatology Reports, June 2005, Volume 7, Issue 3, pp 188 – 194

46 “Gastrointestinal involvement in rheumatoid arthritis: a biopsy study”. J Rheumatol. 1979 Mar-Apr;6(2):163-73

47 Autoimmune diseases can be arrested by re-establishing the intestinal barrier “Leaky gut and autoimmune diseases”. Clin Rev Allergy Immunol. 2012 Feb;42(1):71-8. doi: 10.1007/s12016-011-8291-x

48 “Intestinal permeability and inflammation in patients on NSAIDs”, G Sigthorsson et al, Gut. Oct 1998; 43(4): 506–511 Baillieres Clinical Rheumatology 10:165, 1996

49 "Intestinal permeability and inflammation in Rheumatoid Arthritis: Effects of non-steroidal anti-inflammatory drugs" The Lancet. Volume 324, Issue 8413, 24 November 1984, Pages 1171-1174. Originally published as Volume 2, Issue 8413. Ingvar Bjarnason, Alex So, A.Jonathan Levi, TimothyJ. Peters, Peter Williams, GiuseppeD. Zanelli, J.Michael Gumpel, Barbara Ansell

50 Whitfield-Cargile CM, Cohen ND, Chapkin RS, Weeks BR, Davidson LA, Goldsby JS, Hunt CL, Steinmeyer SH, Menon R, Suchodolski JS, Jayaraman A, Alaniz RC. The microbiota-derived metabolite indole decreases mucosal

References:

inflammation and injury in a murine model of NSAID enteropathy. Gut Microbes. 2016 May 3;7(3):246-61

51 Iijima K, Shimosegawa T. Geographic differences in low-dose aspirin-associated gastroduodenal mucosal injury. World J Gastroenterol. 2015 Jul 7;21(25):7709-17

52 Takeuchi K, Satoh H. NSAID-induced small intestinal damage--roles of various pathogenic factors. Digestion. 2015;91(3):218-32

53 Endo H, Sakai E, Kato T, Umezawa S, Higurashi T, Ohkubo H, Nakajima A. Small bowel injury in low-dose aspirin users. J Gastroenterol. 2015 Apr;50(4):378-86

54 "Gastric tolerance of high-dose pulse oral prednisone in multiple sclerosis".Neurology. 1999 Dec 10;53(9):2093-6. Metz LM1, Sabuda D, Hilsden RJ, Enns R, Meddings JB

55 Meng Y, Zhang Y, Liu M, Huang YK, Zhang J, Yao Q, Zhao YL, Xiong JJ. Evaluating Intestinal Permeability by Measuring Plasma Endotoxin and Diamine Oxidase in Children with Acute Lymphoblastic Leukemia Treated with High-dose Methotrexate. Anticancer Agents Med Chem. 2016;16(3):387-92.

56 Beutheu S, Ghouzali I, Galas L, Déchelotte P, Coëffier M. Glutamine and arginine improve permeability and tight junction protein expression in methotrexate-treated Caco-2 cells. Clin Nutr. 2013 Oct;32(5):863-9.

57 Sharkey KA, Savidge TC. Role of enteric neurotransmission in host defense and protection of the gastrointestinal tract. Auton Neurosci. 2014 Apr;181:94-106

58 Schäper J, Wagner A, Enigk F, Brell B, Mousa SA, Habazettl H, Schäfer M. Regional sympathetic blockade attenuates activation of intestinal macrophages and reduces gut barrier failure. Anesthesiology. 2013 Jan;118(1):134-42

59 Keita AV, Söderholm JD. The intestinal barrier and its regulation by neuroimmune factors. Neurogastroenterol Motil. 2010 Jul;22(7):718-33

60 Vaziri ND, Liu SM, Lau WL, Khazaeli M, Nazertehrani S, Farzaneh SH, Kieffer DA, Adams SH, Martin RJ. High amylose resistant starch diet ameliorates oxidative stress, inflammation, and progression of chronic kidney disease. PLoS One. 2014 Dec 9;9(12):e114881

61 Zhou XL, Kong XF, Lian GQ, Blachier F, Geng MM, Yin YL. Dietary supplementation with soybean oligosaccharides increases short-chain fatty acids but decreases protein-derived catabolites in the intestinal luminal content of weaned Huanjiang mini-piglets. Nutr Res. 2014 Sep;34(9):780-8

62 Kong JS, Yoo SA, Kim HS, Kim HA, Yea K, Ryu SH, Chung YJ, Cho CS, Kim WU. Inhibition of synovial hyperplasia, rheumatoid T cell activation, and experimental arthritis in mice by sulforaphane, a naturally occurring isothiocyanate. Arthritis Rheum. 2010 Jan;62(1):159-70

63 Zhao J, Moore AN, Redell JB, Dash PK. Enhancing expression of Nrf2-driven genes protects the blood brain barrier after brain injury. J Neurosci. 2007 Sep 19;27(38):10240-8

64 Cerhan JR, Saag KG, Merlino LA, Mikuls TR, Criswell LA. Antioxidant micronutrients and risk of rheumatoid arthritis in a cohort of older women. Am J Epidemiol. 2003 Feb 15;157(4):345-54

65 Kim J, Cha YN, Surh YJ. Mutat Res. 2010 Aug 7;690(1-2):12-23. doi: 10.1016/j.mrfmmm.2009.09.007. Review. A protective role of nuclear factor-erythroid 2-related factor-2 (Nrf2) in inflammatory disorders

References:

66 Liu TW, Cephas KD, Holscher HD, Kerr KR, Mangian HF, Tappenden KA, Swanson KS. Nondigestible Fructans Alter Gastrointestinal Barrier Function, Gene Expression, Histomorphology, and the Microbiota Profiles of Diet-Induced Obese C57BL/6J Mice. J Nutr. 2016 May;146(5):949-56

67 Guarner F. J Nutr. 2007 Nov;137(11 Suppl):2568S-2571S. Review. Studies with inulin-type fructans on intestinal infections,permeability, and inflammation.

68 Campbell SC, Wisniewski PJ, Noji M, McGuinness LR, Häggblom MM, Lightfoot SA, Joseph LB, Kerkhof LJ. The Effect of Diet and Exercise on Intestinal Integrity and Microbial Diversity in Mice. PLoS One. 2016 Mar 8;11(3):e0150502

69 Yuan TF, Ferreira Rocha NB, Paes F, Arias-Carrión O, Machado S, de Sá Filho AS. Neural Mechanisms of Exercise: Effects on Gut Microbiota and Depression. CNS Neurol Disord Drug Targets. 2015;14(10):1312-4

70 Bermon S, Petriz B, Kajėnienė A, Prestes J, Castell L, Franco OL. The microbiota: an exercise immunology perspective. Exerc Immunol Rev. 2015;21:70-9

71 Luo B, Xiang D, Nieman DC, Chen P. The effects of moderate exercise on chronic stress-induced intestinal barrier dysfunction and antimicrobial defense. Brain Behav Immun. 2014 Jul;39:99-106

72 Role of Glutamine in Protection of Intestinal Epithelial Tight Junctions. J Epithel Biol Pharmacol. Author manuscript; available in PMC 2015 Mar 23.RadhaKrishna Rao and Geetha Samak

73 Achamrah N, Déchelotte P, Coëffier M. Glutamine and the regulation of intestinal permeability: from bench to bedside. Curr Opin Clin Nutr Metab Care. 2017 Jan;20(1):86-91

74 Shu X, Zhang J, Wang Q, Xu Z, Yu T. Glutamine decreases intestinal mucosal injury in a rat model of intestinal ischemia-reperfusion by downregulating HMGB1 and inflammatory cytokine expression. Exp Ther Med. 2016 Sep;12(3):1367-1372

75 Wang B, Wu Z, Ji Y, Sun K, Dai Z, Wu G. L-Glutamine Enhances Tight Junction Integrity by Activating CaMK Kinase 2-AMP-Activated Protein Kinase Signaling in Intestinal Porcine Epithelial Cells. J Nutr. 2016 Mar;146(3):501-8

76 Akobeng AK, Elawad M, Gordon M. Glutamine for induction of remission in Crohn's disease. Cochrane Database Syst Rev. 2016 Feb 8;2:CD007348

77 Chaudhry KK, Shukla PK, Mir H, Manda B, Gangwar R, Yadav N, McMullen M, Nagy LE, Rao R. Glutamine supplementation attenuates ethanol-induced disruption of apical junctional complexes in colonic epithelium and ameliorates gut barrier dysfunction and fatty liver in mice. J Nutr Biochem. 2016 Jan;27:16-26

78 Bertrand J, Ghouzali I, Guérin C, Bôle-Feysot C, Gouteux M, Déchelotte P, Ducrotté P, Coëffier M. Glutamine Restores Tight Junction Protein Claudin-1 Expression in Colonic Mucosa of Patients With Diarrhea-Predominant Irritable Bowel Syndrome. JPEN J Parenter Enteral Nutr. 2016 Nov;40(8):1170-1176

79 Wang H, Zhang C, Wu G, Sun Y, Wang B, He B, Dai Z, Wu Z. Glutamine enhances tight junction protein expression and modulates corticotropin-releasing factor signaling in the jejunum of weanling piglets. J Nutr. 2015 Jan;145(1):25-31

80 Tian S, Guo R, Wei S, Kong Y, Wei X, Wang W, Shi X, Jiang H. Curcumin protects against the intestinal ischemia-reperfusion injury: involvement of the tight junction protein ZO-1 and TNF-α related mechanism. Korean J Physiol Pharmacol. 2016 Mar;20(2):147-52

81 Yucel AF, Kanter M, Pergel A, Erboga M, Guzel A. The role of curcumin on intestinal oxidative stress, cell proliferation and apoptosis after ischemia/reperfusion injury in rats. J Mol Histol. 2011 Dec;42(6):579-87

References:

82 Bereswill S, Muñoz M, Fischer A, Plickert R, Haag LM, Otto B, Kühl AA, Loddenkemper C, Göbel UB, Heimesaat MM. Anti-inflammatory effects of resveratrol, curcumin and simvastatin in acute small intestinal inflammation. PLoS One. 2010 Dec 3;5(12):e15099

83 Ren W, Yin J, Wu M, Liu G, Yang G, Xion Y, Su D, Wu L, Li T, Chen S, Duan J, Yin Y, Wu G. Serum amino acids profile and the beneficial effects of L-arginine or L-glutamine supplementation in dextran sulfate sodium colitis. PLoS One. 2014 Feb 5;9(2):e88335

84 Beutheu S, Ghouzali I, Galas L, Déchelotte P, Coëffier M. Glutamine and arginine improve permeability and tight junction protein expression in methotrexate-treated Caco-2 cells. Clin Nutr. 2013 Oct;32(5):863-9

85 Shing CM, Peake JM, Lim CL, Briskey D, Walsh NP, Fortes MB, Ahuja KD, Vitetta L. Effects of probiotics supplementation on gastrointestinal permeability, inflammation and exercise performance in the heat. Eur J Appl Physiol. 2014 Jan;114(1):93-103

86 Lamprecht M, Bogner S, Schippinger G, Steinbauer K, Fankhauser F, Hallstroem S, Schuetz B, Greilberger JF. Probiotic supplementation affects markers of intestinal barrier, oxidation, and inflammation in trained men; a randomized, double-blinded, placebo-controlled trial. J Int Soc Sports Nutr. 2012 Sep 20;9(1):45

87 "Hypochlorhydria and hypergastrinaemia in rheumatoid arthritis" Annals Rheumatic Disease. 1979 Feb; 38(1): 14–17.

88 de Witte TJ, Geerdink PJ, Lamers CB, Boerbooms AM, van der Korst JK. Hypochlorhydria and hypergastrinaemia in rheumatoid arthritis. Ann Rheum Dis. 1979 Feb;38(1):14-7

89 "Molecular Mimicry and Autoimmunity" N Engl J Med 1999; 341:2068-2074 December 30, 1999 DOI: 10.1056/NEJM199912303412707

90 Cares K, Al-Ansari N, Macha S, Zoubi N, Zaghloul H, Thomas R, Lalinsky P, El-Baba M. Eur J Gastroenterol Hepatol. 2016 Dec 27 Risk of small intestinal bacterial overgrowth with chronic use of proton pump inhibitors in children.

91 Bures J, Cyrany J, Kohoutova D, Förstl M, Rejchrt S, Kvetina J, Vorisek V, Kopacova M. World J Gastroenterol. 2010 Jun 28;16(24):2978-90 Small intestinal bacterial overgrowth syndrome.

92 "Low gastric hydrochloric acid secretion and mineral bioavailability". Adv Exp Med Biol. 1989;249:173-84. Champagne ET

93 Wright JV. Treatment of childhood asthma with parenteral vitamin B12, gastric re-acidification, and attention to food allergy, magnesium and pyridoxine. Three case reports with background and an integrated hypothesis. J Nutr Med 1990;1:277-282

94 Yin J, Levanon D, Chen JD. Inhibitory effects of stress on postprandial gastric myoelectrical activity and vagal tone in healthy subjects. Neurogastroenterol Motil. 2004 Dec;16(6):737-44

95 Muth ER, Koch KL, Stern RM. Significance of autonomic nervous system activity in functional dyspepsia. Dig Dis Sci. 2000 May;45(5):854-63

96 Hausken T, Svebak S, Wilhelmsen I, Haug TT, Olafsen K, Pettersson E, Hveem K, Berstad A. Low vagal tone and antral dysmotility in patients with functional dyspepsia. Psychosom Med. 1993 Jan-Feb;55(1):12-22

97 Chen YJ, Lin CL, Li CR, Huang SM, Chan JY, Fang WH, Chen WL. Psychoneuroendocrinology. 2016 Dec;74:342-349 Associations among integrated psychoneuroimmunological factors and metabolic syndrome

References:

98 McMenamin CA, Travagli RA, Browning KN. Exp Biol Med (Maywood). 2016 Jun;241(12):1343-50 Inhibitory neurotransmission regulates vagal efferent activity and gastric motility.

99 Shichijo K, Ito M, Taniyama K, Sekine I. The role of sympathetic neurons for low susceptibility to stress in gastric lesions. Life Sci. 1993;53(3):261-7

100 Holst JJ, Skak-Nielsen T, Orskov C, Seier-Poulsen S. Vagal control of the release of somatostatin, vasoactive intestinal polypeptide, gastrin-releasing peptide, and HCl from porcine non-antral stomach. Scand J Gastroenterol. 1992 Aug;27(8):677-85

101 Gupta SC, Tyagi AK, Deshmukh-Taskar P, Hinojosa M, Prasad S, Aggarwal BB. Arch Biochem Biophys. 2014 Oct 1;559:91-9. doi: 10.1016/j.abb.2014.06.006. Review. Downregulation of tumor necrosis factor and other proinflammatory biomarkers by polyphenols

102 Arango D, Diosa-Toro M, Rojas-Hernandez LS, Cooperstone JL, Schwartz SJ, Mo X, Jiang J, Schmittgen TD, Doseff AI. Mol Nutr Food Res. 2015 Apr;59(4):763-72. doi: 10.1002/mnfr.201400705. Dietary apigenin reduces LPS-induced expression of miR-155 restoring immune balance during inflammation

103 Muthukrishnan S, Jain R, Kohli S, Batra S. J Clin Diagn Res. 2016 Apr;10(4):CC05-8 Effect of Mindfulness Meditation on Perceived Stress Scores and Autonomic Function Tests of Pregnant Indian Women.

104 Sinha AN, Deepak D, Gusain VS. J Clin Diagn Res. 2013 May;7(5):821-3. Assessment of the effects of pranayama/alternate nostril breathing on the parasympathetic nervous system in young adults

105 Stewart A. Joint ventures: helping those with rheumatoid arthritis live well. Int J Yoga Therap. 2013;(23):91-100

106 Singh VK, Bhandari RB, Rana BB. Effect of yogic package on rheumatoid arthritis. Indian J Physiol Pharmacol. 2011 Oct-Dec;55(4):329-35

107 Yago MR, Frymoyer A, Benet LZ, Smelick GS, Frassetto LA, Ding X, Dean B, Salphati L, Budha N, Jin JY, Dresser MJ, Ware JA. The use of betaine HCl to enhance dasatinib absorption in healthy volunteers with rabeprazole-induced hypochlorhydria. AAPS J. 2014 Nov;16(6):1358-65

108 Yago MR, Frymoyer AR, Smelick GS, Frassetto LA, Budha NR, Dresser MJ, Ware JA, Benet LZ. Gastric reacidification with betaine HCl in healthy volunteers with rabeprazole-induced hypochlorhydria. Mol Pharm. 2013 Nov 4;10(11):4032-7

109 Pang J, Dalziel G, Dean B, Ware JA, Salphati L. Pharmacokinetics and absorption of the anticancer agents dasatinib and GDC-0941 under various gastric conditions in dogs--reversing the effect of elevated gastric pH with betaine Hcl. Mol Pharm. 2013 Nov 4;10(11):4024-31

110 "Dietary, metabolic, physiologic, and disease-related aspects of acid-base balance: foreword to the contributions of the second International Acid-Base Symposium". Journal of Nutrition. 2008 Feb;138(2):413S-414S

111 Effect of age on blood acid-base composition in adult humans: role of age-related renal functional decline". Am J Physiol. 1996 Dec;271(6 Pt 2):F1114-22

112 "Significance of the hydrogen ion concentration in synovial fluid in rheumatoid arthritis". Clin Exp Rheumatol. 1985 Apr-Jun;3(2):99-104

113 Farr M, Garvey K, Bold AM, Kendall MJ, Bacon PA. Significance of the hydrogen ion concentration in synovial fluid in rheumatoid arthritis. Clin Exp Rheumatol. 1985 Apr-Jun;3(2):99-104

References:

114 "Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents." Am J Clin Nutr. 1998 Sep;68(3):576-83

115 Della Guardia L, Roggi C, Cena H. Diet-induced acidosis and alkali supplementation. Int J Food Sci Nutr. 2016 Nov;67(7):754-61

116 Niekamp K, Zavorsky GS, Fontana L, McDaniel JL, Villareal DT, Weiss EP. Systemic acid load from the diet affects maximal-exercise RER. Med Sci Sports Exerc. 2012 Apr;44(4):709-15

117 Vormann J, Remer T. Dietary, metabolic, physiologic, and disease-related aspects of acid-base balance: foreword to the contributions of the second International Acid-Base Symposium. J Nutr. 2008 Feb;138(2):413S-414S

118 Jehle S, Zanetti A, Muser J, Hulter HN, Krapf R. Partial neutralization of the acidogenic Western diet with potassium citrate increases bone mass in postmenopausal women with osteopenia. J Am Soc Nephrol. 2006 Nov;17(11):3213-22

119 Pattison DJ, Symmons DP, Young A. Does diet have a role in the aetiology of rheumatoid arthritis? Proc Nutr Soc. 2004 Feb;63(1):137-43

120 Maurer M, Riesen W, Muser J, Hulter HN, Krapf R. Neutralization of Western diet inhibits bone resorption independently of K intake and reduces cortisol secretion in humans. Am J Physiol Renal Physiol. 2003 Jan;284(1):F32-40

121 Adeva MM, Souto G. Clin Nutr. 2011 Aug;30(4):416-21 Diet-induced metabolic acidosis.

122 Bushinsky DA. Eur J Nutr. 2001 Oct;40(5):238-44 Acid-base imbalance and the skeleton.

123 Burckhardt P. The role of low acid load in vegetarian diet on bone health: a narrative review. Swiss Med Wkly. 2016 Feb 22;146:w14277

124 Hänninen, Kaartinen K, Rauma AL, Nenonen M, Törrönen R, Häkkinen AS, Adlercreutz H, Laakso J. Antioxidants in vegan diet and rheumatic disorders. Toxicology. 2000 Nov 30;155(1-3):45-53

125 Hänninen O, Rauma AL, Kaartinen K, Nenonen M. Vegan diet in physiological health promotion. Acta Physiol Hung. 1999;86(3-4):171-80

126 Hietavala EM, Stout JR, Hulmi JJ, Suominen H, Pitkänen H, Puurtinen R, Selänne H, Kainulainen H, Mero AA. Eur J Clin Nutr. 2015 Mar;69(3):399-404. Effect of diet composition on acid-base balance in adolescents, young adults and elderly at rest and during exercise

127 Sethi G, Sung B, Kunnumakkara AB, Aggarwal BB. Targeting TNF for Treatment of Cancer and Autoimmunity. Adv Exp Med Biol. 2009;647:37-51

128 Linos A, Kaklamani VG, Kaklamani E, Koumantaki Y, Giziaki E, Papazoglou S, Mantzoros CS. Dietary factors in relation to rheumatoid arthritis: a role for olive oil and cooked vegetables? Am J Clin Nutr. 1999 Dec;70(6):1077-82. Erratum in: Am J Clin Nutr 2000 Apr;71(4):1010

129 Rodriguez J, Caille O, Ferreira D, Francaux M. Mol Nutr Food Res. 2016 Nov 2 Pomegranate extract prevents skeletal muscle of mice against wasting induced by acute TNF-α injection.

130 "Alkaline Mineral Supplementation Decreases Pain in Rheumatoid Arthritis Patients: A Pilot Study" The Open Nutrition Journal, 2008, 2, 100-105

131 Krapf R. Partial neutralization of the acidogenic Western diet with potassium citrate increases bone mass in postmenopausal women with osteopenia. Interview by Nicola Zitzmann. Int J Prosthodont. 2007 Mar-Apr;20(2):113-4

132 Journal of Pain. 2008 Aug;9(8):722-31. doi: 10.1016/j.jpain.2008.03.006. Epub 2008 May 12

References:

133 “Nutritional status in patients with rheumatoid arthritis”. Annals Rheumatic Disease 1984;43:386-390 doi:10.1136/ard.43.3.386

134 Mielants H, Veys EM, Cuvelier C, De Vos M. Course of gut inflammation in spondylarthropathies and therapeutic consequences. Baillieres Clin Rheumatol. 1996 Feb;10(1):147-64

135 Satoh H, Urushidani T. Soluble Dietary Fiber Can Protect the Gastrointestinal Mucosa Against Nonsteroidal Anti-Inflammatory Drugs in Mice. Dig Dis Sci. 2016 Jul;61(7):1903-14

136 Jin J, Wu F, Xiao Z, Liu Z, Xie X, Zhou H. [Preventive effect of misoprostol against nonsteroidal anti-inflammatory drug-induced enteropathy in mice]. Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi. 2015 Jul;31(7):928-32. Chinese

137 Amagase K, Nakamura E, Kato S, Takeuchi K. [Glutamate as a potential protective drug in the gastrointestinal mucosa]. Yakugaku Zasshi. 2015;135(6):779-82. doi: 10.1248/yakushi.14-00250-3

138 Ueda T, Hokari R, Higashiyama M, Yasutake Y, Maruta K, Kurihara C, Tomita K, Komoto S, Okada Y, Watanabe C, Usui S, Nagao S, Miura S. Beneficial effect of an omega-6 PUFA-rich diet in non-steroidal anti-inflammatory drug-induced mucosal damage in the murine small intestine. World J Gastroenterol. 2015 Jan 7;21(1):177-86

139 Brzozowski B, Mazur-Bialy A, Pajdo R, Kwiecien S, Bilski J, Zwolinska-Wcislo M, Mach T, Brzozowski T. Curr Neuropharmacol. 2016;14(8):892-900 Mechanisms by which Stress Affects the Experimental and Clinical Inflammatory Bowel Disease (IBD): Role of Brain-Gut Axis.

140 "African Journal of Food Science" Article Number - 4218DCC61625, Vol.10(12), pp. 374-378, December 2016, DOI: 10.5897/AJFS2016.1479, ISSN: 1996-0794

141 Han M, Song P, Huang C, Rezaei A, Farrar S, Brown MA, Ma X. Dietary grape seed proanthocyanidins (GSPs) improve weaned intestinal microbiota and mucosal barrier using a piglet model. Oncotarget. 2016 Nov 18.

142 Chen H, Mao X, He J, Yu B, Huang Z, Yu J, Zheng P, Chen D. Dietary fibre affects intestinal mucosal barrier function and regulates intestinal bacteria in weaning piglets. Br J Nutr. 2013 Nov;110(10):1837-48

143 Barnett AM, Roy NC, McNabb WC, Cookson AL. Food Funct. 2012 Jul;3(7):690-9. doi: 10.1039/c2fo30017f. Review. The interactions between endogenous bacteria, dietary components and the mucus layer of the large bowel

144 Gulcicek OB, Solmaz A, Yiğitbaş H, Ercetin C, Yavuz E, Ozdogan K, Arici S, Akkalp AK, Sarac T, Çelebi F, Celik A. Comparison of the Effects of Glutamine, Curcumin, and Nesfatin-1 on the Gastric Serosal Surface Neomucosa Formation: An Experimental Rodent Model. Gastroenterol Res Pract. 2016;2016:2081962

145 Xun W, Shi L, Zhou H, Hou G, Cao T, Zhao C. Effects of curcumin on growth performance, jejunal mucosal membrane integrity, morphology and immune status in weaned piglets challenged with enterotoxigenic Escherichia coli. Int Immunopharmacol. 2015 Jul;27(1):46-52

146 Yao Q, Ye X, Wang L, Gu J, Fu T, Wang Y, Lai Y, Wang Y, Wang X, Jin H, Guo Y. Protective effect of curcumin on chemotherapy-induced intestinal dysfunction. Int J Clin Exp Pathol. 2013 Oct 15;6(11):2342-9

147 Shu X, Zhang J, Wang Q, Xu Z, Yu T. Exp Ther Med. 2016 Sep;12(3):1367-1372 Glutamine decreases intestinal mucosal injury in a rat model of intestinal ischemia-reperfusion by downregulating HMGB1 and inflammatory cytokine expression.

148 Chaudhry KK, Shukla PK, Mir H, Manda B, Gangwar R, Yadav N, McMullen M, Nagy LE, Rao R. J Nutr Biochem. 2016 Jan;27:16-26 Glutamine supplementation attenuates ethanol-induced disruption of apical junctional complexes in colonic epithelium and ameliorates gut barrier dysfunction and fatty liver in mice.

149 “Enzyme Nutrition” by Dr. Edward Howell. ISBN 9780895292216. 28 January 1995, Penguin Publishing Group

References:

150 Hänninen O, Rauma AL, Kaartinen K, Nenonen M. Acta Physiol Hung. 1999;86(3-4):171-80. Review Vegan diet in physiological health promotion

151 Rovenská E, Svík K, Stancíková M, Rovenský J. Clin Exp Rheumatol. 2001 May-Jun;19(3):303-9. Inhibitory effect of enzyme therapy and combination therapy with cyclosporin A on collagen-induced arthritis

152 Abnormal intestinal permeability and microbiota in patients with autoimmune hepatitis. Lin R, Zhou L, Zhang J, Wang B. Int J Clin Exp Pathol. 2015 May 1;8(5):5153-60.

153 The intestinal microbiome, barrier function, and immune system in inflammatory bowel disease: a tripartite pathophysiological circuit with implications for new therapeutic directions. Vindigni SM, Zisman TL, Suskind DL, Damman CJ. Therap Adv Gastroenterol. 2016 Jul;9(4):606-25.

154 Arthritis susceptibility and the gut microbiome. Taneja Veena. FEBS Lett. 2014 Nov 17;588(22):4244-9. doi: 10.1016/j.febslet.2014.05.034. Review.

155 Roles of the gut in the metabolic syndrome: an overview. Fändriks L. J Intern Med. 2016 Dec 19.

156 Gut permeability is related to body weight, fatty liver disease, and insulin resistance in obese individuals undergoing weight reduction. Damms-Machado A, Louis S, Schnitzer A, Volynets V, Rings A, Basrai M, Bischoff SC. Am J Clin Nutr. 2017 Jan;105(1):127-135.

157 The role for gut permeability in the pathogenesis of type 1 diabetes--a solid or leaky concept? Li X, Atkinson MA. Pediatr Diabetes. 2015 Nov;16(7):485-92.

158 Craig WJ, Mangels AR; American Dietetic Association. Position of the American Dietetic Association: vegetarian diets. J Am Diet Assoc 2009 Jul;109(7):1266-82. DOI: https://doi.org/10.1016/j.jada.2009.05.027.

159 Farmer B, Larson BT, Fulgoni VL III, Rainville AJ, Liepa GU. A vegetarian diet pattern as a nutrient-dense approach to weight management: an analysis of the national health and nutrition examination survey 1999-2004. J Am Diet Assoc 2011 Jun;111(6):819-27. DOI: https://doi.org/10.1016/j.jada.2011.03.012.

160 Peters MJ, Symmons DP, McCarey D et al. EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis 2010;69:325–31.

161 Meune C, Touze E, Trinquart L, Allanore Y. Trends in cardiovascular mortality in patients with rheumatoid arthritis over 50 years: a systematic review and meta-analysis of cohort studies. Rheumatology 2009;48:1309–13.

162 Avina-Zubieta JA, Choi HK, Sadatsafavi M et al. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. Arthritis Rheum 2008;59:1690–7.

163 Orlich MJ, Singh PN, Sabaté J, et al. Vegetarian dietary patterns and mortality in Adventist Health Study 2. JAMA Intern Med 2013 Jul 8;173(13):1230-8. DOI: https://doi.org/10.1001/jamainternmed.2013.6473.

164 Rosell M, Appleby P, Spencer E, Key T. Weight gain over 5 years in 21,966 meat-eating, fish-eating, vegetarian, and vegan men and women in EPIC-Oxford. Int J Obes (Lond) 2006 Sep;30(9):1389-96. DOI: https://doi.org/10.1038/sj.ijo.0803305.

165 Ornish D. Statins and the soul of medicine. Am J Cardiol 2002 Jun 1;89(11):1286-90. DOI: https://doi.org/10.1016/S0002-9149(02)02327-5.

166 Jenkins DJ, Kendall CW, Marchie A, et al. Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants. Am J Clin Nutr 2005 Feb;81(2):380-7.

167 Barnard ND, Cohen J, Jenkins DJ, et al. A low-fat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74-wk clinical trial. Am J Clin Nutr 2009 May;89(5):1588S-1596S. DOI: https://doi.org/10.3945/ajcn.2009.26736H.

168 Huang T, Yang B, Zheng J, Li G, Wahlqvist ML, Li D. Cardiovascular disease mortality and cancer incidence in vegetarians: a meta-analysis and systematic review. Ann Nutr Metab 2012;60(4):233-40. DOI: https://doi.org/10.1159/000337301.

169 Tuso PJ, Ismail MH, Ha BP, Bartolotto C. Nutritional update for physicians: plant-based diets. Perm J 2013 Spring;17(2):61-6. DOI: https://doi.org/10.7812/TPP/12-085.

170 Tonstad S, Butler T, Yan R, Fraser GE. Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. Diabetes Care 2009 May;32(5):791-6. DOI: https://doi.org/10.2337/dc08-1886.

171 Appleby PN, Davey GK, Key TJ. Hypertension and blood pressure among meat eaters, fish eaters, vegetarians and vegans in EPIC-Oxford. Public Health Nutr 2002 Oct;5(5):645-54. DOI: https://doi.org/10.1079/PHN2002332.

172 Ferdowsian HR, Barnard ND. Effects of plant-based diets on plasma lipids. Am J Cardiol 2009 Oct 1;104(7):947-56. DOI: https://doi.org/10.1016/j.amjcard.2009.05.032.

173 Ornish D, Scherwitz LW, Billings JH, et al. Intensive lifestyle changes for reversal of coronary heart disease. JAMA 1998 Dec 16;280(23):2001-7. DOI: https://doi.org/10.1001/jama.280.23.2001.

174 Esselstyn CB Jr, Gendy G, Doyle J, Golubic M, Roizen MF. A way to reverse CAD? J Fam Pract 2014 Jul;63(7):356-364b.

175 Barnard ND, Cohen J, Jenkins DJ, et al. A low-fat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74-wk clinical trial. Am J Clin Nutr 2009 May;89(5):1588S-1596S. DOI: https://doi.org/10.3945/ajcn.2009.26736H.

176 Faecal microbial flora and disease activity in rheumatoid arthritis during a vegan diet. Br J Rheumatol. 1997 Jan;36(1):64-8. Peltonen R1, Nenonen M, Helve T, Hänninen O, Toivanen P, Eerola E.