

Introduction, Prerequisites & How to Use This Guide

Autoimmunity: A Growing Epidemic

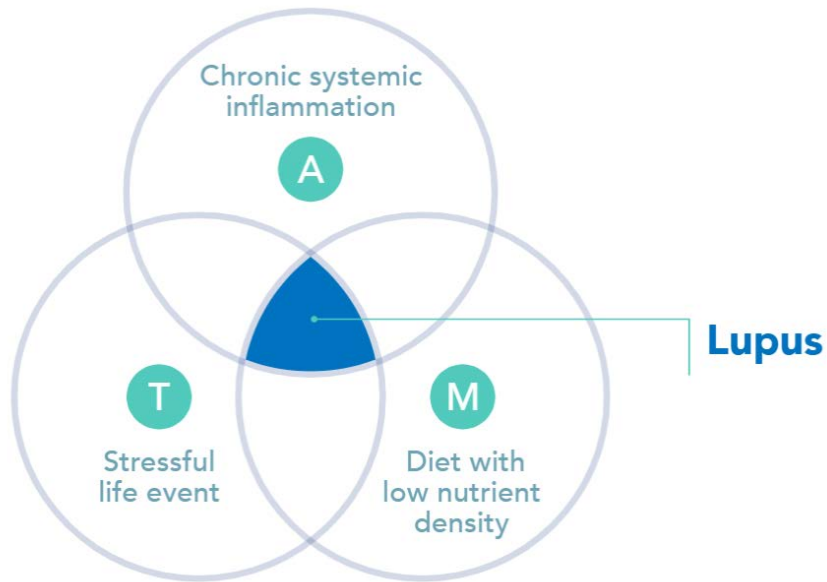
Autoimmune disease affects hundreds of millions of people worldwide, and its prevalence is increasing.ⁱ There are 100+ known autoimmune disease types. Some of the more prevalent include type 1 diabetes, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and inflammatory bowel disease (IBD).ⁱⁱ Incidence rates vary with estimates ranging from less than one newly diagnosed case of systemic sclerosis to more than 20 cases of adult-onset RA per 100,000 person-years; prevalence rates range from less than three per 100,000 (e.g., autoimmune hemolytic anemiaⁱⁱⁱ and uveitis) to more than 500 per 100,000 (Grave's disease, RA, and thyroiditis).^{iv} Researchers report autoimmune conditions are increasing in prevalence.^v

In the US, autoimmune disease annually affects 50 million people and costs over \$100 billion annually.^{vi,vii} Latent or pre-autoimmune disease often exists for 7–14 years before diagnosis. Nearly 80% of those affected with autoimmune disease are women.^{viii} Many autoimmune conditions are increasing, as indicated by increased rates of type 1 diabetes,^{ix,x} rheumatoid arthritis,^{xi,xii} and possibly psoriasis^{xiii} and lupus.^{xiv,xv,xvi} Furthermore, diagnosis of one autoimmune condition increases the likelihood of diagnosis for a second (or a third) by 25%–34%.^{xvii,xviii,xix,xx} This comorbidity is likely due to common underlying mechanisms across many autoimmune conditions.^{xxi}

Standard treatment approaches involve anti-inflammatory and immunosuppressive therapies, including nonsteroidal anti-inflammatory drugs (NSAIDs), salicylates, steroids, immune modulators, and biologic therapies. While these medications are often effective in suppressing symptoms and can be lifesaving in the short term, they can be expensive, have serious side effects,^{xxii,xxiii} and may not confer long-term remission.^{xxiv} Some patients suffer degraded quality of life even with treatment,^{xxv} and one-third of RA patients on biologics develop antibodies against the medication.^{xxvi} Biologics also have very low long-term retention rates, as low as 10% for RA patients after ten years.^{xxvii}

Alessio Fasano, MD, pediatric gastroenterologist and research scientist¹ proposes a causal autoimmune triad: genetic susceptibility, antigen exposure, and increased intestinal permeability.^{xxviii} Recently, advances in the...

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For a patient with a history of chronic systemic inflammation (an antecedent),^{xxix} an inflammatory diet^{xxx, xxxi, xxxii, xxxiii} can play a large role in mediating their health, and a psychological stressor^{xxxiv, xxxv, xxxvi} could act as a trigger for either developing systemic lupus erythematosus (SLE) or disease flares.

Nutrition Domain

Introduction

Patterns of food consumption over time have an enormous impact on overall health. Food intake patterns can be immunomodulating; for instance, switching to the Mediterranean diet can decrease inflammation, reduce T-cell activity, and downregulate lymphocytes and monocytes.^{xxxvii} Even in healthy patients, high-fat, high-carbohydrate meals increase immune activation transiently but significantly (specifically nuclear kappa B)^{xxxviii, xxxix} as well as increasing endotoxin concentrations.^{xl}

Dietary food choices and nutrient balance may trigger or mediate autoimmune phenomena via short-term and long-term effects on the immune system. For example, specific food antigens so often represent the most

significant trigger of autoimmune phenomena, and we have previously highlighted (in the Foundational Lifestyle Factors chapter) the need to immediately initiate a food plan that eliminates suspect antigens. This type of intervention will be addressed in full detail in the Antigens Domain of this Guide. This Nutrition Domain focuses on long-term nutritional influences on the immune system, most notably key excesses and deficiencies of macro- and micronutrients.

In the long term, the balance of macronutrients and micronutrients plays a foundational role in the development and perpetuation of autoimmune disease. Macronutrients (proteins, fats, and carbohydrates) provide much of the structure and energy substrate for life. Micronutrients (minerals, vitamins, and phytonutrients) provide the cofactors, adaptogens, and information-mediating molecules that promote balance and allostasis.

For many patients, nutritional factors can be antecedents, triggers, and mediators of autoimmune conditions. As a frontline intervention, personalized nutrition can dramatically alter the disease trajectory while improving overall health.

Recommendations

KEY CLINICAL RECOMMENDATIONS	STRENGTH OF RECOMMENDATION	REFERENCES
Recommend an anti-inflammatory diet high in phytonutrients and with low glycemic load.	C	xli, xlii, xliii, xlv, xlv, xlv, xlvii, xlviii, xlix
Perform a comprehensive functional nutrition evaluation to assess nutrient deficiencies and imbalances.	C	i, li, lii, liii, liv, lv
For appropriately selected patients, consider clinically supervised caloric restriction, intermittent fasting, and/or ketogenic diet.	C	lvi, lvii, lviii, lix, lx, lxi, lxii, lxiii, lxiv, lxv

WHAT NOT TO DO:

- Do not order laboratory tests of specific nutrients unless indicated by clinical symptoms or signs.
- Do not order nutritional supplements unless indicated by symptoms, signs, or diagnostic test results.

Autoimmune Intake Questionnaire: Interpretative Considerations

Disclaimer: The content in this interpretive guide is intended to serve as a starting point for thought processing about the implications of a patient's response to these questions. This is by no means meant to be all inclusive, or diagnostic for any one patient, nor is it intended to remove the need for thorough assessment, physical exam, and personalized treatment for every patient. Specific sections and questions for which there are no additional considerations provided are assumed to have clinical indications that are common knowledge.

NUTRITION

1. *What colors of foods (natural colors, not artificial) do you have during the following meal times? (Please check all colors that apply.)*

Considerations:

- Missing colors: Patients may not be getting all the nutrients and phytonutrients needed to maintain health.
- Over- or under-consuming one color of food: Lack of diversity in the diet can also lend toward nutrient excesses or deficiencies.
- Missing meals: Meal timing is an important consideration in maintaining health.

Consider addressing MLFs: Nutrition

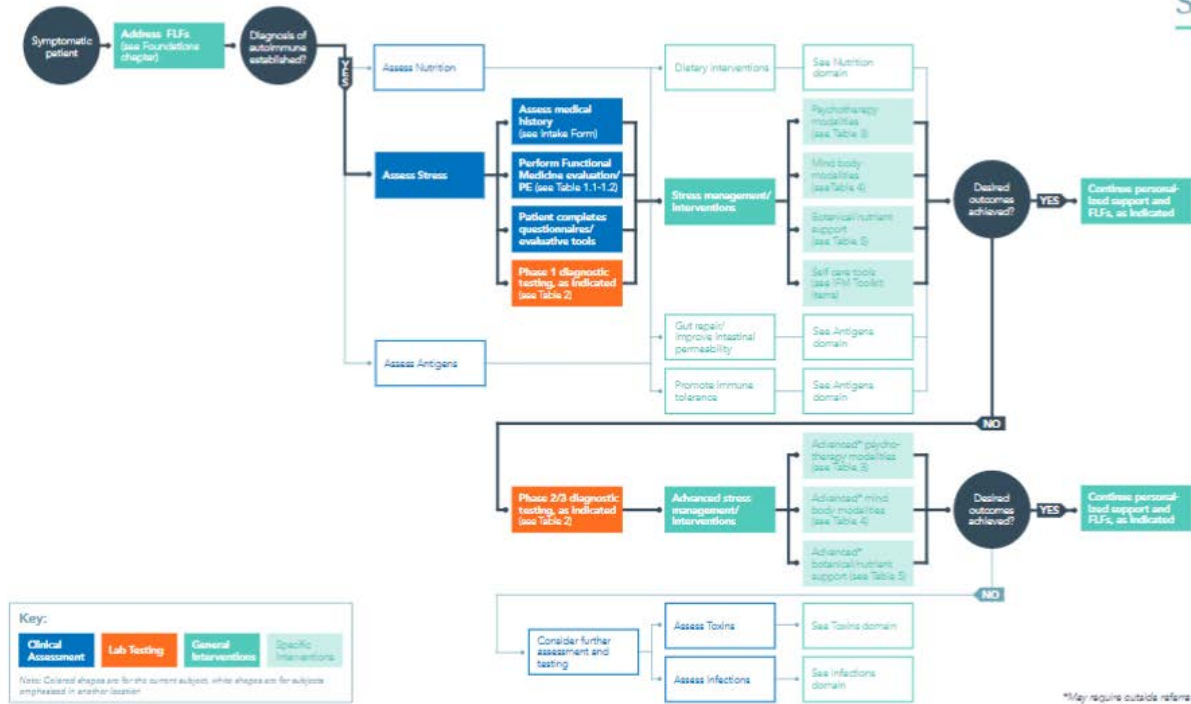
2. *How often do you add additional salt to your food?*

Considerations:

- Adverse effects on health: Frequent salt use can potentially impact blood pressure and lead to systemic imbalance (e.g., electrolyte imbalance, kidney disease, etc.).
- Potential loss of senses: As salt is a flavor enhancer, more frequent use can indicate the loss of taste or smell.

Stress: Table 2. Diagnostic Tests

CONCERN/ TEST	TEST	COMPANY	COST	REFERENCE RANGE	SIGNIFICANCE/ CONSIDERATIONS
PHASE 1 LABS					
Thyroid Studies	Hyperthyroid <ul style="list-style-type: none"> ■ Free T3 (fT3) ■ Free T4 (fT4) ■ Thyroid Stimulating Immunoglobulin (TSI) ■ TSH ■ TSH Receptor Ab (TRAb) If above abnormal, then: <ul style="list-style-type: none"> ■ Radioactive iodine uptake (RAIU) scan ■ Radioactive iodine uptake test (unless diagnosis of Grave's disease is established clinically) 	Many companies		Overt Hyperthyroidism <ul style="list-style-type: none"> ■ <0.38 mIU/L TSH ■ >4.2 pg/mL fT3 ■ >1.8 ng/dL fT4 ■ >1.75 IU/L TSH-receptor Ab (TRAb) 	If other tests are negative but the patient has warning signs or symptoms of hyperthyroidism, consider additional testing. If needed, a thyroid-stimulating immunoglobulin (TSI) test may be helpful.
	Hypothyroid Comprehensive thyroid profile: <ul style="list-style-type: none"> ■ Free T3 (fT3) ■ Free T4 (fT4) ■ rT3 ■ TPO ■ TSH ■ TG ab (serum) 	Many providers (e.g., Quest, LabCorp, etc.)		Optimal Ranges: <ul style="list-style-type: none"> ■ <0.38 mIU/L TSH ■ 1.2–4.9 mg/dL fT3 ■ 1.0–1.53 ng/dL fT4 ■ 13.5–34.2 ng/dL rT3 ■ 0.5–1.5 mIU/L TSH ■ <20 IU/mL Thyroglobulin Ab ■ <20 IU/mL Ab (TPO) Thyroid peroxidase 	



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