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## Shark Cartilage to Treat Cancer

*By Dónal P. O'Mathúna, PhD*

**S**HARK CARTILAGE IS A POPULAR CANCER REMEDY FRAUGHT WITH controversy. William Lane, PhD, did much to bring the remedy to public attention through his books *Sharks Don't Get Cancer* (1992) and *Sharks Still Don't Get Cancer* (1996). Subsequent publicity led to significant media attention, including an appearance on "60 Minutes" (1993). While that television show reported remarkable improvements in cancer patients treated with shark cartilage, the medical literature has been consistently critical of the findings.<sup>1</sup> Although one study found it was the most popular cancer remedy recommended in health food stores,<sup>2</sup> the FDA sought an injunction against manufacturers for promoting the product as a cancer treatment.<sup>3</sup> Among Dutch cancer patients, 60% have used the Houtsmuller Diet, named after a Dutch physician who claimed a diet rich in shark cartilage and other vitamins cured his malignant melanoma; but the doctor has since admitted he never had cancer.<sup>4</sup> Given the popularity of shark cartilage products, professionals should be aware of the evidence available for its use in treating cancer.

### Background

Although shark cartilage is recommended for psoriasis, inflammatory joint diseases, and macular degeneration, most interest and research has focused on its use in treating cancer. Interest in cartilage to treat cancer began in the 1950s, primarily focused on bovine cartilage. Attention was directed toward shark cartilage in the 1970s, and basic research through the 1980s produced interesting in vitro findings. Then Lane's books brought public attention. His book *Sharks Don't Get Cancer* claimed that some substance in sharks' cartilage protected them from cancer. However, several dozen documented cases of benign and malignant cancers in sharks date back to 1913.<sup>5</sup> Lane's 1996 book acknowledged this, but noted that the incidence of cancer in sharks is very low. However, a recent review of marine research concluded that shark cancer rates are unknown because they have never been systematically examined.<sup>5</sup> Even if the incidence of cancer in sharks is low, this provides no support for using cartilage to treat cancer. Nonetheless, research is demonstrating that extracts made from shark cartilage hold promise as cancer treatments.<sup>6</sup>

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## Pharmacology

Commercial shark cartilage products consist of powdered shark skeletons, which make up 6% of a shark's whole body weight.<sup>7</sup> This powder contains 40% protein, up to 20% chondroitin sulfate and glucosamine, up to 25% calcium, and glycoproteins.<sup>4</sup> Several extracts of shark cartilage are also under investigation for anticancer activity. U-995 had *in vitro* activity, but not when given orally to animals. Another, AE-941 (Neovastat, Aeterna Laboratories, Canada), is a water-soluble extract from which 95% of inert cartilage material has been removed. It has *in vitro* activity, is orally active, and is the first shark cartilage extract to reach phase III clinical trials as an anti-cancer agent.<sup>6</sup> This extract also has been shown to stimulate tissue plasminogen activator (t-PA) and thus to have potential in treating vascular disorders.<sup>8</sup> A clear distinction must be made between such purified extracts and the crude material typically marketed as shark cartilage.

## Mechanism of Action

Although several mechanisms of action have been proposed, the one with some supportive evidence is that of antiangiogenesis. In 1971, Judah Folkman published a seminal paper proposing that agents that block the

development of blood vessels could be used to treat cancer.<sup>9</sup> Angiogenesis is the production of new blood vessels that occurs in humans primarily during fetal development, inflammation, wound healing, and malignancy. Tumor growth requires new vascularization to permit exchange of nutrients and waste. Inhibiting this process would prevent tumors from growing beyond a couple of millimeters in diameter.<sup>10</sup> Antiangiogenic factors have been found in bovine, human, and shark cartilage.<sup>7</sup> Some from other sources are in various stages of clinical trials as anticancer agents.<sup>11</sup>

## Clinical Studies

Early animal experiments demonstrated that shark cartilage and its extracts had antiangiogenic and antitumor activity in mice, rabbits, and chick embryos.<sup>10</sup> However, shark cartilage was not administered orally in these experiments. Oral administration was examined in mice with the SCCVII tumor model, which is known to be responsive to conventional anticancer therapies, including antiangiogenic agents.<sup>12</sup> Mortality, tumor size, and metastatic spread were not reduced compared to controls.

Human studies with shark cartilage began with two conducted by Lane.<sup>1</sup> In the first, 29 patients with a variety of cancers were given 0.5 g/kg/d rectally. Lane reported improvements in 55% of the patients, but the details remain unpublished in peer-reviewed literature. In another open trial, eight patients with end-stage cancers of various types were given 30 g/d shark cartilage by enema and, for women, also vaginally. After 11 weeks, seven patients reported improvements and five were reported as tumor-free. Improvement was not measured objectively. The National Cancer Institute concluded that these studies provide little evidence to support the use of shark cartilage.

Abstracts from five trials were identified by the authors of an extensive review of shark cartilage research.<sup>4</sup> Three abstracts reported no benefit from shark cartilage in patients with breast, prostate, or refractory brain cancers; one found a positive trend among cancer patients; and another found improved quality of life in 10 of 20 subjects enrolled. Analysis of all these studies is limited by the lack of published details.

One clinical trial has been published in the peer-reviewed literature.<sup>11</sup> Miller et al enrolled 60 patients with several types of advanced, previously treated cancers. All subjects received 1 g/kg shark cartilage orally, divided into three doses taken before meals. Predetermined criteria for a complete response and a partial response were not met by any patient. Overall, no improvement in quality-of-life scores was found. The

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median time to tumor progression was similar to that reported elsewhere for patients receiving supportive care only or placebo in controlled trials. The authors concluded that for the dose and types of cancer involved in this trial, shark cartilage showed no anticancer activity.

As mentioned above, AE-941 is an extract of shark cartilage that has demonstrated anticancer activity in Phase I and II trials. These studies have been in non-small cell lung cancer and renal cell carcinoma. For example, 80 patients with advanced, refractory lung cancer were enrolled in a multicenter, open-label, dose-escalation study.<sup>13</sup> Of the 48 patients with unresectable, advanced non-small cell lung cancer, those receiving more than 2.6 mL/kg/d survived significantly longer than those receiving lower doses (median, 6.1 v. 4.6 months;  $P = 0.026$ ). In addition, 26% of the high-dose patients had stable disease compared to 14% in the low-dose group. This purified shark cartilage extract is now in Phase III trials.

### Adverse Effects

In the Miller et al trial, the most common adverse effects were gastrointestinal disturbances, with 10% of the subjects discontinuing shark cartilage because of their severity.<sup>11</sup> In general, crude shark cartilage, and its extracts, are tolerated well in recommended doses. Theoretically, the high calcium content of crude preparations could be problematic in patients with renal disease or at risk for arrhythmias.<sup>4</sup> Antiangiogenic effects could interfere with wound healing after surgery or trauma. Participants in clinical trials of other antiangiogenic agents should avoid shark cartilage to prevent interference or potentially adverse synergistic effects. Shark cartilage should be avoided during pregnancy and breast feeding due to the risk of interference with normal fetal and infant angiogenesis.

### Formulation

Manufacturers of powdered shark cartilage products typically recommend between 500 mg and 4.5 g daily, taken in 2-6 divided doses.

### Conclusion

The oral use of powdered shark cartilage to treat cancer is not supported by clinical studies. As a recent review concluded, "It is notable that despite more than a decade of evaluation of shark cartilage, not a single controlled study has established any efficacy of crude cartilage extracts against cancer."<sup>5</sup> However, shark cartilage is a source of antiangiogenic products, some of which are progressing through clinical trials and may lead to effective treatments. Such products also hold the poten-

tial to be synthetically derived, thus sparing the natural shark population which has been measurably depleted over the past 15 years (sharks are also fished for their meat and oil, and for sport, as well as for their cartilage).<sup>5</sup>

### Recommendation

Patients with cancer should be encouraged not to place hope in powdered shark cartilage products. Although the products are generally well tolerated, they do carry some risk of gastrointestinal discomfort and may interfere with other conditions. In addition, a month's supply can cost \$700-1000.<sup>4</sup> Such costs may be acceptable with an effective product, but not with one that has failed to produce results that have stood up to professional review. Patients should instead be encouraged to pursue the treatments that have been shown to be effective for their particular form of cancer. ❖

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## An Overview of Osteopathic Medicine: Principles and Practice

By Tiffani Singleton, DO,  
Janet M. Burns, DO, and  
Katherine A Clark, DO, FAAFP,

OSTEOPATHIC MEDICINE IS PARALLEL AND DISTINCT from conventional medicine. It has been practiced for more than 100 years. Its founder, Andrew Taylor Still, MD, formulated a philosophy of medical care that, while not unique in the history of medicine, was controversial at the time. The reigning medical paradigm of Still's day was that disease came from without and, therefore, the cure must come from without as well. Disease was regarded as the sum total of all the symptoms manifested in the patient and, therefore, treatments were aimed at eliminating or suppressing the symptoms one by one. Still concluded that disease was the result of dysfunction, most noticeably in structure, and that if structure was optimized, function could be improved or restored. Treatment therefore was aimed at the whole person: mind, body, and spirit. It focused on optimizing host structure and function and not on treating a particular disease entity.

Today, osteopathic physicians (DOs) are recognized for the unlimited practice of medicine in all 50 states, the District of Columbia, and U.S. territories. Conventional and osteopathic physicians train and practice together in offices, hospitals, and the Armed Forces. Despite this, many physicians are not aware of the distinctions between osteopathic and conventional medicine.

Osteopathic medicine is "... a complete system of medical care with a philosophy that combines the needs

of the patient with current practice of medicine, surgery, and obstetrics, that emphasizes the interrelationship between structure and function; and that has an appreciation of the body's ability to heal itself."<sup>1</sup> While differing in philosophy, the most noticeable difference between DOs and conventional physicians (MDs) is the use of osteopathic manipulative treatment (OMT).

OMT is a therapeutic adjunct that is utilized to treat a wide variety of disorders. As with any form of treatment, it has indications, contraindications, side effects, and dosing requirements. This article will discuss osteopathic medicine, its history, philosophy, and utilization of manipulative techniques.

### History of Osteopathic Medicine

Andrew Taylor Still was born in Virginia in 1828. After studying medicine and serving an apprenticeship under his father, who was a Methodist minister and physician, Still became a licensed physician in the state of Missouri. He served as a surgeon in the Union Army during the Civil War.<sup>2</sup>

After the Civil War and following the death of three of his children from spinal meningitis in 1864, Still became dissatisfied with the effectiveness of 19th-century medicine. He grew to reject the prevailing medical practices, many of which, including blood-letting and the use of certain drugs with serious side effects such as mercury and strychnine, were ineffective and even harmful. Still spent the next 10 years studying human anatomy and developing an alternate method of treating disease.<sup>2</sup>

Still developed a medical approach based on anatomy. He used the bony skeleton as his reference point for understanding clinical problems and their pathological processes. He wrote: "Osteopathy is compounded of two words; *osteon*, meaning bone, (and) *pathos*, (or) pathine, to suffer."<sup>3</sup> Through his cadaver dissections, he reasoned that strains or distortions of the fascia, ligaments, or muscle fibers surrounding blood and lymph vessels and nerve bundles could be the cause of ischemia and congestion.<sup>3</sup> In the course of treating his patients, he applied his knowledge of physiology and made clinical correlations between structural imbalances, including misaligned vertebrae, and his patients' disorders. He found that correcting these imbalances resulted in partial or complete cure.

In 1874, Still began practicing osteopathy exclusively. He traveled around Missouri and successfully treated many patients who had been treated unsuccessfully by other physicians. As his reputation grew, he established an infirmary in Kirksville, MO, in 1889 to care for his growing number of patients.

Table 1 The four principles of osteopathy
<ul style="list-style-type: none"> <li>• The body is a unit.</li> <li>• The body possesses self-regulatory mechanisms.</li> <li>• Structure and function are reciprocally interrelated.</li> <li>• Rational therapy is based upon an understanding of body unity, self-regulatory mechanisms, and the interrelationship of structure and function.</li> </ul>

Still's attempts to incorporate osteopathic principles into mainstream medicine were not accepted.<sup>2,4</sup> In 1892, he opened the American School of Osteopathy (ASO) in Kirksville. He was an advocate of training women and minorities in the medical profession. The first class enrolled 21 students, including several women. They were granted the degree of Doctor of Osteopathy (DO) at the end of their training.

By 1897, all subjects covered in traditional medical education were taught at ASO, with the exception of the materia medica, the current drug formulary.<sup>2</sup> In retrospect, such distrust of medication was not totally unwarranted. As late as 1899, the Merck Manual of Therapeutics listed 68 different treatments for diabetes mellitus—including arsenic, codeine, iron, and belladonna. He did, however, sanction the use of antiseptics and anesthetics in surgical and obstetrical practice, and the use of antidotes in poisoning cases. As pharmacology improved and use of toxic treatments declined, many DOs sought to provide their patients with the best of both worlds. After much heated debate, the profession officially added the materia medica to the curriculum in 1929,<sup>2</sup> but continued to differ fundamentally from conventional medical training in its philosophic approach to health and disease. Osteopathic medicine emerged as many U.S. medical activities had begun to converge under the American Medical Association. As a result, the profession worked for many years to solidify its own professional identity and to achieve professional credibility.<sup>2,4</sup>

### Osteopathic Philosophy, Principles, and Practice

Osteopathic medicine is both a philosophy of health care and a distinctive art. It is supported by expanding scientific knowledge, considers the unity of the patients' structure and function, and applies the philosophy in the practice of medicine and surgery. Its practice combines behavioral, chemical, physical, spiritual, and biological factors related to the establishment and maintenance of health as well as the prevention and alleviation of disease.<sup>3</sup> The four principles of osteopathy are summarized in Table 1.

Table 2 Diagnostic criteria for somatic dysfunction
S = Sensitivity
T = Tissue texture change (feel)
A = Asymmetry or positional change (look)
R = Restriction of motion (move)

Osteopathic medicine is based on a health-oriented, patient-centered philosophy. The physician's primary roles are to:

- address primary cause(s) of disease using available evidence-based practices.
- enhance the patient's healing capacity.
- individualize management plans with an emphasis on health restoration and disease prevention.
- use physical examination and manipulative treatment to improve altered structural, mechanical, and physiologic function.<sup>3</sup>

### Somatic Dysfunction

Somatic dysfunction is defined as impaired or altered function of related components of the somatic (body framework) system (i.e., skeletal, arthrodiar, and myofascial structures) and related vascular, lymphatic, and neural elements.<sup>1</sup> Somatic dysfunction exhibits a change in quantity and quality of motion, and is palpable. Such structural and functional disturbances may be of postural, traumatic, or behavioral origin (i.e., neglect, misuse, or abuse by the patient).<sup>5</sup> Four diagnostic criteria of somatic dysfunction are summarized using the mnemonic STAR in Table 2.<sup>1</sup>

Impairment or failure of visceral function may be reflected in the musculoskeletal system. This is referred to as a viscerosomatic reflex. Similarly, impairment of musculoskeletal function may be reflected in the visceral system, a somatovisceral reflex. Visceral and somatic systems can become linked in a vicious cycle of afferent and efferent impulses, which sustain and exacerbate the disturbance.<sup>5</sup> Palpatory findings of viscerosomatic origin consistently return after appropriate OMT treatment. Osteopathic physicians recognize this as a sign that somatic findings may be of visceral origin, which assists them in further differential diagnosis of the problem.<sup>6</sup>

An example of a viscerosomatic reflex would be palpable tissue texture changes overlying the 2nd-5th thoracic vertebrae as a result of a disease and inflammation of the lung tissue. It has been demonstrated that electrical stimulation of inflamed tracheobronchial mucosa causes decreased electrical skin resistance in the T2-5 dermatomes, followed by cutaneous hyperalgesia hours

later.<sup>7</sup> Appropriate treatment of the somatic component with OMT may reduce afferent and efferent sympathetic input into the vicious cycle, potentially decreasing vasoconstriction and improving tissue perfusion.<sup>5</sup>

### Osteopathic Manipulative Treatment

OMT is designed to treat somatic dysfunction and to remove musculoskeletal and myofascial impediments to normal physiologic processes. It addresses all tissues and is not limited to the spine.

Osteopathic manipulative techniques are categorized by several parameters, including:

- The initial set up of treatment: direct or indirect. Direct techniques engage the restrictive barrier (i.e., with the goal of stretching the connective tissue around the restricted joint), whereas indirect techniques are positioned away from the barrier and follow the sense of tissue ease.
- Activating force: force utilized to effect change. It may be physician-initiated, with deep pressure, compression, or traction. It also may be patient-initiated, with voluntary muscle contraction or deep breathing applied at the physicians' direction.<sup>3</sup>
- Target tissue and mechanism of action: joint, neuromyofascial elements, or viscera.

### Dosing of OMT and Treatment Reactions

The dose of OMT is limited by the patient's ability to respond to it. The sicker the patient, the lower the dose. Pediatric patients can be treated more frequently, while geriatric patients need longer intertreatment intervals. Chronic disease requires chronic treatment. Acute problems initially can have a shorter interval between treatments. The interval can be increased as the patient improves.<sup>8</sup>

Symptom exacerbation following OMT, such as transient soreness, may occur and is considered a normal, temporary outcome of the treatment process. There are few absolute contraindications to OMT, and it is difficult to list general contraindications to all techniques because of the wide variety of procedures available. These techniques vary from mild ones utilizing only the force of the patient's breath, to more forceful impulse- or thrust-based techniques.<sup>6</sup>

True complications are rare. A review of the literature reveals that most complications involved thrust techniques and focused on the cervical spine. The estimated risk of major impairment following cervical spine manipulation is 6.39 per 10 million manipulations. Vertebrobasilar artery stroke is the most commonly cited injury.<sup>9</sup> However, the actual risk of vertebrobasilar artery stroke from manipulation is less than the risk of a spon-

Table 3
Indications for HVLA
<ul style="list-style-type: none"><li>• Hypomobility</li><li>• Motion restriction</li><li>• Joint fixation</li><li>• Acute joint locking</li><li>• Motion loss with somatic dysfunction</li><li>• Restoration of bony alignment</li><li>• Meniscoid entrapment</li><li>• Adhesions</li><li>• Pain modulation</li><li>• Reflex relaxation of muscles</li></ul>

taneous one.<sup>10</sup> However, a nested case-control study of patients with cervical arterial dissection or transient ischemic arrhythmia (TIA) found that cervical arterial dissections were independently associated with spinal manipulative therapy within 30 days, even after controlling for neck pain.<sup>11</sup>

**High-Velocity/Low-Amplitude (mobilization by impulse).** High-velocity/low-amplitude (HVLA) mobilization employs a rapid therapeutic force of brief duration that travels a short distance within the anatomic range of the joint.<sup>1</sup> It is a direct technique that involves moving a dysfunctional joint through its restrictive barrier to restore appropriate physiologic motion. Table 3 lists several indications for the use of HVLA technique. A common misconception is that the bone is out of place, and that treatment puts it back in place. Instead, HVLA is designed to improve motion and allow the joint to return to the normal neutral or midline position. Following precise positioning against the restrictive barrier, a short (low-amplitude), quick (high-velocity) impulse is applied. Often a click or pop (cavitation) is heard, but is not required for successful treatment. Manipulation of a hypermobile joint can alleviate pain and improve motion, however it can also contribute to further joint instability.<sup>12,13</sup> Of note, studies have failed to show that habitual joint cracking leads to degenerative joint disease in the MCP joints in the elderly, and is not associated with osteoarthritis of the hand.<sup>14</sup>

**Soft Tissue.** The soft-tissue technique is similar to massage and is one of the most adaptable techniques. By adjusting the intensity, it can be well tolerated by most patients regardless of age and co-morbidity. The technique focuses on the subcutaneous tissue, muscles, and fascia, utilizing varying amounts of pressure and friction. The goals are to decrease abnormal tissue tension and assist in the movement of fluids, blood, and lymph.<sup>15</sup> Soft-tissue techniques may be applied directly using inhibition, which is application of steady pressure

to soft tissues to relax muscle tension and normalize reflex activity,<sup>16</sup> kneading; stretching; deep pressure; or effleurage. It also may be applied indirectly using the patients' breathing as the activating force.

**Muscle Energy Techniques.** Muscle energy techniques were developed by Frederic L. Mitchell, Sr., DO. They utilize the patient's own isometric muscle contractions to alter restriction of motion. They most commonly are used as a direct technique. The hypothesized mechanism of action is activation of golgi tendon organs, which inhibit tension in muscle fibers. It shares similarities with the proprioceptive neuromuscular facilitation techniques used by physical therapists.<sup>17</sup>

**Strain-Counterstrain.** Strain-counterstrain is an indirect technique developed by Lawrence Jones, DO. Jones found that patients with painful strains would tolerate being returned to the position in which the strain originally occurred. A tender point is defined as a small hypersensitive area in the myofascial tissues that does not have a pattern of pain radiation. These points are a manifestation of somatic dysfunction.<sup>1</sup> The physician identifies a tender point in a region of muscle or fascial strain. The patient is placed into a position of comfort, maintained for approximately 90 seconds, then returned to a neutral position.<sup>18</sup> This technique is thought to reset the proprioceptive reflex toward the normal resting length. It is a very gentle, well-tolerated technique, to which gentle massage may be added.

**Facilitated Positional Release.** Facilitated positional release is an indirect myofascial method of treatment developed by Stanley Schiowitz, DO. The dysfunctional region of the body is placed in a neutral position, diminishing tissue and joint tension in all planes. An activating force (compression or torsion) is added for 3-5 seconds. The patient is returned to the neutral position, and the somatic dysfunction is reevaluated.<sup>1</sup>

**Functional Methods.** Functional methods are indirect techniques used by A. T. Still. Their most recent refinement is attributed to William L. Johnston, DO.<sup>19</sup> They utilize the body's tendency to change toward an optimum steady state. The segment is placed in a position where a state of greatest ease is achieved between all of its physiologic movements. The patient's respirations provide the activating force. The motions of ease are followed until motility and tissue texture no longer improve.<sup>20</sup> Functional methods often are well tolerated when other techniques are not.

**Myofascial and Ligamentous Articular Release Treatment.** A. T. Still taught what used to be called traction methods. Most of these became known as ligamentous articular strain or myofascial release techniques. They address fascial, muscular, and ligamentous ten-

**Table 4**

**Key points in the lymphatic circulatory system<sup>28</sup>**

- Thoracic inlet
- Upper ribs
- Sternum
- First thoracic vertebrae
- Superior mediastinum
- Thoracic spine
- Lower ribs
- Thoraco-lumbar junction

sions or imbalances in any part of the body. The fundamental principles are to disengage, exaggerate, and balance. Activating forces may be supplied by the physician (compression or distraction/stretching) or by the patient's respiration.<sup>21</sup> William G. Sutherland, DO, generally is credited with formalizing these concepts into a method of treatment.

**Osteopathy in the Cranial Field.** William G. Sutherland, DO, also applied the fundamental principles of myofascial and ligamentous release techniques to the diagnosis and treatment of somatic dysfunction of the head. Cranial manipulation is a gentle treatment in which the physician detects stresses and strains of connective tissue or bony skeleton of the cranium through light but focused palpation.<sup>22</sup> The physician applies gentle forces with the hands to the dysfunctional regions, aiming for a reduction of these strains and improved symmetry of the bony skeleton. Oleski et al have shown that external manipulation treatment of the cranium alters select parameters of the cranial vault and base as measured by pre- and post-treatment X-ray.<sup>23</sup>

Cranial techniques have been found to be useful in treating a variety of disorders, including structural sequelae of long labor on the infant and the mother,<sup>24</sup> headaches including migraine headaches, sinusitis, hay fever, otitis media, colic,<sup>25</sup> and diminished infant suck reflex.

**Visceral Manipulation.** Visceral techniques can be direct or indirect and involve palpation and mobilization of organs and the fascia that suspends and envelops them. Sustained abnormal mechanical tension in these tissues is palpable. It contributes to functional impairment of the organ by adversely affecting the exchange of fluids and nutrients, pressure differentials, and neurologic function.<sup>26</sup> The goal is to restore physiologic motion and relieve tissue congestion. Physiologic motion can be divided into two components: visceral mobility (movement of the viscera in response to voluntary movement or to the movement of the diaphragm in

respiration); and visceral motility (inherent motion of the viscera themselves).<sup>27</sup>

**Lymphatic Techniques.** Proper lymphatic flow relies on a balance among the three pumps that control the cardiovascular-pulmonary system: the heart; the diaphragm, an abdomino-thoracic pump; and the skeletal muscles, a peripheral pump. Lymphatic flow disturbance can be diagnosed by the presence of edema, palpation of lymph nodes, or both. The tissues may become tender and the muscles contracted. Lymphatic techniques focus on freeing key areas of restriction to lymphatic flow. (See Table 4.) Lymphatic flow can be increased using active or passive lymphatic pump techniques.<sup>28</sup> One type of active lymphatic pump utilizes an external force to mimic the skeletal muscle pump by gently rocking the patient in the supine position from the feet in both dorsi- and plantar-flexion. Another technique uses gentle pumping motions on the chest to stimulate lymph flow by augmenting abdomino-thoracic cavity pressure changes. Passive techniques involve optimizing diaphragmatic excursion to allow increased generation of abdomino-thoracic pressure differentials. Thoracic and abdominal pump treatments have been shown to cause significant increases in thoracic duct lymph flow.<sup>29</sup>

### Treatment with OMT

Early osteopathic philosophy viewed disease as the result of imbalanced physiology and overwhelmed host defenses. Treatment and technique, therefore, were not specific to any particular disease. Early research in the field reflects this philosophy and was focused on identifying and defining “osteopathic lesions” referred to today as somatic dysfunction. Today, OMT is utilized to improve function, decrease pain, and is useful in prevention as well as in treatment.

### System Specific Disorders Responsive to OMT

Recent research has emphasized efficacy of OMT in specific disease entities, as well as continued inquiry into underlying mechanisms of action. The following illustrate specific disorders that have been addressed with OMT.

**Low Back Pain.** Low back pain is the second most common cause of absence from the work place among people younger than 55 years, second only to the common cold. Somatic dysfunction in low back pain is a diagnosis of exclusion. Low back pain also can be the result of referred pain from the viscera. Viscerosomatic reflexes can be seen with pathology in the prostate, stomach, colon, uterus, kidney, urinary bladder, liver, and spleen.<sup>30</sup>

Table 5
Benefits of manipulation in rheumatic disease
<ul style="list-style-type: none"><li>• Increased range of motion</li><li>• Decreased pain</li><li>• Increased function</li><li>• Relaxation of muscle spasm</li><li>• Improved symmetric balance of muscle activity</li></ul>

Somatic dysfunction may be the primary cause of low back pain or may coexist with other musculoskeletal problems, both acute and chronic. Eighty to ninety percent of non-traumatic low back pain is related to poor posture.<sup>31</sup> OMT is useful as an adjunct in the treatment of low back pain. Patients also should be taught stretches to increase mobility of the hip flexors, hip extensors, and hamstrings as well as exercises to strengthen the abdominal musculature and improve pelvic stability.<sup>32</sup>

In a study involving 155 patients with low back pain for at least three weeks but fewer than six months, 83 patients received OMT, and 72 patients received standard medical therapy. Although the researchers found no statistical difference in clinical outcome between the two groups, the use of medication was found to be greater in the standard-care group than in the osteopathic treatment group, with significant differences for NSAIDs and muscle relaxants. Physical therapy also was used more frequently in the standard-care group.<sup>33</sup>

**Headache.** Headache is a prevalent condition with substantial socioeconomic impact. The structural exam, neurologic examination, and, when appropriate, radiographic studies, are used in the evaluation of biomechanical function of the neuro-musculoskeletal system. Cervicogenic headache, when associated with moderate-to-severe motion loss in the upper three cervical vertebrae, responds favorably to manipulative intervention.<sup>34</sup> The suboccipital myofascial release technique addresses these areas and decreases the tension in the musculature and improves lymphatic drainage of the tissues.

The efficacy of spinal manipulation for chronic headache was studied in a systematic review of randomized clinical trials. Manipulation was found to be more effective than massage for cervicogenic headache. Spinal manipulation also was found to have results comparable to commonly used first-line prophylactic prescription medications for tension-type and migraine headache.<sup>35</sup> Grimshaw reviewed literature on manipulation and mobilization of the cervical spine and concluded that mobilization is probably of at least short-term benefit for patients with acute neck pain; manipulation is probably slightly more effective than mobilization or

physical therapy for some patients with subacute or chronic neck pain; and manipulation and/or mobilization may be beneficial for muscle tension headache.<sup>34</sup>

**Rheumatic Disease.** Treatment of the somatic component in an arthritic process by administration of manipulative treatment has been helpful in relieving pain and distress.<sup>36</sup> The effects of manipulation on myofascial pain can be immediate. Manipulation has been shown to decrease joint pain and normalize function. Manual techniques are beneficial for back and neck muscle imbalance when compared with no treatment or placebo, and have adjunctive usefulness in a comprehensive treatment program. (See Table 5.) Manual techniques are useful for painful conditions as a means to break the pain cycle and increase tolerance of exercise.<sup>37</sup>

Mobilizing joints and decreasing muscle/fascial/ligamentous imbalance or tension increases range of motion, improves local circulation and lymphatic drainage, and balances neuromuscular relationships that alter muscle tone. Treating postural muscles may improve balance and gait. Improved biomechanical function may reduce somatovisceral reflexes. Indirect treatments are useful for patients with osteoporosis or acute inflammation.<sup>36</sup>

**Fibromyalgia.** Fibromyalgia syndrome is a common nonarticular, rheumatic musculoskeletal pain disorder for which a definite cause has yet to be identified. Fibromyalgia is characterized by diffuse pain and aching, the presence of multiple tender points, morning stiffness, as well as many other associated symptoms including irregular sleep patterns, irritability, numbness and tingling of extremities, chronic fatigue, cognitive dysfunction, bladder irritability, and headaches.<sup>38</sup>

In one study, 24 female patients were randomized to either OMT only, OMT and education, application of moist heat to tender points only, or a control group. Those receiving OMT had significantly higher pain thresholds, were more satisfied, comfortable, and relaxed as well as confused compared to patients not receiving OMT. The OMT-treated patients also reported fewer symptoms related to failure, frustration, inhibition, struggling, helplessness, guilt, incapacity, insomnia, and tiredness associated with pain. They were less bothered and depressed, had good appetites more often, had less frequent losses of energy, and were restless and lonely less often.<sup>39</sup>

**Chronic Pain Syndromes.** The experience of pain is mediated by stimulation that occurs at the periphery, spinal cord, and multiple regions of the cerebral cortex. Improper treatment of acute pain may lead to central nervous system remodeling or facilitation, one of the most common causes of chronic pain. OMT has been

shown to be helpful in both acute and chronic pain syndromes. The pain relief resulting from joint manipulation appears to involve descending inhibitory mechanisms that utilize serotonin and noradrenaline.<sup>40</sup>

**Pulmonary Disorders.** Respiration has been described as a dynamic process involving reflex neural activity; abdominal, diaphragmatic, and other muscular activity; motion of fascial planes; and the movements of more than 146 joints. Pathologic alterations in structure, including restricted rib motion, result in inefficient or decreased ability to function.<sup>41</sup> Goals of OMT in pulmonary disorders are to optimize cervical, rib cage, and diaphragmatic motion, allowing the patient to generate improved pressure gradients necessary for efficient movement of air and fluid, and decreasing the work of breathing. Rib raising can improve rib excursion<sup>42</sup> while diaphragm redoming aims to improve the excursion of the diaphragm, which may tend to tighten and flatten in chronic respiratory conditions such as asthma.

Many osteopathic primary care and specialty physicians have utilized OMT for patients with asthma or chronic obstructive pulmonary disease (COPD).<sup>43</sup> In adults hospitalized with COPD, OMT has been shown to reduce the severity of illness, residual volume, and retained pCO<sub>2</sub>, while increasing oxygen saturation and lung capacity.<sup>44</sup> One study evaluated the immediate effects of osteopathic manipulative procedures on respiratory excursion, peak expiratory flow rates, and subjective measures of symptoms compared with sham procedures on chronic asthma patients. Measurements of both upper and lower thoracic forced respiratory excursion statistically increased after OMT compared with sham procedures. Changes in peak expiratory flow rates and asthma symptoms were not statistically significant.<sup>45</sup>

OMT combined with conventional treatment has been reported to reduce the length of stay in the hospital in patients with respiratory tract infections, asthma, and COPD. Researchers took these findings further by conducting a prospective, randomized study to evaluate the efficacy of adjunctive OMT in elderly patients hospitalized with pneumonia. Results showed mean duration of IV antibiotic use was shorter for the osteopathic-treated group than for the control group, which received a light touch protocol (P = 0.005). The treatment group also had significantly shorter length of hospital stay (P = 0.014) and greater decrease in white blood cell count between days 1 and 3 (P = 0.014).<sup>44</sup>

## Conclusion

The osteopathic approach to care of the whole patient is consistent with current practice in primary care. OMT

is a safe and effective adjunct to conventional therapy for many disorders. As there has been increased interest in alternative and manual medicine, other health care providers have sought training in OMT. The osteopathic profession provides training in OMT to physicians and dentists through continuing medical education programs sponsored by the American Academy of Osteopathy and the Michigan State University College of Osteopathic Medicine. ❖

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## Clinical Briefs

*With Comments from Russell H. Greenfield, MD*

### **Probiotic Infant Formula and Infectious Disease Prevention**

**Source:** Weizman Z, et al. Effect of a probiotic infant formula on infections in child care centers: Comparison of two probiotic agents. *Pediatrics* 2005;115:5-9.

**Goal:** To compare the effect of two different probiotics on preventing infections in children attending day care centers.

**Design:** Prospective, randomized, double-blind, placebo-controlled trial at 14 Israeli child care centers.

**Subjects:** Healthy infants from 4-10 months of age (n = 201).

**Methods:** Participants were random-

ized to receive standard formula (n = 60), or formula supplemented with either *Bifidobacterium lactis* (also called BB-12, n = 73) or *Lactobacillus reuteri* (n = 68) for 12 weeks. Children were evaluated at baseline, 4, 8, and 12 weeks. Parents filled out a questionnaire daily (which included questions on feeding, stools, and behavior) and were asked to report on symptoms. With onset of illness, each child was examined daily by a pediatrician. Primary outcome measures included number of days/episodes of fever, respiratory illness, or diarrhea. Secondary outcome measures focused on the need for conventional medical intervention.

**Results:** Those infants not receiving probiotic therapy experienced significantly more episodes of fever. The control group also had more episodes of diarrhea, which lasted longer than simi-

lar illness in the treatment groups. No difference was noted between groups with respect to incidence of respiratory tract infections. For the children who did receive probiotics, those getting *L. reuteri* experienced fewer days of fever, missed fewer days of child care, and had lower rates of clinic visits and antibiotic use than those in the BB-12 group.

**Conclusions:** Healthy infants offered formula supplemented with either BB-12 or *L. reuteri* experienced less febrile illness, and both fewer and shorter episodes of diarrhea, than children receiving standard formula. Effects noted were more prominent in the group receiving *L. reuteri*.

**Study Strengths:** Compared two microbes accepted as viable probiotics; amount and viability of microbes

monitored every three months; degree of follow-up.

**Study Weaknesses:** Short duration; no fecal analysis of gut colonization.

**Of Note:** Infants in the study were not breastfed based on prior parental decision; information from seven children was not included in the final analysis due to non-compliance with the protocol; probiotic-supplemented infant formulas are currently available in several countries; the 21-month study period spanned two winter and two summer seasons; children with atopic disorders were not permitted to participate in the study (previous probiotic studies have suggested benefit for atopic disorders); each supplemented formula contained  $1 \times 10^7$  colony-forming units of the specified microbe and mean daily formula intake did not differ between the groups; no adverse effects were noted; improvements with probiotic therapy in established illness were modest (e.g., differences in duration of fever and diarrhea were less than one day).

**We Knew That:** Probiotics may enhance host immunity beyond the gas-

trointestinal tract; human breast milk is a source of lactic acid bacteria for the infant gut, and breastfed infants develop a probiotic-rich intestinal milieu as compared with formula-fed infants, which may explain the lower incidence of infectious diarrhea in breastfed babies; children attending day care centers have a higher incidence of both respiratory and gastrointestinal infections; prior studies suggest that probiotic therapy may lessen the incidence of recurrent infectious disease in children attending day care centers; bifidobacteria and lactobacilli are generally regarded as safe since they are normally found in human intestines.

**Clinical Import:** Any means of keeping infants healthy has worldwide implications, and although some of the improvements noted in this study were modest, one need only ask any parent if one day less of their child's illness would be deemed beneficial. The idea that taking bacteria orally could have an impact on immune system function far from the digestive tract was once incredible, but data have shown the concept to be true and research into the benefits of probiotic therapy has exploded.

This is one of the few studies pitting one microbe against another to evaluate therapeutic effectiveness. The issue is significant, as many people, patient and practitioner alike, consider probiotic therapy to be therapeutically equivalent across numerous microbial strains. Such a stance is incorrect. The effect of probiotic therapy is strain-specific and likely disease-specific, but with so many organisms touted as effective probiotics, it is as yet unclear which agents should be used in specific clinical situations.

This study offers a framework for comparing organisms with probiotic activity, and suggests that *L. reuteri*, even more than BB-12, may help keep infants healthy while attending day care. Longer trials are warranted, and data comparing *L. reuteri* with *Lactobacillus GG* (the organism currently associated with the most supportive data) in specific clinical situations would be valuable. Readers should keep in mind that probiotic therapy usually involves live organisms, which could put immunocompromised children at risk.

**What to do with this article:** Keep a hard copy in your file cabinet. ❖

## CME Questions

**CME Instructions:** Physicians participate in this continuing medical education program by reading the articles, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, participants must complete the evaluation form provided at the end of each semester (June and December) and return it in the reply envelope provided to receive a certificate of completion. When an evaluation form is received, a certificate will be mailed to the participant.

**20. The most popular types of shark cartilage products are made from:**

- a. water extracts of shark cartilage.
- b. powdered crude shark cartilage.

- c. alcohol extracts of shark cartilage.
- d. powdered cartilage of various sources.

**21. The most common adverse effect of oral shark cartilage is:**

- a. heart attack.
- b. psoriasis.
- c. gastrointestinal disturbance.
- d. All of the above

**22. Which of the following are included in the diagnostic criteria of somatic dysfunction?**

- a. Sensitivity
- b. Tissue texture changes
- c. Asymmetry
- d. Restricted range of motion
- e. All of the above

**23. Which of the following is an osteopathic principle?**

- a. Taking care of the whole person
- b. The relationship of structure and function
- c. Prevention
- d. Homeostasis

Answers: 20. b, 21. c, 22. e, 23. b.

# ALTERNATIVE MEDICINE ALERT™

*A Clinician's Evidence-Based Guide to Alternative Therapies*

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## Cancer: Resources and Screening Guidelines

**C**ANCER, THE SECOND LEADING CAUSE OF DEATH AMONG AMERICANS, IS RESPONSIBLE FOR one of every four deaths in the United States. In 2005, more than 570,000 Americans—or more than 1,500 people a day—will die of cancer. Close to 1.4 million new cases will be diagnosed in 2005. This estimate does not include preinvasive cancer or the more than 1 million cases of nonmelanoma skin cancer expected to be diagnosed this year.

The number of new cancer cases can be reduced substantially, and many cancer deaths can be prevented. Adopting healthier lifestyles—for example, avoiding tobacco use, increasing physical activity, achieving optimal weight, improving nutrition, and avoiding sun exposure—can significantly reduce a person's risk for cancer. Making cancer screening, information, and referral services available and accessible to all Americans is also essential for reducing the high rates of cancer and cancer deaths (*See Tables 1 and 2*).

**Table 1**

### Cancer: Information Resources

National Cancer Institute National Institutes of Health 9000 Rockville Pike, Bethesda, MD 20892 Web site: <a href="http://www.nci.nih.gov">www.nci.nih.gov</a> Telephone: (800) 4-CANCER	Center for Disease Control and Prevention 1600 Clifton Rd, Atlanta, GA 30333 Web site: <a href="http://www.cdc.gov">www.cdc.gov</a> Telephone: (404) 639-3311
American Cancer Society 1599 Clifton Rd. NE, Atlanta, GA 30329 Web site: <a href="http://www.cancer.org">www.cancer.org</a> Telephone: (800) ACS-2345	MD Anderson Cancer Center The University of Texas 1515 Holcombe Blvd., Houston, TX 77030 Web site: <a href="http://www.mdanderson.org">www.mdanderson.org</a> Telephone: (800) 392-1611
The Sidney Kimmel Cancer Center at Johns Hopkins University 401 North Broadway, Baltimore, MD 21231 Web site: <a href="http://www.hopkinskimmelcancercenter.org">www.hopkinskimmelcancercenter.org</a> Telephone: (410) 955-8964	Harvard Center for Cancer Prevention 677 Huntington Ave., Landmark 3 East Boston, MA 02115 Web site: <a href="http://www.hsph.harvard.edu/cancer">www.hsph.harvard.edu/cancer</a> Telephone: (617) 998-1034
Carol Ann Schwartz Cancer Initiative Richard and Hinda Rosenthal Center for Complementary and Alternative Medicine Columbia University College of Physicians & Surgeons 630 W. 168 St., Box 75, New York, NY 10032 Web site: <a href="http://www.rosenthal.hs.columbia.edu">www.rosenthal.hs.columbia.edu</a> Telephone: (212) 342-0101	National Breast Cancer Coalition 1101 17th St., NW, Suite 1300 Washington, DC 20036 Web site: <a href="http://www.stopbreastcancer.org">www.stopbreastcancer.org</a> Telephone: (800) 622-2838

Table 2

## American Cancer Society's Screening Guidelines for the Early Detection of Cancer in Asymptomatic People

Site	Recommendation
<b>Breast</b>	<ul style="list-style-type: none"> <li>Yearly mammograms are recommended starting at age 40. The age at which screening should be stopped should be individualized by considering the potential risks and benefits of screening in the context of overall health status and longevity.</li> <li>Clinical breast exams should be part of a periodic health exam, about every 3 years for women in their 20s and 30s, and every year for women 40 and older.</li> <li>Women should know how their breasts normally feel and report any breast change promptly to their health care providers. Breast self-exam is an option for women starting in their 20s.</li> <li>Women at increased risk (e.g., family history, genetic tendency, past breast cancer) should talk with their doctors about the benefits and limitation of starting mammography screening earlier, having additional tests (i.e., breast ultrasound and MRI), or having more frequent exams.</li> </ul>
<b>Colon &amp; rectum</b>	<p>Beginning at age 50, men and women should begin screening with one of the examination schedules below:</p> <ul style="list-style-type: none"> <li>A fecal occult blood test (FOBT) or fecal immunochemical test (FIT) every year</li> <li>A flexible sigmoidoscopy (FSIG) every 5 years</li> <li>Annual FOBT or FIT and flexible sigmoidoscopy every 5 years*</li> <li>A double-contrast barium enema every 5 years</li> <li>A colonoscopy every 10 years</li> </ul> <p>* Combined testing is preferred over either annual FOBT or FIT, or FSIG every 5 years, alone. People who are at moderate or high risk for colorectal cancer should talk with a doctor about a different testing schedule.</p>
<b>Prostate</b>	<p>The PSA test and the digital rectal examination should be offered annually, beginning at age 50, to men who have a life expectancy of at least 10 years. Men at high risk (African American men and men with a strong family history of one or more first-degree relatives diagnosed with prostate cancer at an early age) should begin testing at age 45. For both men at average risk and high risk, information should be provided about what is uncertain about the benefits and limitation of early detection and treatment of prostate cancer so that they can make an informed decision about testing.</p>
<b>Uterus</b>	<p><b>Cervix:</b> Screening should begin approximately three years after a woman begins having vaginal intercourse, but no later than 21 years of age. Screening should be done every year with regular Pap tests or every two years using liquid-based tests. At or after age 30, women who have had three normal test results in a row may get screened every 2-3 years. Alternatively, cervical cancer screening with HPV DNA testing and conventional or liquid-based cytology could be performed every three years. However, doctors may suggest a woman get screened more often if she has certain risk factors, such as HIV infection or a weak immune system. Women 70 years and older who have had three or more consecutive normal Pap tests in the last 10 years may choose to stop cervical cancer screening. Screening after total hysterectomy (with removal of the cervix) is not necessary unless the surgery was done as a treatment for cervical cancer.</p> <p><b>Endometrium:</b> The American Cancer Society recommends that at the time of menopause all women should be informed about the risks and symptoms of endometrial cancer, and strongly encouraged to report any unexpected bleeding or spotting to their physicians. Annual screening for endometrial cancer with endometrial biopsy beginning at age 35 should be offered to women with or at risk for hereditary nonpolyposis colon cancer (HNPCC).</p>
<b>Cancer-related checkup</b>	<p>For individuals undergoing periodic health examinations, a cancer-related checkup should include health counseling, and, depending on a person's age and gender, might include examinations for cancers of the thyroid, oral cavity, skin, lymph nodes, testes, and ovaries, as well as for some nonmalignant diseases.</p>

American Cancer Society guidelines for early cancer detection are assessed annually in order to identify whether there is scientific evidence sufficient to warrant a reevaluation of current recommendations. If evidence is sufficiently compelling to consider a change or clarification in a current guideline or the development of a new guideline, a formal procedure is initiated. Guidelines are formally evaluated every five years regardless of whether new evidence suggests a change in the existing recommendations. There are nine steps in this procedure, and these "guidelines for guideline development" were formally established to provide a specific methodology for science and expert judgment to form the underpinnings of specific statements and recommendations for the Society. These procedures constitute a deliberate process to ensure that all Society recommendations have the same methodological and evidence-based process at their core. This process also employs a system for rating strength and consistency of evidence that is similar to that employed by the Agency for Health Care Research and Quality and the U.S. Preventive Services Task Force.

*Adapted from:* American Cancer Society. *Cancer Facts & Figures 2005*. Atlanta, GA; 2005.