

# CLINICAL SUMMARY

## Evaluation of Adjunctive Nutritional Support Combining an Inflammatory-Modulating Medical Food, Reduced Iso-Alpha Acids (RIAA), Vitamin D, Selenium, Zinc, and Dietary Modifications in Patients with Autoimmune Conditions: Summary of Clinical Experience

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### Introduction

Autoimmune disorders are comprised of more than 80 distinct, chronic illnesses in which the body's compromised immune system fails to distinguish *self* from *non-self*, and include conditions such as Crohn's disease, ulcerative colitis, rheumatoid arthritis, Raynaud's phenomenon, erythromelalgia, and systemic lupus erythematosus. In addition, autoimmune disease can affect any system, organ, or tissue in the body such as the joints, gastrointestinal tract, kidneys, skin and other connective tissues, endocrine system, and nervous system.<sup>1-6</sup>

According to recent statistics, as many as 50 million Americans are thought to suffer from some form of autoimmune disease, with 8.5 million (or 1 in 31) individuals afflicted by the most common autoimmune disorders. Not surprisingly, autoimmune conditions collectively rank as the third most prevalent health complaint in the United States (U.S.), and the eighth leading cause of mortality for women between the ages of 15 and 64. While the cause(s) of these conditions remain largely unknown, research has shown that gender, race, and heredity are among the major risk factors for autoimmune disorders.<sup>7-8</sup>

Autoimmune disease remains a major problem in the U.S. and abroad despite an improvement in symptoms control through non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and disease-modifying antirheumatic drugs (DMARDs). Thus, the present direction of research into the development of new therapeutic agents emphasizes the identification of agents that can modulate the immune system, resulting in the ability to target specific cell types involved in the inflammatory response.

Interestingly, diet may represent a significant immune-modulating part of a patient's environmental exposure, and adjunctive diet strategy and counseling may have a noticeable impact on modifying the underlying inflammatory signals associated with autoimmune disorders. In support, the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) has noted that diet and lifestyle may have a considerable influence in the progression and potential management of autoimmune diseases.<sup>9</sup>

### *Chronic Inflammation, Nutritional Deficiencies, and Oxidative Stress: Three Key Factors in Autoimmune Diseases*

Several triggers and mediators considered to be critical in the autoimmune disease pathway have recently emerged as promising targets for condition management. In particular, chronic inflammation, nutritional deficiencies, and oxidative stress are believed to be involved in the pathogenesis of autoimmune disorders.

Mounting scientific evidence indicates that inflammation is intrinsic to autoimmune conditions. In fact, during inflammation, an array of cytokines, eicosanoids, reactive oxygen species, and other mediators that can overwhelm and disrupt Th1/Th2 balance are released, which can potentially damage body tissues.<sup>10-13</sup> Furthermore, common nutritional deficiencies have been associated with abnormal autoimmune response. For example, inadequate vitamin D intake has been linked to a higher risk of autoimmune diseases.<sup>14-16</sup> The roles of selenium and zinc have also been the source of heightened interest because of the participation of these nutrients in metabolic processes involving joint tissues and immune system function.<sup>17-21</sup>

Additionally, accumulating data suggest that oxidative stress may trigger autoimmune symptoms in susceptible individuals by inducing pro-inflammatory cytokines, activating macrophages, and stimulating cellular proliferation.<sup>22-23</sup>

### *Natural Adjunctive Therapies for Autoimmune Disorders*

The goal of a natural approach is not to simply address the symptoms, but to offer safe and effective disease management strategies for patients by targeting the core issues implicated in the progression of autoimmune disorders. Optimal nutritional programs have also been proposed to help reduce the risk of autoimmune conditions in some genetically predisposed populations.

The purpose of this clinical summary is to present results from a series of selected case histories that demonstrate how nutritional support utilizing an anti-inflammatory medical food, targeted nutraceuticals, and dietary changes may benefit patients with autoimmune conditions. This nutritional program promoted optimal immune system balance and health of body tissues.

### Patients and Methods

Case summaries of 10 female patients presenting with autoimmune disorders who received adjunctive nutritional support at the Functional Medicine Research Center<sup>SM</sup> (FMRC) are presented (**Table 1**). Patients ranged in ages from 40 to 59, and the follow-up period ranged from 10 to 30 weeks.

During the course of observation, all patients received dietary counseling, and a daily regimen comprised of an inflammatory-modulating medical food, RIAA (450-900 mg), vitamin D (1000-2000 IU), selenium (100-200 mcg), and zinc (10-20 mg). To measure the possible effects of the aforementioned nutritional support, the Medical Symptoms Questionnaire (MSQ) scores were obtained from all 10 subjects, and the Medical Outcomes Study Short-Form 36 (MOS SF-36) health survey data were assessed in 9 participants. The MOS survey was incomplete for 1 patient (case no. 091RA1105).

### Results

The MSQ scores from all 10 cases demonstrated greater than 45% improvement in subjective symptoms (**Table 1**). The physical component summary of MOS SF-36 from 9 subjects displayed an improved or optimized response in physical status. Moreover, improvement, optimization, and maintenance of mental status were indicated in 8 of the 9 patients, while 1 case showed evidence of worsened condition.

### Conclusion

The overall outcome of these 10 clinical observations suggest that a tailored adjunctive approach incorporating an inflammatory-modulating medical food, RIAA, vitamin D, selenium, and zinc in conjunction with dietary changes and standard medical therapies may help to promote function and well-being in patients with underlying issues of immune system imbalance, thereby reducing the intensity of subjective symptoms in these patients.

**Table 1.** Functional significance of nutritional support featuring a combination of an inflammatory -modulating medical food, RIAA, vitamin D, selenium, zinc, and dietary modifications in patients with autoimmune conditions.

<i>Patient* and Therapy Description</i>			<i>MSQ<sup>†</sup></i>			<i>MOS-PCS<sup>‡</sup></i>			<i>MOS-MCS<sup>‡</sup></i>		
<u>Age</u>	<u>Condition**</u>	<u>Follow-Up Period</u>	<u>Initial Evaluation</u>	<u>Final Evaluation</u>	<u>Percent Improvement</u>	<u>Initial Evaluation</u>	<u>Final Evaluation</u>	<u>Physical Response<sup>§</sup></u>	<u>Initial Evaluation</u>	<u>Final Evaluation</u>	<u>Mental Response<sup>§</sup></u>
57	CD	22 weeks	39	10	74.4 %	44.4 (@ 3 weeks)	51.3 (@ 16 weeks)	Optimized	47.9 (@ 3 weeks)	57.3 (@ 16 weeks)	Optimized
56	CD	30 weeks	84	6	92.9%	35.3	40.6	Improved	45.0	55.1	Optimized
47	UC	10 weeks	48	8	83.3%	40.6	52.6	Optimized	60.5	63.4	Maintained
51	RA	25 weeks	21	9	57.1%	38.7 (@ 3 weeks)	55.3	Optimized	55.6 (@ 3 weeks)	62.1	Maintained
51	RA	20 weeks	43	23	46.5%	26.5	35.9 (@ 16 weeks)	Improved	27.4	45.2 (@ 16 weeks)	Improved
52	RA	18 weeks	14	4	71.4%		—			—	
59	RA	16 weeks	52	9	82.7%	41.6 (@ 2 weeks)	52.0	Optimized	35.7 (@ 2 weeks)	45.7	Improved
54	RP	22 weeks	33	8	75.8%	49.2 (@ 2 weeks)	53.4 (@ 17 weeks)	Optimized	61.1 (@ 2 weeks)	14.2 (@ 17 weeks)	Worsened
44	RP & EM	16 weeks	24	5	79.2%	16.6	47.0	Improved	53.7	56.9	Maintained
40	SLE	19 weeks	23	8	65.2%	33.7	52.3 (@ 9 weeks)	Optimized	58.3	56.3 (@ 9 weeks)	Maintained

\* Case No: 092CD1105; 100CD0106; 099UC1105; 090RA1105; 093RA1105; 091RA1105; 097RA206; 094RD1105; 095EM1105; 098SLE1105

\*\*CD: Crohn's Disease; UC: Ulcerative Colitis; RA: Rheumatoid Arthritis; RP: Raynaud's Phenomenon; EM: Erythromelalgia; SLE: Systemic Lupus Erythematosus

<sup>†</sup>The MSQ is a clinical tool for the evaluation of general physical symptoms. Total scores above 75 are generally associated with substantial symptomatology and disability, and scores below 30 generally indicate few or low intensity symptoms.

<sup>‡</sup>The MOS SF-36 is a well-validated general quality of life questionnaire that summarizes health outcome in two reliable reproducible scores: The Physical Component Summary (PCS) and the Mental Component Summary (MCS). On a scale of 0-100, 50 is the mean for the US. Higher scores are associated with healthier individuals.

<sup>§</sup>"Optimized": Positive change from initial score below 50 to final score of 50 and above; "Improved": Positive change from initial to final scores below 50;

"Maintained": Positive/negative change from initial to final scores of 50 and above; "Worsened": Negative change from initial score of 50 and above to final score below 50.

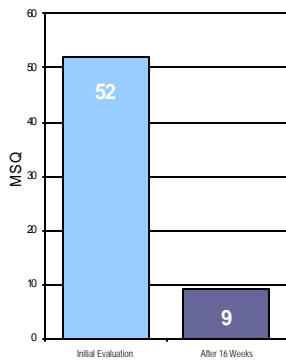
### Case Study Highlight #1 (Case #097RA206)

A 59-year-old female presented with a previous diagnosis of rheumatoid arthritis and osteoarthritis, for which she was currently under the care of a rheumatologist and taking medications, including methotrexate and hydroxychloroquine. Chief complaints included pain in wrists, fingers, feet and ankles, stiffness, and body ache 3-4 times per day (each episode in duration of 30-60 minutes) accompanied with fatigue.

At the initial clinic visit, laboratory tests revealed positive anti-nuclear antibody; elevated rheumatoid factor and female hormones; and evidence of *Candida albicans* in stool. The patient received a daily adjunctive regimen of an inflammatory-modulating medical food, RIAA (900 mg), vitamin D<sub>3</sub> (2000 IU), selenium (200 mcg), and zinc (20 mg). In addition, 3 softgels twice daily of a supplement combination of EPA-DHA (300 mg and 200 mg, respectively), and a probiotic were added at the 2-week time point. After 8 weeks, the patient reported 75% improvement in pain and fatigue. Sensitivity to gluten was discovered and the patient was placed on an elimination diet, with no other changes to the prescribed protocol. Following 16 weeks of recommended nutritional support and diet, the patient's subjective pain and mental well-being symptoms had dramatically improved as indicated by the MSQ, AIMS-2 (the new Arthritis Impact Measurement Scales), and MOS-MCS scores, respectively, shown in Figures 1-3. The patient was considered in remission by her rheumatologist and taken off methotrexate.

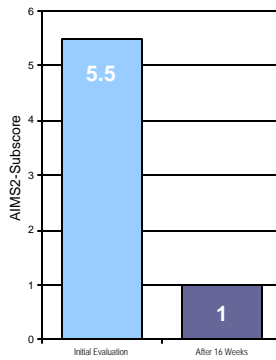
**Figure 1.** The MSQ score substantially decreased from 52 to 9 after 16 weeks of nutritional support and diet.

#### 83% Improvement in Symptoms



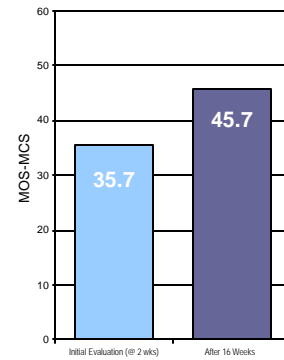
**Figure 2.** The AIMS2 symptoms subscore significantly decreased from 5.5 to 1.0 after 16 weeks of nutritional support and diet.

#### 82% Improvement in Symptoms



**Figure 3.** The MOS-MCS score notably increased from 35.7 (at 2 weeks) to 45.7 after 16 weeks of nutritional support and diet.

#### Substantial Improvement of Mental Score



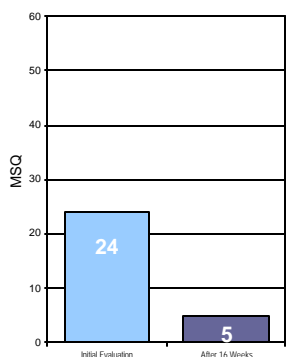
### Case Study Highlight #2 (Case #095EM1105)

A 44-year-old female presented with a history of erythromelalgia and Raynaud's phenomenon, for which she was currently taking medications under the care of a rheumatologist. Chief complaints included hot painful feet, cold painful fingers, increased fatigue, abdominal bloating, and indigestion, as well as asthma and migraines. The subject's past medical conditions included mycoplasma pneumonia, anemia, bronchitis, and mononucleosis.

At the initial clinic visit, laboratory tests revealed elevated lactulose recovery and lactulose/mannitol ratio; increased ALT; and low-to-normal level of 25-OH vitamin D. Initially, the patient was placed on an elimination diet, and received vitamin D<sub>3</sub> (2000 IU) with isoflavones, 2 softgels bid of a supplement combination of EPA-DHA (300 mg and 200 mg, respectively), and vitamin B<sub>12</sub>/folate combination supplement. At the 5-week time point, the patient was instructed to begin a daily adjunctive regimen of an inflammatory-modulating medical food, RIAA (450 mg), vitamin D (1000 IU), selenium (100 mcg), and zinc (10 mg). After only 5 weeks, the patient noted 100% reduction in hand pain and migraines. Following up on positive results for gluten sensitivity and lack of beneficial intestinal bacteria, the subject was placed on a gluten-free diet and probiotics. After 12 weeks of the recommended nutritional support and diet, all pain medications were stopped and the patient was able to stand on her feet. Following 16 weeks of the program, the subject was able to walk for extended periods without pain. During final evaluation, the patient's subjective pain and physical well-being symptoms had dramatically improved as indicated by the MSQ and MOS-PCS scores, while maintaining her healthy mental status, respectively, as seen in Figures 1-3.

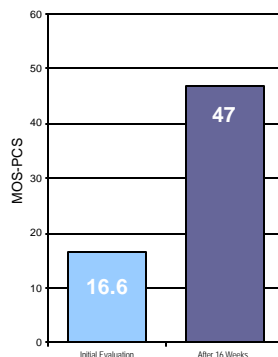
**Figure 1.** The MSQ score significantly decreased from 24 to 5 after 16 weeks of nutritional support and diet.

#### 79.2% Improvement in Symptoms



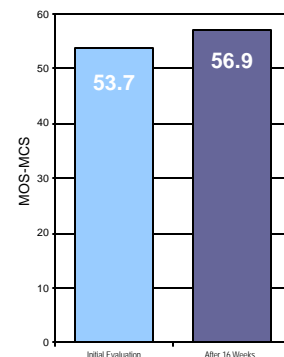
**Figure 2.** The MOS-PCS score substantially increased from 16.6 to 47 after 16 weeks of nutritional support and diet.

#### Substantial Improvement of Physical Score



**Figure 3.** The MOS-MCS score increased from 53.7 to 56.9 after 16 weeks of nutritional support and diet.

#### Maintenance of Healthy Mental Score



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## Note

The information provided in each of the case studies presented in this summary describes the results of one patient under the care of a licensed healthcare practitioner and may not be a typical response.

This study was provided by Jack Kornberg, MD and Robert H. Lerman, MD, PhD, and conducted at the Functional Medicine Research Center<sup>SM</sup> (FMRC), the clinical research arm of Metagenics, Inc. The methodology and results of these case studies were reviewed by FMRC. Financial support for this study was provided by Metagenics, Inc.