

# Patient Report: Evidence that Intravenous Administration of Glutathione and Vitamin C Relieved Acute Pain from Rheumatoid Arthritis Flare

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## Abstract

Rheumatoid arthritis (RA) is classified as an autoimmune disease, with underlying inflammation and oxidative stress. While some patients go into remission, most RA patients experience occasional bouts of intense disease activity in a specific joint or multiple joints, called flares. No single cause of RA flares has yet been identified. RA patients have exhibited reduced antioxidant levels, including glutathione and vitamin C. Vitamin C levels have been inversely correlated with disease activity markers. Administration of glutathione and vitamin C intravenously induced a rapid reduction in acute pain from an RA patient flare.

## Introduction

Rheumatoid arthritis (RA) is classified as an autoimmune disease. Characteristics of RA include painful, swollen joints (especially wrists, finger joints near palm, balls of feet, toes, knees, etc.), a symmetrical pattern of affected joints, stiffness lasting over 30-60 min in the morning or after inactivity, elevated blood markers of inflammation, and often antibodies called RF factor and anti-CCP. While some patients go into remission, most RA patients experience occasional flares, which are increased bouts of disease activity in a specific joint or multiple joints. Traditionally, treatment has involved changes in the dosing, and/or types of allopathic

medication, chiropractic adjustment, complementary modalities (homeopathic remedies, acupuncture, herbals, bioenergy adjustment, etc.) as well as improved nutrition, meditation, and exercise.

Most RA patients have the hallmarks of oxidative stress with significantly raised levels of inflammatory oxidized fats called lipid peroxidation,<sup>1-3</sup> an overabundance of reactive oxygen species, and insufficient levels of antioxidants<sup>3-5</sup> in the blood and joints.<sup>6-8</sup> In addition, most RA patients exhibit significantly lower serum levels of total antioxidant capacity in their blood, including antioxidant vitamins A, C, and E and the mineral selenium, than healthy controls.<sup>3,9,10</sup> Interestingly, the level of vitamin C in the plasma was inversely correlated with markers of disease activity.<sup>11</sup> In other words, patients with higher vitamin C levels in the blood had less disease activity.<sup>11</sup> The balance between antioxidant defense and oxidant production is essential for healthy cell function and is maintained by four major redox pairs. Oxidative stress in the cell reflects a reduced antioxidant capability and usually has indicated insufficient levels of glutathione because glutathione is the most abundant free thiol in cells.<sup>12,13</sup>

The concentrations of glutathione (GSH) and its oxidized partner GSSH are regulated by the glutathione pathways, which include the enzymes glutathione reductase, glutathione peroxidases, and glutathione-S-transferases (GST). RA patients have exhibited significantly lower levels of glutathione,<sup>14,15</sup> glutathione peroxidase,<sup>1,3,10,15,16</sup> and glutathione

reductase in the blood<sup>1</sup> in comparison to healthy controls. The intracellular glutathione concentration in leukocytes was also significantly reduced.<sup>13</sup> Synovial fluids of RA patients contained a 30-fold increase in collagenase and elastase activities, which degrade the joint tissue, but only a threefold boost in glutathione reductase levels.<sup>17</sup> These synovial fluids still exhibited the presence of oxidative stress.<sup>17</sup> Recently, patients with a null genotype at GSTM1 locus (which encodes a type of glutathione-S-transferase) had a significantly increased relative risk of RA and RA severity.<sup>18,19</sup> Glutathione (GSH) and its redox partner, GSSH, also play a major role in detoxification and immune function.

A small clinical trial has shown that RA patients benefited from antioxidant supplementation.<sup>14</sup> In addition, intravenous (IV) vitamin C treatment has improved patients with acute inflammation, including pancreatitis<sup>20</sup> and Hepatitis C virus infections.<sup>21</sup> Intravenous administration of glutathione has decreased the toxicity of several chemotherapy regimens<sup>22-26</sup> and did not induce any novel toxicities. Below, we describe an RA patient's response to IV-administered ascorbic acid and glutathione.

## Material and Methods

Glutathione (200 mg/ml) and ascorbic acid (15 g in 0.5 L sterile PBS) were obtained from Hopewell Pharmacy (Hopewell, New Jersey) and McGuff Pharmaceuticals, (Santa Ana, California), respectively. Ascorbic acid, also called vitamin C in this and other reports, was administered at 4 to

6 ml / min. Glutathione (600 mg) was administered as bolus near completion of ascorbic acid administration.

### Patient Report

A female RA patient (48 yr, > 30 yr RA history) presented with X-ray evidence of prominent, chronic erosive changes in left elbow with joint space narrowing and spur formation. Clinically, the left elbow was very tender, hot, and swollen with minimal movement. Patient was intravenously administered ascorbic acid in 0.5 L sterile PBS, followed by glutathione. The patient observed that the first treatment stopped the acute, throbbing rheumatoid arthritis pain for more than six hours. Although some pain returned within a day or two, it was diminished. A subsequent eight treatments provided further relief. Thereafter, the patient was initially administered glutathione (600 mg) intramuscularly (IM) weekly. Now, glutathione is administered IM on an as needed basis to quell flares.

### Discussion

Excess inflammation, oxidative stress, and autoimmune responses have been described as underlying disease characteristics of RA. The sudden onset of a flare presents difficult challenges for the patient and the clinician. While no single cause of RA flares has been identified, approaches that help reduce the oxidative stress of the RA patient and foster the healing process of the body with sufficient nutrients may be beneficial.

This patient report describes the rapid reduction of pain from an RA flare of a single patient by administration of ascorbic acid and glutathione. This high dose of ascorbic acid may have rapidly shifted the oxidative stress balance, as vitamin C is a well-known antioxidant. The results are consistent with the blood level of vitamin C being inversely correlated to disease activity variables.<sup>11</sup> This patient report supports the hypothesis that adding antioxidant supplements provides a benefit to some rheumatoid arthritis patients.<sup>14</sup> It also is consistent with

the hypothesis that lower glutathione levels due to GSTM1 null allele are conversely associated with RA severity.<sup>18</sup> These results raise the possibility that supplementation with the glutathione precursor N-Acetylcysteine (NAC)<sup>27</sup> may also benefit RA patients, similar to benefits seen by HIV patients<sup>28</sup> and trauma patients.<sup>29</sup> This patient report suggests that further studies on modulation of glutathione levels and antioxidant levels in rheumatoid arthritis patients are warranted.



Katherine L. Molnar-Kimber, PhD, has been an Immunologist, Virologist, and Molecular Biologist for over 20 years as well as a writer. She recently began writing about rheumatoid arthritis, including potential causes of RA flares and tips

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### Notes

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