

The role of nutrition and diet in rheumatoid arthritis

Rosemary H. Martin

Human Nutrition Research Group, University of Ulster, Coleraine BT52 1SA, UK

The nutritional implications of rheumatoid arthritis (RA) are due to a combination of the underlying disease pathology, disability and drug treatment. A wide range of conflicting dietary advice is available, yet the lack of scientific information regarding its efficacy often leaves sufferers vulnerable to exploitation. The recent increase in scientific investigations by the medical and related professions in this area represents an extremely welcome approach to remedy this situation.

Characteristics of rheumatoid arthritis

RA is a chronic, systemic inflammatory disease of unknown aetiology which principally affects the joints (Kumar *et al.* 1992). Worldwide, RA affects approximately 1% of the adult population and also occurs among one in 1000 children as juvenile RA (Di Toro & Polito, 1997). RA can strike at any age, yet typically occurs between 40 and 60 years of age (Bodman & Roitt, 1994). Approximately three females are affected for every male, and during pregnancy 70% of women suffering from RA experience remission, with flare-ups after birth (Nelson & Ostenson, 1997). As yet no definitive marker exists for RA. However, the auto-antibody rheumatoid factor is found in 70–80% of patients (Harris, 1990). There is an increased risk of RA among individuals positive for the human leucocyte antigen-DR4 allele of the major histocompatibility complex class II gene involved in antigen expression (Oiller & Thompson, 1992).

RA is characterized by painful, swollen joints, particularly of the fingers, wrists and knees. Symptoms may be 'symmetrical', with the same joints affected on opposite sides of the body. Typically, there is 'morning stiffness' of the joints (Kumar *et al.* 1992). Low-grade fever with flu-like symptoms, such as shivering, aching and fatigue, contributes to reduced appetite, weight loss and general malaise (Semble, 1995). The clinical course features periods of remission and relapse that are highly variable. Some patients remain stable, while sadly in others the disease is extremely aggressive, inflicting early disability (Hilliquin & Menkes, 1994).

Pathophysiology of inflammatory processes in rheumatoid arthritis

Normal human inflammatory responses are an essential component of the body's defence mechanisms against invading pathogens (Coleman *et al.* 1992). However, in RA these processes, once initiated, persist, resulting in the formation of a destructive, tumour-like tissue called 'pannus' (Bodman & Roitt, 1994). This invades soft tissues causing cartilage breakdown and bone erosion (Palmer, 1995). Inflammation is mediated by soluble proteins or cytokines (Panayi, 1993), the actions of which may be crudely simplified into those that are pro-inflammatory, e.g. interleukin-1 β and tumour necrosis factor- α , or anti-inflammatory, e.g. interleukin-10 and transforming growth factor- β (Koch *et al.* 1995).

Factors affecting nutrition in rheumatoid arthritis

Metabolic effects of inflammation

Tumour necrosis factor- α and interleukin-1 β bring about fever, increased catabolism, muscle wasting, connective tissue remodelling and anorexia associated with RA (Roubenoff *et al.* 1994). High levels of reactive oxygen species increase the oxidative stress on antioxidant defences (Grimble, 1990). Elevated plasma Cu, decreased plasma Zn and Fe are features of inflammation (Milanino *et al.* 1993) which are poorly understood, especially in RA. Recently, Roubenoff *et al.* (1997) have published findings indicating abnormal homocysteine metabolism in RA.

Physical disability

Ultimately, RA sufferers experience some degree of physical disability. Hands may become immobilized in a claw-like position (Kumar *et al.* 1992), making daily activities such as food preparation, eating and drinking extremely difficult. Poor mobility increases the dependence on others for shopping and cooking. Reduced physical activity contributes to loss of bone mass in long-standing RA (Hansen *et al.* 1996b), although this also depends on disease activity and drug therapy. Housebound individuals

Abbreviation: RA, rheumatoid arthritis.

Corresponding author: R. H. Martin, fax +44 (0)1265 324965, email RH.martin@ulst.ac.uk

may also be at risk of vitamin D deficiency in cases where there is little exposure to sunlight.

Drug treatment

RA sufferers undergo lifelong drug treatment to alleviate symptoms and delay disease progression. Most of the drugs used have significant side effects, involving the liver, kidneys, gastrointestinal tract and eyes (Semble, 1995). There are also nutritional implications in terms of altered appetite, nausea, vomiting, taste changes and altered nutrient absorption, metabolism and excretion (Brooks, 1994; Semble, 1995). Methotrexate is a known folate antagonist (Dijkmans, 1995), while non-steroidal anti-inflammatory drugs may increase gut mucosal permeability (Parke *et al.* 1996). Increased Ca and vitamin D intakes may protect against bone loss during steroid treatment for RA (Gulko & Mulloy, 1996), particularly in children where poor bone mineralization and growth failure are potential problems (Di Toro & Polito, 1997). Drugs place stress on detoxification systems operating via cytochrome P450, which utilizes riboflavin and thiamin (Parke *et al.* 1996).

Malnutrition in rheumatoid arthritis

The increased catabolism raises resting energy expenditure, which leads to weight loss and reduced lean body mass, especially if energy and protein requirements are not met (Roubenoff *et al.* 1994). This phenomenon is recognized as 'rheumatoid cachexia'. Helliwell *et al.* (1986) identified 26% of their RA group who were malnourished according to established anthropometric and biochemical indices. Malnutrition has been identified also among Finnish (Nenonen, 1995) and Spanish patients (Hernandez-Berriain *et al.* 1996) and, unsurprisingly, was more common among those who had severe disease. Low dietary intakes of Cu, Mg, Zn, vitamins D, E and A, pyridoxine, folate and *n*-3 fatty acids have been consistently reported by different investigators (Kremer & Bigaouette, 1996; Hansen *et al.* 1996a; Morgan *et al.* 1997).

Dietary approaches to rheumatoid arthritis

Dietary approaches to RA range from those based on sound nutritional principles to fads, myths and quackery. Rheumatologists have traditionally been sceptical, although viewpoints are changing. In contrast, RA patients are well known for their enthusiasm for dietary approaches. Of those surveyed, 75% of UK RA sufferers (Garret *et al.* 1993) and 33% of Danish RA sufferers (Haughen *et al.* 1991) believe that food plays a part in the severity of their symptoms. At least 20% will have tried a diet in their attempt to alleviate symptoms (Haughen *et al.* 1991). RA sufferers collectively spend billions of dollars on alternative treatments, including dietary therapies (Panush *et al.* 1983). Unfortunately, much of the advice is contradictory (Darlington *et al.* 1990), leaving RA sufferers confused as to what strategy to follow.

Some 'cultural beliefs' hold that RA is a 'cold' disease to be treated with 'hot' foods such as chilli, garlic and peas,

and 'hot' medicines such as aspirin, cod-liver oil, Fe and vitamins (Champion, 1994). Low-acid diets emerged from the belief that RA is due to acid-alkaline imbalance, and advocate the avoidance of citrus fruits and other acidic foods (Champion, 1994). Some authors have attempted to produce benefits via alteration of bowel flora using 'living' food (holistic) diets rich in lactobacilli (Nenonen, 1995).

'Cleansing', 'detoxifying' diets aim to purge the disease-causing toxins from the body. Fasting is a component of 'detoxifying', which can produce immediate relief from RA symptoms (Palmbad *et al.* 1991). However, the benefits are not lasting and symptoms generally deteriorate on return to normal eating or a vegetarian diet (Kjeldsen-Kragh *et al.* 1991). The mechanism behind such observations is unknown, but may relate to changes in intermediary metabolism or the removal of aggravating food antigens (Parke *et al.* 1996). Fasting is not recommended except under clinical supervision where genuine food allergy is suspected.

Elimination approach

Foods associated with symptoms of rheumatoid arthritis

Oils, fish and fresh vegetables are commonly associated with improvements in symptoms, while citrus fruits, chocolate, alcohol, red meats, flour products, spices and fizzy drinks are often implicated in the aggravation of symptoms (Darlington *et al.* 1990; Haughen *et al.* 1991; Garret *et al.* 1993). Such lists reflect those of the popular 'Dong' diet (Dong & Banks, 1975) for RA, based on the Chinese poor man's diet: rich in seafood, vegetables and rice, but eliminating dairy produce, alcohol, additives, spices and meat, allowing occasional poultry. In a clinical trial of this type of diet, Panush *et al.* (1983) found no consistent effect on disease, with the exception of two patients who experienced considerable improvement. Given that immunological mechanisms are important in RA pathology, and that despite research no 'trigger' antigens have yet been isolated, many patients and some clinicians have asked: 'Are there dietary causes of RA?'

Food intolerance in rheumatoid arthritis

Potential food antigens may be intrinsic to the actual foodstuff or arise from chemicals added to the food as preservatives, fertilizers or pesticides. The gut is a major organ in immune defence, and intestinal antigens may cross the gut barrier, eventually circulating as immune complexes (Buchanan *et al.* 1991). Absorption of dietary antigens from the gut may be enhanced by changes in gut permeability owing to immaturity, immunodeficiency, allergy or concomitant disease such as Crohn's disease (Parke *et al.* 1996).

Evidence to date for the role of food intolerance in RA is inconclusive, derived mainly from anecdotal reports. Milk and dairy produce, cereals, maize, wheat gluten, tartrazine and azo dyes have all been implicated in RA in recent reviews (Buchanan *et al.* 1991; Darlington & Ramsey, 1993). Overall, there seem to exist 'subgroups' of RA patients for whom food intolerance plays a significant role

in their disease. Carefully-designed double-blind clinical trials are needed to distinguish true intolerance from disease which spontaneously relapses and remits.

Dietary supplementation

Nutrient megadosing

The old adage: 'if a little is good, more is better' reflects the practice of nutrient megadosing, whether self administered or prescribed by 'alternative practitioners'. Commonly advocated are vitamin E, Zn and Se (Champion, 1994). Se supplementation trials in RA have improved Se status without any consistent effect on disease activity (Tarp, 1995). Apart from the expense and risk of toxicity, moderate nutritional supplementation may interfere with normal regulation of nutrient bioavailability; for example, high doses of Zn inhibit Cu absorption (Bremner & Beattie, 1995).

Novel food supplements

Novel food supplements are common to the shelves of any health food shop and some pharmacies. There is only slight evidence that the New Zealand green-lipped mussel (*Perna canaliculus*) extract, or 'Seatone' is of value in RA (Larkin, 1994). Devil's claw (*Harpagophytum*)-root extract, sea kelp, ginseng, and lactobacillus are others recommended in books (Darlington *et al.* 1990). Such products undoubtedly have powerful placebo effects, necessitating properly-controlled clinical trials to investigate their reported efficacy in RA.

Fish and plant oils

Oil-based supplements have emerged as the most promising area of dietary manipulation in RA. Pharmacological doses (3–10 g/d) of the long-chain *n*-3 fatty acids found in fish oils reduce stiffness and pain in RA (Kremer, 1996). Their mechanisms of action include the inhibition of pro-inflammatory eicosanoids (De Luca *et al.* 1995) and cytokines (Endres & von Shacky, 1996), although clearly other mechanisms exist. The value of low doses of long-chain *n*-3 fatty acids is unclear; however, frequent intakes of oily fish may reduce the risk of RA (Shapiro *et al.* 1996), or limit its severity (Recht *et al.* 1990).

Summary

Given the lack of understanding of the nutritional requirements in RA, plus the variability in its clinical course, it is difficult to produce specific dietary recommendations for RA. In general, sufferers should consume as varied a diet as possible, based on current Department of Health (1991) guidelines. Dietary counselling is important to help patients achieve this. Self-imposed elimination diets should be avoided and suspected food intolerance tested under strict clinical supervision. Nutrient megadosing is inadvisable, although dietary supplementation with Ca,

vitamin D, folic acid or multivitamins and minerals should be recommended where necessary.

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