

c0050 **Chronic pelvic pain
and nutrition**

8.3

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Introduction

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p0090 This brief summary section lists current evidence relating to the influence of nutritional features on pelvic pain in general, and a number of specific conditions in particular. Some of the evidence is clear, while much of it remains equivocal, with a mixture of conflicting research evidence, and anecdotal evidence, clouding the conclusions. Despite some uncertainty, there is evidence that inflammatory processes can safely be modulated by a variety of nutrients and dietary strategies that involve anti-inflammatory and

antioxidant substances in the diet. Several preventative measures also appear to be fairly solidly established (involving the balance of lipid substances omega-3, omega-6, etc. in the diet). In general two areas stand out, the influence of diet on inflammatory processes, and the influence of vitamin D deficiency on a number of pelvic floor disorders affecting women.

Inflammation

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Butrick (2009) notes that when muscle fibre trauma occurs, inflammatory mediators (e.g. bradykinin, serotonin, prostaglandins, adenosine triphosphate, histamine) are released locally, resulting in sensitization of muscle nociceptors, reducing their mechanical threshold. This results in muscle hyperalgesia and mechanical allodynia in which innocuous pressure may be perceived as painful. If prolonged, this peripheral sensitization leads to central sensitization, via a series of neuroplastic changes that occur in the central nervous system (CNS). These processes are described in greater detail in Chapter 3.

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While pharmacological control of inflammation is clearly an option, there are also well-founded strategies for modulating this process, via dietary manipulation.

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Dietary anti-inflammatory strategies

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- Herbs such as turmeric can suppress expression of cyclo-oxygenase-2 (COX-2); and nutmeg inhibits release of tumor necrosis factor (TNF-alpha) (Sanders & Sanders-Gendreau 2007).

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B978-0-7020-3532-6.00010-9, 00010

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- u0095 • Lopez-Miranda et al. (2010) report that phenolic compounds in olive oil have antioxidant and anti-inflammatory properties, prevent lipoperoxidation, induce favourable changes of lipid profile, improve endothelial function and have antithrombotic properties. Oleocanthal, a compound in olive oil retards the production of pro-inflammatory enzymes cyclo-oxygenase-1 (COX-1) and COX-2.
- TS1 u0100 • A study by Beauchamp et al. (2006) suggests that 50 ml or 3.5 tablespoons of olive oil has the same effect as a 200-mg tablet of ibuprofen. Note however that consumption of 50 ml olive oil as an anti-inflammatory intervention requires caution, as this volume of olive oil contains in excess of 400 calories. This is of importance in chronic pelvic pain (CPP), since studies (Greer et al. 2008) have noted that weight loss leads to significant improvements in pelvic floor disorder symptoms.
- u0105 • Moschen et al. (2010) confirmed that weight loss is an effective anti-inflammatory strategy, achieving its effects by decreasing expression of TNF- α and IL-6 as well as by increasing anti-inflammatory adipokines such as adiponectin.
- u0115 • Resveratrol has been found to be a more potent anti-inflammatory agent than aspirin or ibuprofen (Takada et al. 2004)
- u0120 • Carvacrol (derived from the essential oils of oregano and thyme) efficiently suppresses COX-2 expression (Baser 2008, Hotta et al. 2010)
- u0125 • Antioxidant anthocyanins from pomegranate (POMx), and blueberry extract (*Vaccinium corymalosum*) which is also rich in anthocyanins, have been shown to have active antioxidant and antinociceptive properties (Torri et al. 2007).
- u0130 • POMx inhibited inflammation associated with activated human mast cells, involved in disease processes associated with connective tissues (Zafar et al. 2009).
- u0135 • Mixtures of antioxidants – resveratrol, green tea extract, α -tocopherol, vitamin C, omega-3 PFA, tomato extract – were found, in a placebo-controlled study, to modulate inflammation in overweight males.
- u0140 • Bromelain, an aqueous extract obtained from both the stem and fruit of the pineapple plant, contains a number of proteolytic enzymes with anti-inflammatory and analgesic properties (Maurer 2001, Brien et al. 2004).
- u0145 • Catechins and epicatechins, found in red wine and tea (particularly green tea), are polyphenolic antioxidant plant metabolites that quench free radicals and provide protection against oxidative damage to cells (Hara 1997, Yang et al. 2001, Sutherland et al. 2006, Kim et al. 2008).
- u0150 • In a 14-day, prospective randomized study, involving a total of 284 patients affected by chronic bacterial prostatitis (NIH class II prostatitis), Cai et al. (2009) evaluated the therapeutic antioxidant effects of extracts from the plants *Serenoa repens*, *Urtica dioica* (ProstaMEV[®]) and curcumin[®], as well as the antioxidant plant-derived nutrient quercetin (FlogMEV[®]) extracts, compared with prulifloxacin. One month after treatment, 89.6% of patients who had received prulifloxacin as well as ProstaMEV[®] and FlogMEV[®] (Group A) reported no symptoms related to CBP, whilst only 27% of patients who received antibiotic therapy alone (Group B) were recurrence-free ($P < 0.0001$). Six months after treatment, no patients in Group A had recurrence of disease whilst two patients in Group B did.
- s0025 **Antioxidants and anti-inflammatory nutrients**
- p0130 Mier-Cabrera et al. (2009) and Kamencic & Thiel (2008) have demonstrated that in endometriosis, oxidative stress may be improved by use of antioxidant compounds. Antioxidant nutrients have been shown to protect against cell-damaging free radicals, and to reduce activity of COX-2, a major cause of inflammation (Nijveldt 2001, Kim et al. 2004). Closely tied to anti-inflammatory strategies are nutritional approaches that emphasize enhanced intake of antioxidant foods containing phytochemicals such as carotenoids, flavonoids, limonene, indole, ellagic acid, allicin (from garlic) and sulphoraphane.
- p0135 Examples include:
- u0110 • Resveratrol, a polyphenolic found in the skins of red fruits, including grapes, is an antioxidant and is also found in wine. It has antichemotactic activities, as well as being a regulator of aspecific leukocyte activation (Jang et al. 1997, Bertelli et al. 1999, Szewczuk et al. 2004, Indraccoloa & Barbieri 2010).

s0030 **Anti-inflammatory effects of omega 3 and 6 oils**

p0185 Eicosanoids – biologically active substances including prostaglandins, prostacyclins, thromboxanes and leukotrienes – are derived either from omega-3 or omega-6 fatty acids. Since essential fatty acids cannot be synthesized by the body and must be supplied through dietary intake, the type of fatty acid that predominates in the diet can promote or oppose the inflammatory response. Metabolism of saturated fats and omega-6 fatty acids (e.g. arachidonic acid), leads to the biosynthesis of inflammatory prostaglandins, prostacyclins, thromboxanes, leukotrienes and lipoxins.

p0190 Omega-3 fatty acids are essential nutrients, which means that humans cannot manufacture their own, and so must be found in the diet. The main food sources are found in flaxseed oil, walnut oil and oily fish. Omega 3 oils reduce inflammation, by competing with arachidonic acid in the cell membrane, reducing the available amount and also compete with cyclo-oxygenase and lipo-oxygenase enzymes which are up-regulated in the inflammatory process (Obata et al. 1999, Ringbom et al. 2001).

p0195 The ratio of omega-6:omega-3 fatty acids appears to be critical (Simopoulos et al. 2002). Although the optimal ratio remains under review, it is suggested that approximately four parts omega-6 to one part omega-3 essential fatty acids should be the target for optimum balance (Yehuda et al. 2000, 2005). A ratio of 3:1, and lower, is also recommended by some authorities (Chrysohoou 2004).

p0200 Simopoulos (2002) has observed that the ratio of omega-6 to omega-3 is clinically variable:

A ratio of 2–3/1 suppressed inflammation in patients with rheumatoid arthritis, and a ratio of 5/1 had a beneficial effect on patients with asthma, whereas a ratio of 10/1 had adverse consequences. These studies indicate that the optimal ratio may vary with the disease under consideration. This is consistent with the fact that chronic diseases are multigenic and multifactorial. Therefore, it is quite possible that the therapeutic dose of omega-3 fatty acids will depend on the degree of severity of disease resulting from genetic predisposition. A lower ratio of omega-6/omega-3 fatty acids is more desirable in reducing the risk of many of the chronic diseases of high prevalence in Western societies.

p0205 This emphasizes the need for careful assessment and testing of fatty-acid status prior to prescription of changes in patient's omega 6:3 ratio. As a generalization, a nutritionist would test fatty acid status, and make recommendations ranging from 4:1 through to

a 1:1 ratio based on the test results, although the 4:1 ratio is the 'ideal' for someone who is optimally healthy.

- Short-chain omega-3 fatty acids oppose inflammation through decreased production of inflammatory prostaglandins, leukotrienes and arachidonic acid. Food sources include flaxseed, hempseed, walnuts, canola and rapeseed oils, as well as dark green leafy vegetables, pumpkin seeds and oily fish (Saldeen & Saldeen 2004). u0155
- Long-chain omega-3 fatty acids are found in the following food sources and should be widely integrated into the anti-inflammatory diet: oily fish from cold northern waters such as salmon and mackerel; sardines, herring, black cod (sablefish or butterfish); fish oil, algae and DHA-rich eggs. u0160
- PUFAs, and especially total omega-3 fatty acids, were independently associated with lower levels of proinflammatory markers (IL-6, IL-1ra, TNF, C-reactive protein) and higher levels of anti-inflammatory markers (soluble IL-6r, IL-10, TGF) independent of confounders. Ferrucci et al. (2006) suggest that these findings support omega-3 fatty acids as being beneficial in patients affected with diseases characterized by active inflammation. u0165

Vitamin D and pelvic floor disorders in women s0035

Using 2005–2006 National Health and Nutrition Examination Survey data, Badalian and Rosenbaum (2010) reported on the prevalence of vitamin D deficiency in women with pelvic floor disorders, and the possible associations between vitamin D levels and pelvic floor disorders. Analysis of results collected from 1881 non-pregnant women, over the age of 20 were that:

- One or more pelvic floor disorders were reported by 23% of women. u0170
- Mean vitamin D levels were significantly lower for women reporting at least one pelvic floor disorder and for those with urinary incontinence, irrespective of age. u0175
- In adjusted logistic regression models, it was observed that there was a significantly decreased risk of one or more pelvic floor disorders with increasing vitamin D levels in all women aged 20 or older, and in the subset of women 50 years and older. u0180
- The likelihood of urinary incontinence was significantly reduced in women 50 and older with vitamin D levels 30 ng/mL or higher. u0185

B978-0-7020-3532-6.00010-9, 00010

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p0250 The conclusion was that higher vitamin D levels are associated with a decreased risk of pelvic floor disorders in women.

CPP/endometriosis and diet

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p0255 There is limited evidence – from animal studies – that dietary strategies such as a high fruit and vegetable, and low meat intake, may be useful in preventing endometriosis (Parazzini et al. 2004).

p0260 A 12-year prospective study has linked trans fats with increase risk of endometriosis. The study reported that:

During the 586,153 person-years of follow-up, 1199 cases of laparoscopically confirmed endometriosis were reported. Although total fat consumption was not associated with endometriosis risk, those women in the highest fifth of long-chain omega-3 fatty acid consumption were 22% less likely to be diagnosed with endometriosis compared with those with the lowest fifth of intake [95% confidence interval (CI) = 0.62–0.99; P-value, test for linear trend (Pt) = 0.03]. In addition, those in the highest quintile of trans-unsaturated fat intake were 48% more likely to be diagnosed with endometriosis (95% CI = 1.17–1.88; Pt = 0.001).

[TS4]

(Missner et al. 2010)

p0265 Britton et al. (2000) investigated the relation between diet and benign ovarian tumours (BOT) in a case–control study involving 673 women with BOT, of whom 280 had endometrioid tumours. It was noted that an intake of vegetable fat was positively associated with endometrioid tumours in a dose–response manner. Specifically, there was an elevated risk for intake of polyunsaturated fat.

p0270 A review of the literature on diet and endometriosis (Fjerbæk & Knudsen 2007) noted that evidence (at that time) was sparse. In some instances, dietary modifications, including the intake of fish oils (see discussion of inflammation above) have been shown to beneficially influence dysmenorrhoea.

Dysmenorrhoea: studies and meta-analyses

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p0275 For example, a number of studies have shown that a correlation exists between increased risk of more intense dysmenorrhoea and:

- u0190 • Low fibre intake (Nagata et al 2005);
- u0195 • Low fruit, fish and egg intake, and increased alcohol intake (Balbi et al. 2005);

[TS5]

- Low intake of total fat, saturated fat, omega-3 fatty acids, vitamins D and B12 (Deutsch et al. 2000); [TS6] u0200
- Bernard et al. (2000) demonstrated that during phases of a 'low-fat vegetarian diet, compared to the normal diet phase, sex-hormone binding globulin concentration was significantly higher, and dysmenorrhoea duration and pain intensity fell'; u0205 [TS7]
- In a randomized controlled study Harel (2002) observed a significant reduction in menstrual symptoms, together with a reduction in use of analgesic medication, in adolescents after intake of fish oil; u0210
- Evidence from these studies suggests that coffee and soy intake have no effect on the symptoms of dysmenorrhoea; u0215
- In a Cochrane Collaboration review, Proctor & Murphy (2001) report that there is evidence that vitamin B1 (100 mg daily) and magnesium (no dosage recommended because of conflicting reports) help reduce pain of dysmenorrhoea; u0220
- They also report that omega-3 fatty acids were more effective than placebo for pain relief. u0225

Painful bladder syndrome (PBS)

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- Ward & Haoula (2008), in a review of current literature, suggest that while there is no evidence to link diet with PBS, elimination of substances that are considered to either irritate the bladder or may contribute to bladder inflammation, may help some patients. These substances include caffeine, alcohol, tomatoes, spices, chocolate, citrus and high-acid foods or beverages. u0230

Vulvar vestibulitis syndrome (VVS) and interstitial cystitis

s0055

- Farage & Galask (2005) observe that urinary excretion of oxalates (found naturally in many foods –including spinach and other green leafy vegetables, most nuts, legumes, berries, wheat, and high in vitamin C supplements – and also manufactured by the body) have been proposed as contributing to VVS, based initially on a single case report (Solomons et al. 1991). In that case, symptoms of burning and itching of the urethra, were apparently associated with hyperoxaluria. u0235
- Reports by Fitzpatrick et al. (1993), Stewart & Berger (1997) and Tarr et al. (2003) have all u0240

- suggested a possible shared pathogenesis for VVS and interstitial cystitis, involving high-oxalate presence.
- u0245 • This hypothesis has however not been confirmed in a study involving 130 patients and 23 controls, of a low-oxalate diet (Baggish et al. 1997).
 - A diet low in fermentable oligo-, di-, and monosaccharides and polyols, i.e. sugar alcohols such as sorbitol (Shepherd & Gibson 2006); u0285
 - Eliminate wheat, banana, corn, potato, milk, eggs, peas and coffee. u0290

s0060 Irritable bowel syndrome (IBS) and diet

- [TS8] p0350 Rapin & Weirnsperger (2010) note that increased intestinal permeability is a common feature of irritable bowel syndrome. Management of increased gut permeability, and associated food intolerances, has been shown to be improved by careful nutritional strategies, including use of probiotics (Mennigen & Bruewer 2009, also see below) and glutamine (Li & Neu 2009).
- p0355 In a comprehensive review of IBS, Heizer et al. (2009) suggest that dietary changes are commonly a useful strategy. It is recommended that dietary restrictions should be introduced one at a time, beginning with any food or food group that appears to cause symptoms based on a careful patient history or review of a patient's food diary. The most effective duration for dietary trials has not been well studied, however 2–3 weeks is commonly suggested.
- p0360 A modified exclusion diet, followed by stepwise reintroduction of foods is likely to be more effective in identifying the irritating substance, but is more time-consuming (Parker et al. 1996). Any improvement in symptoms after an unblinded dietary change could be a placebo effect, and may not persist.
- [TS9] p0365 General dietary recommendations for patients with IBS, based on clinical experience and anecdotal reports (Heizer et al. 2009) include:
- u0250 • Avoiding large meals;
 - u0255 • Reducing lactose (eliminate milk, ice cream and yogurt);
 - u0260 • Reducing fat to no more than 40–50 g/day;
 - u0265 • Reducing sorbitol, mannitol, xylitol (mainly 'sugarless' gum, read labels);
 - u0270 • Reducing fructose in all forms, including high-fructose corn syrup (read labels), honey, and high-fructose fruits (e.g., dates, oranges, cherries, apples and pears);
 - u0275 • Reducing gas-producing foods (eg, beans, peas, broccoli, cabbage and bran);
 - u0280 • Eliminating all wheat and wheat-containing products;

Peppermint oil

Many studies suggest that use of peppermint oil is likely to be of benefit in symptomatic treatment of relatively mild cases of IBS (Grigoleit & Grigoleit 2005, Capello et al. 2007). [TS10] s0065 p0415

Turmeric (curcumin)

While some mainly pilot studies have shown potential benefit for use of turmeric (a member of the ginger family of plants) in treatment, noplacbo-controlled studies have as yet been conducted (Bundy et al. 2004, Heizer et al. 2009). p0420

Probiotics

Two meta-analyses (McFarland & Dublin 2008, Nifkar et al. 2008) and two comprehensive narrative reviews (Spiller 2008, Wilhelm et al. 2008) were published in 2008 on the use of probiotics in the treatment of IBS. All concluded that probiotics may be useful but there are many variables affecting the results such as the type, dose and formulation of bacteria comprising the probiotic preparation, the outcome measured as well as size and characteristics of the IBS population studied. [TS11] s0075 p0425

The conclusions of a review of the evidence for use of probiotics in both IBS and inflammatory bowel disease (IBD) are cautiously positive (Iannitti & Palmieri 2010): p0430

Probiotics seem to play an important role in the lumen of the gut elaborating antibacterial molecules such as bacteriocins. Moreover they seem to be able to enhance the mucosal barrier increasing the production of innate immune molecules, including goblet cell derived mucins and trefoil factors and defensins produced by intestinal Paneth cells. Some strains promote adaptive immune responses (secretory immune globulin A, regulatory T cells, IL-10). Some probiotics have the capacity to activate receptors in the enteric nervous system, which could be used to promote pain relief in the setting of visceral hyperalgesia. (Sherman et al 2009) Moreover probiotics exert an important action improving the abnormalities of both the colonic flora and the intestinal microflora. They

B978-0-7020-3532-6.00010-9, 00010

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p0440 This brief chapter has summarized current understanding of nutritional influences on CPP, both in preventive and in therapeutic contexts. While general dietary advice can safely be offered by healthcare providers, it is suggested that skilled and well-trained nutritional experts should be involved before any major dietary modifications are suggested to patients. The following chapter describes the connections between respiratory dysfunction and pelvic pain, as well as means of restoring enhanced breathing function.

could be effective for treating various pathologies preventing the dysbiosis which characterizes or is associated with these conditions. Further future clinical trials, involving large numbers of patients, will be mandatory to achieve definite evidence of the preventive and curative role of probiotics in medical practice.

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Acknowledgement

The editors thank Louise Nicholson FdSc, Dip ION of NutriProVita www.nutriprovita.com for her valuable assistance in the review of the nutritional literature presented in this section.

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TS12

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