

# Administration to Arthritis Patients of a Dietary Supplement Containing Immune Egg: An Open-Label Pilot Study

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## ABSTRACT

Arthritic conditions afflict millions of people worldwide, negatively affecting their physical and mental health and the quality of their lives. Conventional therapeutic modalities frequently provide relief to patients, but it is increasingly evident that other regimens, including nutritional ones, may be beneficial. A drink mix fortified with egg powder derived from specially vaccinated hens ("immune egg") was studied for its ability to modulate symptoms in 13 patients with osteoarthritis, rheumatoid arthritis, or psoriatic arthritis. For the subjects as a whole, statistically significant improvement ( $P < .05$ ) of physician mean global assessment scores was observed at 30 and 60 days after initiation of the study. Compared with baseline values, patients with osteoarthritis exhibited statistically significant improvement ( $P < .05$ ) in their scores 30 and 60 days after start of the program. Improvement was still present even after osteoarthritis patients had stopped taking the product for 30 days. During the 90-day investigation, patients with rheumatoid arthritis demonstrated a similar trend, but their scores were not statistically significant ( $P < .03$ ). No statistically significant effects on blood chemistries, including cholesterol readings, were observed. In conjunction with therapeutic regimens, daily administration of immune egg may provide a safe and effective complementary regimen for amelioration of arthritic symptoms. Potential mechanisms by which orally administered egg antibodies and immunoregulatory products could affect inflammatory processes are discussed.

## INTRODUCTION

**M**ANY MEDICATIONS ARE USED to manage arthritis, but their effectiveness is often inadequate (Trentham et al., 1993; Tilley et al., 1995). Rheumatologists have suggested that arthritis regimens should use a combination of

pharmacologic agents, including those derived from the area of biotechnology (Kavanaugh and Lipsky, 1994). Such a multiregimen approach is based in part on the fact that radiographic abnormalities found within the first 2 years of disease may progress to deformities and, although available drugs may decrease

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the symptoms for a subset of patients, they often do not prevent disease progression. More than 60% of the patients seen in rheumatology clinics have experienced work disabilities (Wolfe and Pincus, 1994), and in a 1-year study of 816 rheumatoid arthritis patients, 122 (15.0%) were hospitalized 160 times, with a mean length of hospitalization of 13.1 days (Wolfe et al., 1986). It is clear that innovative solutions and complementary therapies could be valuable in the treatment of arthritic diseases.

Modulation of arthritis symptoms was seen when diets were supplemented with certain foods (Darlington, 1991; Panush, 1993; Flynn et al., 1994). Clinicians (Klinenberg, 1985; See, 1998) have suggested that, in the future, nutritional therapy may prove to be a viable modality for the treatment of arthritis. Unique products called "immune foods" derived from eggs or milk from specially vaccinated animals, have been shown to provide promising benefit in a number of conditions (Stephan et al., 1990; Ritchie and Becker, 1994; Karge et al., 1998; Karge et al., in preparation). After a specific vaccination procedure in chickens or cows, the host generates high-titer antibodies (Kühlmann et al., 1988) and apparently other factors (Ormrod and Miller, 1991, 1992) that are passively transferred into the eggs or milk. When orally administered, the antibodies contained in these foods reportedly conferred protection against the specific pathogens used in the vaccines (Hammarström et al., 1994; Tsubokura et al., 1997; Yokoyama et al., 1998). Additionally, there is evidence that immunoregulatory factors in immune foods may be involved in regulating cardiovascular (Golay et al., 1990; Karge et al., 1998; Karge et al., in preparation), gastrointestinal (Greenblatt et al., 1998; Jacoby et al., in preparation), and joint health (See, 1998; Trentham et al., 1998).

Encouraging *in vivo* results (Trentham et al., 1998; Hunchar, in preparation) demonstrating antiarthritic and antiinflammatory activity, as well as historical papers suggesting that immune products relieve symptoms in arthritis sufferers (Smith, 1964; Struss, 1964) suggested that a pilot open-label trial was warranted. The clinical trial reported here evaluated the effect on symptoms in arthritic patients of consum-

ing a dietary supplement fortified with immune egg.

## METHODS

### *Patients*

Thirteen previously diagnosed patients, five with rheumatoid arthritis (RA), five with osteoarthritis (OA), and three with psoriatic arthritis (PA), provided informed consent and entered the study. Two of the RA patients were receiving gold-salt therapy, and one was receiving methotrexate. Of those with PA, one was receiving gold-salt therapy and one was receiving methotrexate. These drugs, while providing some benefit, did not alleviate symptoms. The study protocol was reviewed and approved by the Institutional Review Board at the Hospital for Special Surgery, New York. Patients enrolled had been diagnosed with arthritis for at least 6 months and had active disease (i.e., three or more swollen joints and six or more painful and/or tender joints, accompanied by 45 minutes or more of morning stiffness). Prescribed, over-the-counter, or homeopathic medications in high doses, as judged by the physician, were exclusionary. Any patient who had participated in an investigational drug protocol within 60 days before the start of the trial was also excluded. Significant changes in dosing or type of medication were recorded but were not exclusionary when judged suitable by the physician.

Nine women (four with RA, four with OA, one with PA) and four men (one with RA, one with OA, two with PA), ranging in age from 25 to 88 years (mean,  $53.5 \pm 28.5$  years), were admitted to the study.

### *Study design*

This was an open-label study of 12 weeks' duration. Servings were supplied as individual packets of powdered dietary supplement drink mix fortified with 4.5 g of powdered "immune egg" (DCV, Wilmington DE). The powdered egg was processed from eggs of hens vaccinated with a proprietary vaccine consisting of more than 20 different killed enteric human pathogens, including *Shigella*, *Staphylococcus*,

*Escherichia coli*, *Salmonella*, *Pseudomonas*, and *Streptococcus*. The egg was blended with commercially available vitamins and minerals, including vitamins A, B<sub>12</sub>, C, D, and E, thiamine, riboflavin, pyridoxine, pantothenic acid, niacin, folic acid, biotin, calcium, phosphorus, magnesium, copper, iron, iodine, zinc, and potassium. Patients consumed one packet daily in the morning for 8 weeks and then stopped taking the product for the last 4 weeks of the trial. The patients returned packets (either full or empty) for assessment of compliance.

#### Clinical assessments

The same physician investigator examined each patient throughout the study. Examinations were performed at the start of the study and then at 30, 60, and 90 days. The clinical disease variables determined by the physician at each visit consisted of symptoms, functional limitations, and physician global assessments. Blood samples were drawn at each visit.

A scoring system was used to provide a physician global assessment. The following joints were scored: fingers, wrists, elbows, shoulders, toes, feet, ankles, knees, hips, neck, and lower back. Each joint could be scored in three ways: swollen, painful, and/or tender. A point value of 1 was given for each category

that was positive (e.g., if a finger joint was both swollen and painful, the score would be 2). In those cases in which there was only a "slight problem" with the joint, the value of 0.5 was used.

The patient's overall responses to product consumption and comparison with the previous month's quality of life assessment were also recorded.

#### Laboratory assessments

Hematological and blood chemistry profiles were obtained at 4-week intervals. These determinations included hemoglobin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum amyloid A (SAA) (Hemagen, Waltham, MA), low-density lipoprotein (LDL), total cholesterol, platelet count, and leukocyte counts. Liver enzyme tests, including alkaline phosphatase and total bilirubin, were also performed.

## RESULTS

#### Effect on symptoms

Pretrial (baseline) evaluations of the three diagnostic classes of patients (RA, OA, and PA) showed no significant differences in scores

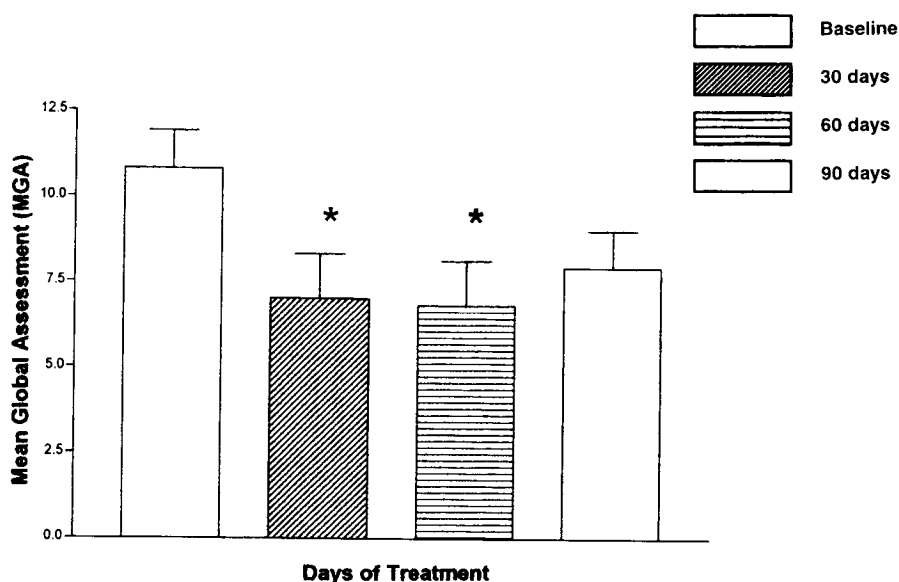


FIG. 1. Effects of dietary supplement (containing 4.5 g of immune egg) in all patients with arthritis (N = 13). Baseline values are compared with assessments made after the test product was taken for 30 and 60 days, and 30 days after treatment was stopped. \*, Significant difference from baseline ( $P < .05$ ).

among the three groups. Considering all three arthritic classes together, there were statistically significant decreases in the mean global assessment (MGA) scores at 30 days ( $7.0 \pm 1.3$ ,  $P < .05$ ) and at 60 days ( $6.8 \pm 1.3$ ,  $P < .05$ ) after the start of product consumption (Fig. 1).

However, among the specific arthritis types, statistically significant improvement over the 2-month period was seen only among the patients with OA (Fig. 2). In this group, statistically significant improvement in MGA scores was still seen even after 30 days without the test product, (Fig. 2), but there was a trend toward a return to baseline values.

Patients with RA showed a strong trend toward reduction in their scores (Fig. 3), but the results were not statistically significant ( $P < .03$ ). Forty percent (2/5) of patients with RA, 60% (3/5) of those with OA, and 30% (1/3) of those with PA reported some degree of improvement in their general well-being and/or quality of life while consuming the supplement. The patients' own responses correlated well with the physician's individual global assessments of each patient (Table 1).

#### Laboratory results

Baseline ESR, CRP and SAA levels were lower in patients with OA compared with pa-

tients with RA. Although a higher percentage of OA patients reported improvement while taking the test product, no statistically significant changes in these laboratory parameters were observed in this group during or after completion of the trial. No significant changes in LDL, total cholesterol, hemoglobin, platelet count, leukocyte count, alkaline phosphatase, or total bilirubin were noted.

#### Patient personal assessments

*Patient #001.* This 29-year-old woman with juvenile RA had a pretrial score of 14 (swollen, painful, and tender fingers, wrists, feet, and knees; toes swollen and painful). After 30 days, her score was 2.0 (fingers still swollen and knees slightly tender). The patient reported feeling "75% better," with more energy and less aches. At her third visit (60 days), the patient reported feeling "slightly worse" than at her previous visit, and her score was 6.0. Thirty days after stopping the product, her score was 8.0, yet she reported that she still felt "75% better" than she did before the trial. This patient had been taking minocycline, the antiinflammatory antibiotic, before the start of the study but discontinued its use within the first 30 days. Thirty days after discontinuing the dietary supplement, the patient reinitiated use of minocycline.

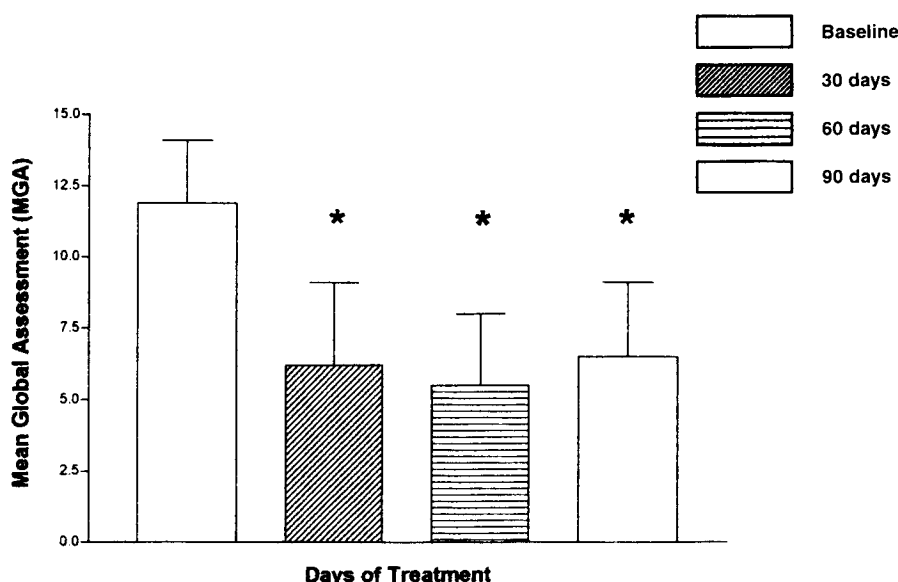


FIG. 2. Effects of dietary supplement (containing 4.5 g of immune egg) in patients with osteoarthritis (N = 5). Baseline values are compared with assessments made after the test product was taken for 30 and 60 days, and 30 days after treatment was stopped. \*, Significant difference from baseline ( $P < .05$ ).

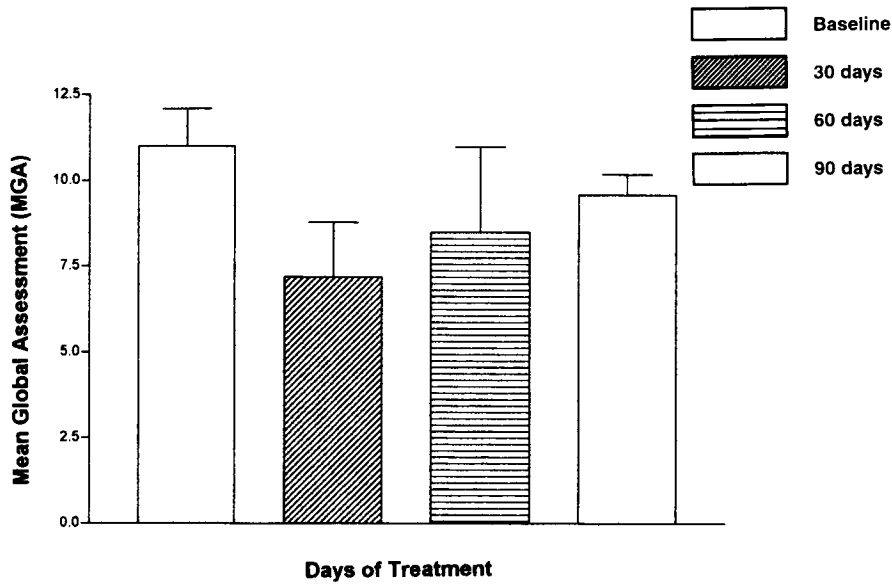


FIG. 3. Effects of dietary supplement (containing 4.5 g of immune egg) in patients with rheumatoid arthritis (N = 5). Baseline values are compared with assessments made after the test product was taken for 30 and 60 days, and 30 days after treatment was stopped.

*Patient #004.* This 88-year-old woman with RA began the study with a score of 10.0. She was taking methotrexate, 5 mg/week; alendronate sodium, 10 mg/day; calcium, 1,500 mg/day; prednisone, 5 mg every other day; and ketoprofen, 12.5 mg twice a day. On entry into the study, the patient found it difficult to bend or lift her arms and could walk only in a limited manner. At her second visit (30 days), the patient reported she felt "generally better" and her

score was 7.0. She walked with less difficulty and was able to bend, open bottles, and reach up to close a window. She was taking 12.5 mg of ketoprofen once a day, and, although still in pain, she reported few attacks. After 60 days (score, 2.0), the patient felt "much better, 98% better," but still reported pain in her legs at night. Thirty days after stopping product, the patient's clinical assessment score had returned to 10.0, and she reported that she felt 50% worse than at her previous visit. Her wrists had become swollen, and she reported severe joint pain. This patient's ESR readings reflected her condition. Her pretrial ESR was 36 mm/hour. At 30 and 60 days, her ESR values were 30 and 21 mm/hour, respectively. At her fourth visit, 30 days after consumption of product had ceased, she had begun to complain of symptoms again and her ESR had climbed to 27 mm/hour.

TABLE 1. PHYSICIAN GLOBAL ASSESSMENT SCORES OF INDIVIDUAL PATIENTS

Patient no.	Baseline	30 Days	60 Days	30 Days after Termination
<b>Rheumatoid arthritis</b>				
001	14	2	6	8
002	13	12	13	11.5
003	8	7	7	9
004	10	7	2	10
007	10	8	15.5	9.5
<b>Osteoarthritis</b>				
008	8	3	2	1
009	7.5	6	3	2.5
011	19.5	17.5	15.6	15.5
013	11.5	2	3	8.5
014	13	2.5	4	5
<b>Psoriatic arthritis</b>				
005	5	3.5	4	6
006	6.5	7	6.5	9.5
015	14	13	7	8

**DISCUSSION AND CONCLUSIONS**

The purpose of this trial was to evaluate the effect on symptoms in arthritic patients of daily consumption of a dietary supplement containing immune egg. Overall, arthritis patients consuming an immune egg-fortified dietary supplement exhibited significant ( $P < .05$ ) im-

provement in their MGA scores at 30 and at 60 days. MGA scores of OA patients at 30 and 60 days showed a statistically significant ( $P < .05$ ) difference compared with their initial scores. Although not statistically significant, there was also a trend toward a decrease in MGA scores compared with baseline values ( $P < .03$ ) in patients with RA. These results correlated with personal evaluations. Overall, 40% of arthritis patients reported some degree of benefit during the 60-day trial period. Sixty percent of those with OA reported feeling "better" during the trial (after consuming the product for 30–60d) than at their initial visit, as did 40% of those with RA and 30% of those with PA.

It is proposed that antibodies and/or immunoregulatory factors (proinflammatory or antiinflammatory) in the immune egg contributed to the improvement observed in these patients. This hypothesis is supported by results from *in vivo* studies and clinical trials carried out with immune egg and milk products, which described reductions in inflammatory responses (Ormrod and Miller, 1991, 1992, 1993; Hunchar, in preparation) and in symptoms associated with arthritic conditions (Smith, 1964; Struss, 1964; Trentham et al., 1998).

Immune eggs are obtained from hens that have been vaccinated over an extended period with a multivalent vaccine of killed human enteric pathogens. These hens passively transfer into their eggs high concentrations of specific antibodies and other products that appear to have immunoregulatory and antiinflammatory activity (See, 1998).

One of the proposed mechanisms by which immune egg may benefit arthritic patients is by lowering levels of intestinal bioburdens with specific antibodies found in the immune egg. There is ample evidence in both human (Hilpert et al., 1987; Tacket et al., 1988; Brunser et al., 1992) and animal (Hammarström et al., 1994; Kuroki et al., 1994; Yokoyama et al., 1998) models that active antibody, derived from a variety of sources, is able to locally neutralize specific bacteria and viruses in the gut. Lipids and other constituents of egg may serve as a natural vehicle to encapsulate antibody from destruction in the digestive tract of humans, providing even greater protection.

It has been suggested that infectious organ-

isms play a critical role in autoimmune diseases via molecular mimicry (Fujinami, 1992; Albani and Carson, 1996). Neutralization of activating pathogens might decrease or eliminate autoimmune processes (Hammarström et al., 1994). Treatment of RA with antibiotics is controversial (Sanchez 1968; Skinner et al., 1971; McPherson-Brown et al., 1985; Breedveld et al., 1990; Langevitz et al., 1992). Double-blind, placebo-controlled, multicenter trials (Kloppenborg et al., 1993, 1994; Tilley et al., 1995) using minocycline have suggested improvement in clinical measures, especially among patients with mild to moderate disease (Tilley et al., 1995). However, because tetracyclines have been shown to inhibit inflammatory events (Plewig and Schopf, 1975; Paulus et al., 1977; Sewell et al., 1996), it is difficult to separate any possible benefits of tetracycline caused by inhibition of inflammation from those caused by suppression of microbial growth (Paulus et al., 1977).

Oral administration of antibodies may be advantageous to patients and others with autoimmune conditions (Hammarström et al., 1994) because these antibodies are localized in the gut, the major access point into the body for many pathogenic organisms (See, 1998). The ability of immune egg specific antibodies to neutralize microbes and decrease autoimmune phenomena may be one mechanism by which some arthritis patients find benefit.

Inflammatory diseases are characterized by infiltrates consisting of cells such as neutrophils, monocytes/macrophages, and helper and suppressor T cells (Luster, 1998; Kamradt and Burmester, 1998). Each class of cells plays a distinct role during the various stages of chronic disease (Kamradt and Burmester, 1998). After activation of a specific subset of T cells by unknown stimuli, immunomodulatory biological components such as cytokines are produced. These in turn stimulate and recruit other cells, including T cells (Kingsley et al., 1990, 1991; Strober and Holoshitz, 1990; Firestein and Zvaifler, 1997). Activated T cells have been implicated in autoimmune diseases such as RA (Sewell and Trentham, 1993).

Albani and Carson (1996) suggested that "[i]ntermittent exposure of the systemic immune system to bacterial antigens at mucosal



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