# Mosaic of Autoimmunity

Subjects: Nutrition & Dietetics

Contributor: Mrinalini Dey , Maurizio Cutolo , Elena Nikiphorou

The “mosaic of autoimmunity” was a term originally coined by Shoenfeld and Isenberg in 1989, and refers to the interplay between genetic, hormonal, immunological, and environmental factors in the pathogenesis of autoimmune diseases, including RA [1].

Mosaic of Autoimmunity | Rheumatoid arthritis | nutrition | autoimmunity | rheumatic diseases

## 1. Introduction

Rheumatoid arthritis (RA) is a chronic, systemic, immune-inflammatory disease, with a complex aetiology, including genetic, environmental, and endogenous triggers [2][3]. Factors such as cigarette smoking, infectious agents, environmental pollution, and chronic stress have been cited as possible triggers for the intense inflammatory response and production of pro-inflammatory mediators seen in RA [4][5][6][7]. In recent years, there has been increasing evidence for the role of nutrition in RA disease onset and activity, although this has failed to filter down to clinical awareness and practice as an adjunct to pharmacological treatments [8][9]. This includes the important role played by beverages and their rich nutritional content [3].

Dietary habits have important effects on human health, for example in hypertension, diabetes, and heart disease [10]. Beverages in particular are a source of a vast array of nutrients, from vitamins and minerals to fats and proteins. In addition to their practical necessity, they have been central to our functioning as humans on a psychosocial level throughout history, from wine consumption in Ancient Rome, to the introduction of afternoon tea in the 1800s, to our modern ritualistic morning coffee or weekend pint of beer with friends. Therefore, from a socio-cultural point of view, beverages serve more than to simply rehydrate or provide nutritional gains. It is therefore unsurprising that research on the role of beverages in the pathogenesis of RA has increased, especially over the last decade, and it stands to reason that clinicians can and should do more to harness this increasing body of evidence in disease management.

Despite being an important and relevant topic, nutrition remains poorly taught through most medical curriculums. The role of the dietician in the multidisciplinary team is important and recognised at least by some, but not always possible. In addition, the controversy surrounding the role of nutrition in RA and a generally poor understanding of the literature mean patients can receive conflicting and confusing information. Meanwhile, we continue to move towards an era of personalised medicine, which includes the consideration of dietary and nutritional needs, and their impact on the individual patient.

## 2. The Mosaic of Autoimmunity in RA and the Role of Nutrition

In recent decades, our understanding of genetic factors in the development of autoimmune conditions has progressed remarkably. Studies in monozygotic twins have demonstrated very high levels (four time or higher) of concordance in not just RA, but other autoimmune conditions such as type 1 diabetes mellitus, systemic lupus erythematosus, and multiple sclerosis [11]. The discovery of human leukocyte antigen (HLA) associations in multiple diseases (e.g., HLA-DR4 and DR1 in RA) has added to our understanding of the genetic basis of disease. However, the incomplete correlation in genotype and disease expression even in monozygotic twins highlights the fact that aetiology is due to more than just genetics [10].

Indeed, several recent studies report on a potential link between dietary factors and alterations in epigenetic pathways, providing compelling insight into the possible effects of environmental factors on fundamental biological processes and aetiology of autoimmune diseases [12]. For example, among beverages, both tea and coffee have been suggested to play an important role in modulating disease risk in humans, mediated by changes in DNA methylation, thereby suppressing tumour progression, decreasing inflammation, and influencing oestrogen metabolism [13].

Many environmental factors have been investigated for their possible role in the development of autoimmune disease. Dietary habits have long been implicated in the development of diseases such as hypertension, heart disease, and cancer [14][15][16]. Specifically, certain beverages, such as sugar-sweetened drinks, have been found to be associated with higher rates of diseases including stroke, hypertension, and chronic kidney disease [17][18][19].

## 3. Conclusions

Beverages are integral to our lives, whether for rehydration, socialising, or as one element of our rich and varied diets. However, with a surprisingly high and diverse nutritional contents, beverages can contribute many benefits for patients with RA, although in some cases may do more harm than good. In fact, as with all food groups, some yield more positive effects than others, and it is particularly important to be aware of the high sugar content of some beverages, especially given the potential for poor cardiovascular outcomes and features of metabolic syndrome in RA patients. Nonetheless, some of our favourite beverages, such as tea, fresh fruit juice, and even moderate amounts of red wine, can confer benefits at the molecular, epigenetic, and clinical level when taken in conjunction with traditional therapies. The growing evidence base for correct nutrition in RA and global health benefits of a healthy diet highlights the need for improved access to dietary counselling for patients, whether this be with a dietician or the physician. In this regard, it is promising that large organisations, including the European League Against Rheumatism (EULAR), have recognised the importance of diet and nutrition in RA, leading to the development of new educational initiatives such as a recent teaching module for online courses dedicated to nutrition and rheumatic diseases [20]. Increased patient and clinician awareness of the role of beverages in RA has the potential to improve the dietary and lifestyle guidance we are able to provide, with positive impacts for the holistic management of patients.

## References


1. Shoenfeld, Y.; Isenberg, D.A. The mosaic of autoimmunity. Immunol. Today 1989, 10, 123–126.
2. Jawaheer, D.; Seldin, M.F.; Amos, C.I.; Chen, W.; Shigeta, R.; Etzel, C.; Damle, A.; Xiao, X.; Chen, N.; Lum, R.F.; et al. Screening the genome for rheumatoid arthritis susceptibility genes: A replication study and combined analysis of 512 multicase families. Arthritis Rheum. 2003, 48, 906–916.
3. Cutolo, M.; Nikiphorou, E. Don’t neglect nutrition in rheumatoid arthritis! RMD Open 2018, 4, e000591.
4. Silman, A.J.; Pearson, J.E. Epidemiology and genetics of rheumatoid arthritis. Arthritis Res. 2002, 4, S265–S272.
5. Catrina, A.I.; Deane, K.D.; Scher, J.U. Gene, environment, microbiome and mucosal immune tolerance in rheumatoid arthritis. Rheumatology 2014, 55, 391–402.
6. Liu, X.; Tedeschi, S.K.; Barbhaiya, M.; Leatherwood, C.L.; Speyer, C.B.; Lu, B.; Costenbader, K.H.; Karlson, E.W.; Sparks, J.A. Impact and Timing of Smoking Cessation on Reducing Risk of Rheumatoid Arthritis Among Women in the Nurses’ Health Studies. Arthritis Rheum. 2019, 71, 914–924.
7. Walker, J.G.; Littlejohn, G.O.; McMurray, N.E.; Cutolo, M. Stress system response and rheumatoid arthritis: A multilevel approach. Rheumatology 1999, 38, 1050–1057.
8. Alunno, A.; Nikiphorou, E.; Philippou, E.; Daien, C.; Wiek, D.; Kouloumas, M.; Cutolo, M. Nutrition in RMDs: Is it really food for thought? Focus on rheumatoid arthritis. BMC Rheumatol. 2020, 4, 1–5.
9. Philippou, E.; Petersson, S.D.; Rodomar, C.; Nikiphorou, E. Rheumatoid arthritis and dietary interventions: Systematic review of clinical trials. Nutr. Rev. 2020.
10. Dahan, S.; Segal, Y.; Shoenfeld, Y. Dietary factors in rheumatic autoimmune diseases: A recipe for therapy? Nat. Rev. Rheumatol. 2017, 13, 348–358.
11. Cooper, G.S.; Miller, F.W.; Pandey, J.P. The role of genetic factors in autoimmune disease: Implications for environmental research. Environ. Health Perspect. 1999, 107, 693–700.
12. Zhang, Y.; Kutateladze, T.G. Diet and the epigenome. Nat. Commun. 2018, 9, 3375.
13. Ek, W.E.; Tobi, E.W.; Ahsan, M.; Lampa, E.; Ponzi, E.; Kyrtopoulos, S.A.; Georgiadis, P.; Lumey, L.H.; Heijmans, B.T.; Botsivali, M.; et al. Tea and coffee consumption in relation to DNA methylation in four European cohorts. Hum. Mol. Genet. 2017, 26, 3221–3231.
14. Fang, X.; Wei, J.; He, X.; An, P.; Wang, H.; Jiang, L.; Shao, D.; Liang, H.; Li, Y.; Wang, F.; et al. Landscape of dietary factors associated with risk of gastric cancer: A systematic review and dose-

response meta-analysis of prospective cohort studies. Eur. J. Cancer 2015, 51, 2820–2832.

15. Ozemek, C.; Laddu, D.R.; Arena, R.; Lavie, C.J. The role of diet for prevention and management of hypertension. Curr. Opin. Cardiol. 2018, 33, 388–393.
16. Ulbricht, T.L.V.; Southgate, D.A.T. Coronary heart disease: Seven dietary factors. Lancet 1991, 338, 985–992.
17. Jayalath, V.H.; De Souza, R.J.; Ha, V.; Mirrahimi, A.; Blanco-Mejia, S.; Di Buono, M.; Jenkins, A.L.; Leiter, L.A.; Wolever, T.M.S.; Beyene, J.; et al. Sugar-sweetened beverage consumption and incident hypertension: A systematic review and meta-analysis of prospective cohorts. Am. J. Clin. Nutr. 2015, 102, 914–921.
18. Pase, M.P.; Himali, J.J.; Beiser, A.S.; Aparicio, H.J.; Satizabal, C.L.; Vasan, R.S.; Seshadri, S.; Jacques, P.F. Sugar- and Artificially Sweetened Beverages and the Risks of Incident Stroke and Dementia: A Prospective Cohort Study. Stroke 2017, 48, 1139–1146.
19. Rebholz, C.M.; Young, B.A.; Katz, R.; Tucker, K.L.; Carithers, T.C.; Norwood, A.F.; Correa, A. Patterns of beverages consumed and risk of incident kidney disease. Clin. J. Am. Soc. Nephrol. 2018, 14, 49–56.
20. Cutolo, M.; Nikiphorou, E. EULAR Online Course on Rheumatic Diseases: Nutrition in Rheumatic Diseases. 2020, Module 42d. Available online: https://www.eular.org/edu_online_course.cfm (accessed on 29 August 2020).