The Joints and Muscles

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There are several reasons for considering the hypothesis that food hypersensitivity might relate to rheumatic diseases.

- Food can evoke immune responses.
- Food can cause immunologically mediated symptoms.
- Immunological mechanisms are important in the pathogenesis of rheumatic diseases.
- Antigens triggering rheumatic responses are unknown.
- Rheumatic diseases have been associated with foods in many reports.

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Adverse Food Reactions and Rheumatic Disease

The notion that rheumatic disease, at least in some patients, might be a manifestation of food hypersensitivity has been an attractive one to physicians and the public. Available information about this possible relationship between food and rheumatic disease is largely anecdotal and, until recently, there were few well-designed, appropriately controlled and blinded studies (2, 3-15).

A relationship between nutrition and rheumatic disease might occur through two possible mechanisms. First, diet and nutritional factors could alter immune or inflammatory responses or both, thus modifying rheumatic symptoms. Second, food antigens might provoke hypersensitivity responses leading to rheumatic symptoms (9).

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The etiology of rheumatoid arthritis and most other forms of inflammatory joint diseases remains unknown. There has been much speculation about the roles of microbial and other environmental agents in the etiopathogenesis of diseases. It may be no less reasonable to consider food antigens as initiating agents that provoke joint inflammation in certain patients (9). If rheumatic diseases resulted from hypersensitivity to foods, then food antigens entering the bloodstream across the gastrointestinal barrier and circulating in antigenic form until recognized by effector or intermediary cells in the immune system may play a role. Experimental data indicate that this occurs (9). Indeed some studies have suggested the gastrointestinal tracts of patients with rheumatoid arthritis may be more penetrable to food antigens than in normal persons, although this finding has been inconsistent (9).

Several investigators have reported compelling examples of patients with rheumatic diseases and possible associated food hypersensitivities. These included a patient who had rheumatoid arthritis along with dairy product sensitivity; uncontrolled

challenge with dairy products produced marked exacerbation of her arthritis (11). Others, in largely uncontrolled studies, reported antirheumatic effects of fasting and noted that certain chemical or food challenges caused clinical deterioration in patients who had rheumatoid arthritis, lupus, Behcet's syndrome, and other rheumatic diseases (2,8-10,12-15). Our own observations identified a patient with rheumatic-like (inflammatory) arthritis who had clinical and immunological sensitivity to milk, in prospective, double-blind, placebo controlled studies carried out in an inpatient clinical research unit. This patient exhibited marked, consistent, subjective, and objective improvement during fasting, which was sustained with elemental nutrition. Four different blind challenges with milk reproducibly exacerbated symptoms, whereas placebo and other foods produced no effects. Symptoms peaked 24 to 48 hours after challenge and resolved over 1 to 3 days. Immunologic studies suggested delayed as well as immediate cutaneous reactivity to milk, no elevation in serum IgE antibodies to milk proteins, anti-milk IgE, marked increases of anti-milk total IgG and IgG4 (directed against alpha lactalbumin), marginally increased IgG milk-circulating immune complexes, and *in vitro* cellular sensitivity to milk. Symptomatic exacerbation of arthritis and immunologic hypersensitivity to milk coexisted in this patient (4). In further studies we noted that many of our patients with rheumatoid arthritis claimed to have food-related ("allergic") arthritis. However of 16 patients who completed 19 double-blind, controlled food-challenge studies, only three patients convincingly demonstrated subjective and objective rheumatologic symptoms following double-blind, encapsulated food challenges (7). They were virtually asymptomatic with elemental nutrition and interestingly were also seronegative patients who showed palindromic symptoms and nonerosive disease and who had no generalized atopy or gastrointestinal disease.

We concluded that immunologic sensitivity to food was an uncommon cause of symptoms among rheumatic disease patients. However our own and others' observations clearly suggested a possible role for food hypersensitivity in at least some patients with rheumatic disease. The mechanism(s) for this is (are) unclear. There is little evidence to suggest that rheumatic disease secondary to "food allergy" is IgE mediated. Given the presence of food antigens, food antibodies, complexes of food antigens and antibodies, and sensitized lymphocytes in the systemic circulation of many individuals after meals, it has been hypothesized that a "delayed" hypersensitivity mechanism, probably not IgE-mediated, may play a role in the food hypersensitivity of these occasional rheumatic disease patients (6,9).

Dietary modification can affect immune responses and thereby moderate symptoms of rheumatic disease. Qualitative and quantitative alterations of polyunsaturated fatty acids in the diet perturb endogenous cellular synthesis of eicosanoids, important mediators of the inflammatory responses. Clinical trials have documented modest anti-inflammatory effects of such interventions for certain patients with rheumatic diseases (9). Similarly fasting improved symptoms of rheumatic disease in some patients, perhaps due to reduced gastrointestinal permeability, decreased neutrophil function, depressed lymphocyte response to mitogens, or increased cortisol concentrations during fasting (1).

Occasional patients with rheumatic diseases may have symptoms associated with hypersensitivity. Most patients who believe that their arthritis is provoked by certain foods can not find support for this belief in blinded, controlled studies. Diet or nutritional therapy for rheumatic disease should be considered experimental. We hope further investigation in this area leads to better understanding of mechanisms of rheumatic disease and to development of better therapies.

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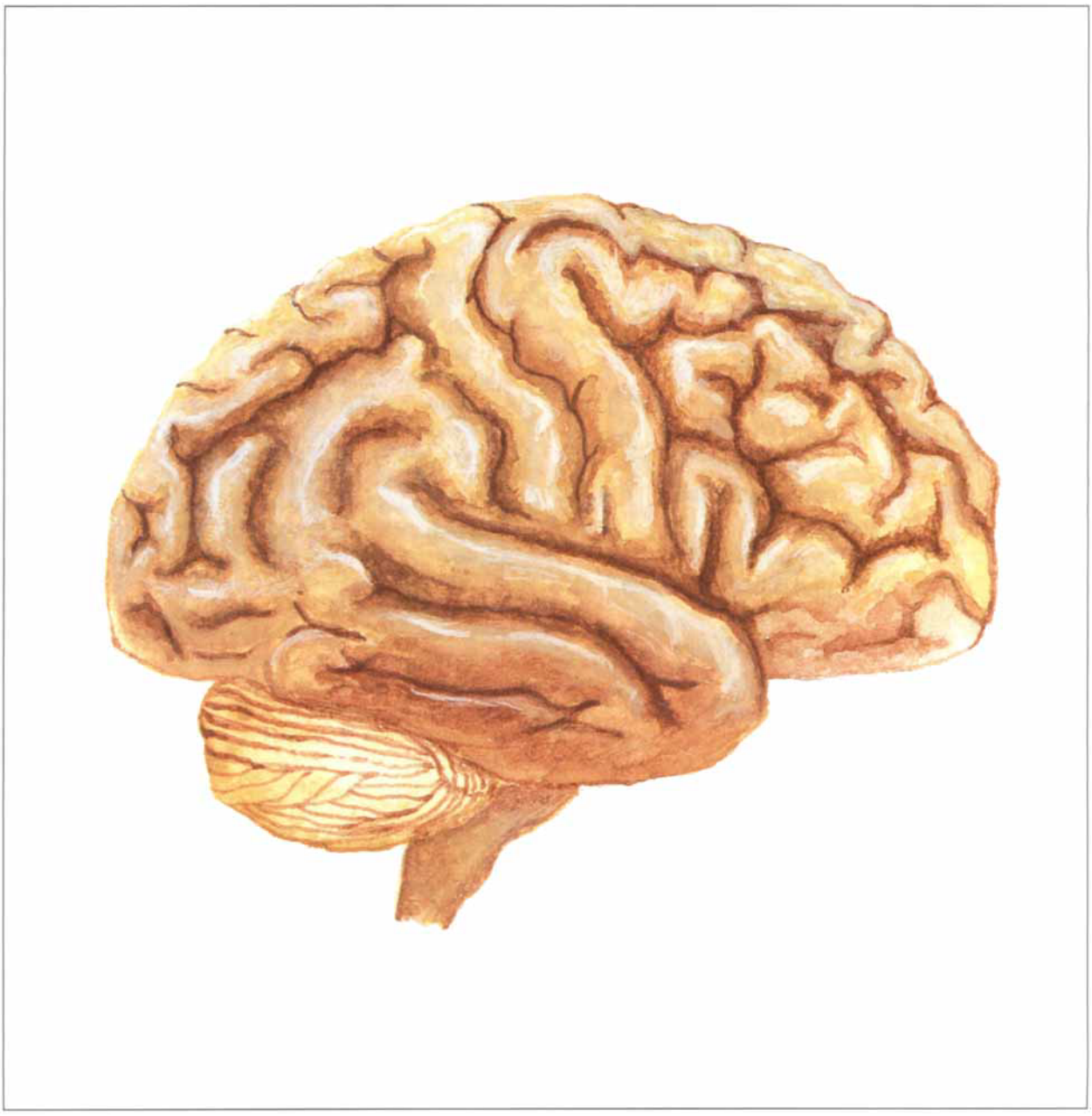
References

1. Hafstrom I, Ringertz B, Gyllenhammar H, Palmblad J, Harns-Ringdahl M. Effects of fasting on disease activity, neutrophil function, fatty acid composition, and leukotriene biosynthesis in patients with rheumatoid arthritis. Arthritis Rheum 31:585-591, 1988.
2. Kjeldsen-Kragh J, Haugen M, Borchgrevink CF, Laerum E, Eek M, Morwinkel P, Hovi K, Forre O. Controlled trial of fasting and one-year vegetarian diet in rheumatoid arthritis. Lancet 338:899-902, 1991.
3. Panush RS, Carter RL, Katz P, Kowsari B, Longley S, Finnie S. Diet therapy for rheumatoid arthritis. Arthritis Rheum 26:462-471, 1983.
4. Panush RS, Stroud RM, Webster E. Food-induced (allergic) arthritis. Inflammatory arthritis exacerbated by milk. Arthritis Rheum 29:220-226, 1986.
5. Panush RS. Nutritional therapy for rheumatic disease. Ann Intern Med (Editorial) 106:619-621, 1987.
6. Panush RS. Possible role of food sensitivity in arthritis: Ann Allergy 61 (Part II): 31-35, 1988.
7. Panush RS. Food induced ("allergic") arthritis: Clinical and serological studies. J Rheum 17:291-294, 1990.
8. Panush RS, Bahna S. Connective tissue reactions to foods. Food Allergy. Edited by D Metcalfe, H Sampson, R Simons, pp. 382-391 Section 4, 1991 (chapter 28).
9. Panush RS, editor. Nutrition and Rheumatic Diseases. Rheum Dis Clin 17:VII-XIV, 197-456, 1991.
10. Panush RS. Diet and Rheumatic Disease. For Textbook of Rheumatology: Update, edited by WN Kelley, ED Harris, CB Sledge, and S Ruddy, WB Saunders Co., Orlando, FL, 994, pp 1-10.
11. Parke AL, Hughes GRV. Rheumatoid arthritis and food. A case study. Br Med J 282:2027-2029, 1981.
12. Ratner P, Scheeyour A, Eshel E, Teitler A. Does milk intolerance affect seronegative arthritis in lactose-deficient women? Israel J Med Sci 21:532-534, 1985.
13. Stroud RM. The effect of fasting followed by specific food challenged on rheumatoid arthritis. In Hahn BH, Arnett FC, Zizic TM, Hochberg MC (eds). Current Topics in Rheumatology. Upjohn, 1983, pp 145-157.
14. van de Laar M, van der Korst JK. Food intolerance in rheumatoid arthritis: I. A double blind, controlled trial of the clinical effects of elimination of milk allergens and AZO dyes. Ann Rheum Dis 51:298-302, 1992.
15. van de Laar, MAFJ, Aalbers M, Bruins FG. Food intolerance in rheumatoid arthritis: II. Clinical and histological aspects. Ann Rheum Dis 51:303-306, 1992.



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