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## Chemoprevention of Colon Cancer by Turmeric and Non-Steroidal Anti-Inflammatory Agents

By Lynn Keegan, RN, PhD, HNC, FAAN,  
and Gerald T. Keegan, MD, FACS

Part 1 of a 2-Part Series

COLORECTAL CANCER IS THE THIRD MOST COMMON MALIGNANCY IN the developed world. This cancer accounts for 60,000 deaths per year in the United States and 20,000 deaths per year in the United Kingdom. Although the incidence of the disease has appeared to drop slightly over just the past few years, the overall incidence and mortality of the disease, as well as the 50% five-year survival rate, has changed little over the past 40 years.<sup>1</sup> Colon cancer affects almost equal proportions of men and women between ages 60 and 80.

The pathogenesis of colorectal cancer is believed to involve both genetic and environmental factors. The most important environmental factor is probably diet.<sup>2</sup> Low-fiber diets have been associated with colon cancer. The effect of fiber has been controversial and some suggest that it is the effect of the phytoestrogens in fruit and vegetables rather than bulk alone that is preventive.<sup>3,4</sup> Studies suggest an inverse relationship between colon cancer and dietary omega-3 fatty acids.<sup>5</sup> The effects of smoking, lack of exercise, colorectal inflammation, and obesity also have been considered risk factors for colon cancer. A personal history of inflammatory bowel disease is a well-established risk factor for colorectal cancer.<sup>6</sup> The presence of colonic polyps is also a concern. Polyps of the colon and rectum generally are benign, but may develop malignant degeneration and are considered precancerous.

### Chemoprevention of Colon Cancer

Chemoprevention is defined as the use of pharmacologic interventions to stop the progression of normal cells to cancer cells. A number of agents—including aspirin, turmeric, and selenium—have been considered preventive for colon cancer. Additionally, there are ongoing studies on the effects of other non-steroidal anti-inflammatory agents (NSAIDs), vitamin D, and calcium as chemopreventive agents. This article will discuss data on turmeric and NSAIDs as

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chemopreventives. Next month, the chemopreventive effects of vitamin D and calcium will be examined.

## Historical Use of Turmeric

Turmeric is a spice that comes from the root *Curcuma longa* and is a member of the Zingiberaceae (ginger) family. In Ayurveda, turmeric has been used for its medicinal properties and is administered topically, orally, and via inhalation.

## Mechanism of Action

**Role of inflammation.** The modulation of the inflammatory cascade may be accomplished by a variety of means. Research is demonstrating that cancer initiation, promotion, progression, angiogenesis, and metastasis all may be related to inflammatory events. There is evidence linking emerging neoplasia and inflammatory eicosanoids (PGE2 and related prostaglandins). Although most research has emphasized the pharmaceutical applications of NSAIDs and selective cyclooxygenase-2 (COX-2) inhibitors, these agents fail to address alternate pathways available for the synthesis of proinflammatory eicosanoids. Evidence suggests the inhibi-

tion of lipoxygenase and its byproducts may be an overlooked but crucial component in complementary cancer therapies. Turmeric, as well as other selected nutritional and botanical agents—such as omega-3 fatty acids, antioxidants, boswellia, bromelain, and quercetin—may inhibit eicosanoid production and modulate both lipoxygenase and COX.<sup>7</sup>

**Turmeric.** Curcuminoids, which are components of turmeric, include mainly curcumin (diferuloyl methane), demethoxycurcumin, and bisdemethoxycurcumin.<sup>8</sup> Turmeric is known to have a variety of pharmacologic effects, including antitumor, anti-inflammatory, anti-infectious, and perhaps immune-enhancing activities. The pleiotropic effects of turmeric are attributable at least in part to inhibition of transcriptional factors, as well as effects on other cytokines.<sup>9</sup> Recently, turmeric has been demonstrated to possess anti-angiogenic effects and pro-apoptotic activities against tumor cell lines.<sup>10</sup>

Many investigators believe turmeric plays a role in prevention of colon cancer, but its mechanism of action is unclear. Studies have shown that treatment with turmeric can prevent and improve murine experimental colitis, a precursor of colon cancer. This finding suggests that turmeric could be a potential therapeutic agent for the treatment of patients with inflammatory bowel disease.<sup>9</sup>

Turmeric has long been known for its anti-inflammatory action.<sup>11</sup> It may exert this activity by inhibition of a number of different molecules that play a role in inflammation.<sup>8</sup> Turmeric has been demonstrated to suppress lipopolysaccharide-induced COX-2 expression in microglial cells.<sup>12</sup>

**NSAIDs.** Generalized colonic inflammation has been hypothesized to play a role in the pathogenesis of colon cancer. A recent prospective study involving more than 22,000 patients assessed the association of C-reactive protein (CRP) and the risk of colon and rectal cancers. CRP is an acute-phase protein produced in the liver in response to stimulation by interleukin-6 and is a non-specific measure of inflammatory disease. The results of this study showed an elevated plasma CRP concentration among persons who subsequently develop colon cancer. The data, although not separating the aspirin group of patients from the other NSAIDs patients, supported the concept that inflammation is a risk factor for the development of colon cancer in average-risk individuals.<sup>13</sup> This article gives further support to considering the use of anti-inflammatory drugs in the chemoprevention of colon cancer.

NSAIDs, such as aspirin or ibuprofen, block COX-1 and COX-2 enzymes. Although COX-1 is necessary for healthy mucosal tissues, blood platelets, and kidneys, and

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COX-2 typically is produced by the body when there is inflammation, these substances also are produced by precancerous tissues such as colonic polyps. Aspirin has properties not shared by the COX-2 inhibitors and probably triggers its own set of endogenous anti-inflammatory mediators through its effect on vascular COX-2.<sup>14</sup> Aspirin and the other NSAIDs may work by different mechanisms. A recent study suggested that selective COX-2 inhibition does not modify CRP levels,<sup>15</sup> and suggested further that COX-2 inhibitors may not have a direct impact on CRP and could influence colon cancer by other, yet unknown mechanisms.<sup>16</sup>

### Research Studies

**Turmeric.** Turmeric has been found to inhibit the growth of malignant cells both in vivo and in vitro. Studies on human tumor cell lines in India show that apoptosis was mediated through the generation of reactive oxygen species.<sup>17</sup> A study comparing celecoxib with turmeric as well as several other agents was undertaken in five hereditary colorectal cell lines. The results of the study showed dose- and time-dependent antiproliferative activities by both celecoxib and turmeric. Celecoxib was the most effective antiproliferative agent, but turmeric displayed a more potent apoptosis-inducing activity.<sup>18</sup>

However, the anti-inflammatory effect of turmeric is only one of its pleiotropic effects on the prevention and perhaps treatment of colon cancer. One of the widely sought approaches is cancer chemoprevention that uses natural agents to reverse or inhibit the malignant transformation of colon cancer cells and to prevent invasion and metastasis. Turmeric possesses chemopreventive activity that works by targeting multiple signaling pathways such as the beta-catenin-mediated transactivation and cell-to-cell adhesion pathways in the prevention of colon cancer development.<sup>19</sup> The apoptotic effect of turmeric in human cancer cells may be related to genetic up regulation at the level of “growth arrest and DNA damage inducible gene 153” messenger RNA transcription.<sup>20</sup>

Turmeric also has been found to protect DNA from damage from alkylating carcinogens in cultured Chinese hamster cells and is believed to be a chemopreventive agent by virtue of its ability to protect DNA as well as to induce DNA repair.<sup>21</sup>

The relationship between cytokines and turmeric has been investigated extensively. Cytokines are small proteins that have a specific effect on the interaction or communication between cells. Mitogen-activated protein kinase (MAPK) and NF-kappa B (NFkappaB) signaling cascades are thought to regulate apoptosis and cell survival. Turmeric is known to inhibit NFkappaB. Scientists in Ireland recently have studied turmeric effects upon MAPK signaling and apoptosis in human

colon cancer cells and showed that c-jun N-terminal kinase played an important role in turmeric-mediated apoptosis in human colon cancer cells that may underlie its chemopreventive effects.<sup>22</sup>

**NSAIDs.** Epidemiologic studies have shown that people who regularly take NSAIDs to treat conditions such as arthritis have lower rates of colorectal polyps, colorectal cancer, and colorectal cancer deaths. Based on these promising epidemiologic data, as well as animal models treated with COX inhibitors, consideration has been given to these substances as chemopreventive. This concept has been reinforced further by the finding of human cancer tissue showing high levels of COX-2 expression.<sup>23</sup> The recent characterization of COX-1 and COX-2 isoforms has led to an expanded understanding of how NSAIDs may help prevent polyp formation and subsequent malignant degeneration. COX enzymes are required for the conversion of arachidonic acid to prostaglandins. COX-2 mediates the inflammatory effects of COX activity. COX also is induced by a wide spectrum of growth factors and pro-inflammatory cytokines, and is as noted above<sup>23</sup> over-expressed in numerous premalignant and malignant lesions.

Treatment with the selective COX-2 inhibitor celecoxib has shown promising results in the prevention of colorectal cancer. Numerous studies show that this selective COX-2 inhibitor is a potent suppressor of colon polyps both in animal models for familial adenomatous polyposis and in patients with this condition. This has led to the U.S. Food and Drug Administration approval of celecoxib for the treatment of patients with familial adenomatous polyposis where multiple polyps are present.<sup>24</sup>

The population-based Pharmacoepidemiologic Prescription Database of North Jutland County, Denmark, identified 113,538 persons who filled prescriptions for ibuprofen during 1989 through 1995 and determined subsequent mortality through 1996. Standardized mortality ratios (SMR) for 25 specific causes of death were computed compared with the general population. For colon cancer, SMRs were significantly below the standard three or more years after ibuprofen prescription. However, there was a nearly threefold increase in the number of deaths from gastrointestinal bleeding.<sup>25</sup>

Multiple studies—experimental, epidemiological, and randomized clinical trials (RCTs)—have provided evidence that aspirin and other NSAIDs can reduce the risk of colorectal adenoma and cancer.<sup>26-28</sup> An extensive study of NSAIDs, colon cancer, and the possible involvement of an insulin-related pathway in more than 2,000 patients supported the protective effect of aspirin and NSAIDs on colorectal cancer risk. In addition, the observed interactions for aspirin/NSAIDs polymorphic genotypes suggest that mechanisms other than COX-2

inhibition may be contributing to the protective effect of aspirin and NSAIDs on colorectal cancer risk.<sup>29</sup>

Because of the gastrointestinal toxicity of aspirin and the non-selective NSAIDs, attention has been directed at the selective COX-2 inhibitors. These agents produce a decrease in the number and size of polyps in patients with familial adenomatous polyposis syndrome (FAP).<sup>30</sup> A review of nine RCTs including more than 24,000 patients using aspirin, sulindac, and celecoxib showed substantial reduction, but not prevention, of precancerous colorectal adenomas in FAP.<sup>31</sup> Prior studies using celecoxib and sulindac have been verified by these findings.<sup>32,33</sup>

### Adverse Effects

**Turmeric.** No reported adverse effects of turmeric have been cited in the research literature.

**NSAIDs.** Gastrointestinal side effects associated with NSAID use are common. NSAID-associated dyspepsia occurs in up to 50% of patients who use these drugs, and heartburn, nausea, vomiting, and abdominal pain also can be observed. Nonselective NSAIDs predictably cause gastrointestinal mucosal injury because they inhibit production of prostaglandins in local tissue.<sup>34</sup> This decline in prostaglandin production may disrupt the mucous layer and decrease secretion of bicarbonate, which can lead to back diffusion of hydrogen ions and damage to the mucosa.<sup>35</sup> The major risk of aspirin and other NSAIDs is the possibility of bleeding secondary to their effects on platelet function. These effects can be particularly serious in the gastrointestinal tract where acute bleeding from ulcers and diverticular disease can be life-threatening and, as noted above in the Danish epidemiologic study, the death rate from gastrointestinal bleeding in patients on ibuprofen was three times that of the normal population.<sup>25</sup>

One case-controlled study found an association between the ingestion of NSAIDs and the development of severe diverticular complications including pericolic abscesses, generalized peritonitis, bleeding, and fistula formation.<sup>36</sup> Selective inhibition of COX-2 by using COX-2 inhibitors allows for the beneficial effects of NSAIDs without adverse gastrointestinal results. COX-2 inhibitors are less likely to produce gastroscopically diagnosed ulcers but, as recent studies have shown, may increase the risk of myocardial infarction.<sup>37</sup> Merck Pharmaceuticals voluntarily withdrew rofecoxib from the market on Sept. 30, 2004. A patient taking rofecoxib has a small absolute risk of a heart attack. The trial prompting Merck to pull the drug involved 2,600 patients, half of whom took 25 mg/d of the drug, and half of whom took a placebo. Among patients taking rofecoxib for more than 18 months, there were 15 heart attacks or

strokes for every 1,000 patients compared with 7.5 per 1,000 who were on placebo, essentially doubling the risk.

The gastric effects of the NSAIDs may be overcome by the concomitant use of H-2 blockers or proton pump inhibitors or a combination of these agents. Misoprostol, a synthetic prostaglandin analogue, also may decrease the risk of NSAID-induced gastrointestinal complications.<sup>38</sup>

### Summary and Conclusion

In summary, population-based observational studies indicate that individuals had lower rates of colorectal cancer if they were taking various agents, including NSAIDs. In placebo-controlled trials in patients with familial adenomatous polyposis and in patients with sporadic colon adenomas, NSAIDs reduced the rates of adenomas. There is significant biologic rationale suggesting that these agents would be effective in reducing colorectal cancer as well.<sup>39</sup>

It is likely that routine use of turmeric may be helpful in prevention of inflammatory processes, which may give rise to or cause the progression of colon cancers. As yet, the literature is not definitive. However, there is certainly no harm in adding turmeric to the daily diet. Some of the ways include using curry sauces as well as adding turmeric to rice, soups, and stews.

### Recommendation

People at high risk for colon cancer, but who have not had ulcer disease or gastrointestinal problems should consider the use of aspirin or non-specific NSAIDs. The concomitant use of H-2 blockers, proton pump inhibitors, and misoprostol can be considered gastrointestinal protectors. COX-2 inhibitors are less likely to produce gastrointestinal complications, but recently the increased incidence of myocardial infarction has been reported with rofecoxib. ♦

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*Gerald T. Keegan, MD, is Emeritus Staff, Scott & White Clinic and Hospital, and former Professor of Surgery (Urology), Texas A&M University School of Medicine.*

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## Safe as a Baby: Is There a Case for the Safety of Herbs During Pregnancy?

**Source:** Nordeng H, Havnen GC. Use of herbal drugs in pregnancy: A survey among 400 Norwegian women. *Pharmacoepidemiol Drug Saf* 2004;13:371-380.

**Abstract:** The authors interviewed 400 postpartum women at Ullevål University Hospital in Oslo, Norway, about use of herbs during pregnancy. The researchers found that 36% of the pregnant women had used herbal drugs during pregnancy with an average of 1.7 products per woman. The proportion of women using herbal drugs increased throughout the first,

second, and third trimesters. The most commonly used herbs were echinacea, iron-rich herbs, ginger, chamomile, and cranberry. Among the women having used herbs in pregnancy, 39% had used herbs that were possibly harmful or herbs where information about safety in pregnancy was missing. Herbal galactagogues had been used by 43% of the women who had breastfed a prior child during their breastfeeding period. The authors concluded that the widespread use of herbal drugs during pregnancy indicates an increased need for documentation about the safety of herbal drugs in pregnancy. To meet the needs of pregnant women, it is necessary for health care personnel to have knowledge about herbal drugs during pregnancy.

**Source:** Belew C. Herbs and the childbearing woman. Guidelines for midwives. *Nurse Midwifery* 1999;44:231-252.

**Abstract:** The use of herbs to promote health or treat disease has become popular, and midwives increasingly encounter questions from childbearing clients regarding herbs. This article provides an overview of key concepts regarding the incorporation of herbs into clinical practice and discusses the preparation and administration of herbal treatments for common concerns of pregnancy. Safety issues are emphasized throughout.

#### ■ COMMENTS BY MARY L. HARDY, MD

HEALTH CARE PROVIDERS KNOW THAT UP TO ONE-THIRD of the adult population uses herbal medicine, but most have not realized how often pregnant women use herbs. Estimates range from a low of 7% to a high of 36% for pregnant women.<sup>1-5</sup> If the patient is also cared for by a naturopath or a midwife, this percentage might be considerably higher.<sup>6,7</sup> All health care providers should be committed to the goal of "First, do no harm," but conventionally trained practitioners may have trouble finding credible information to aid them in advising pregnant patients. This month we will look at an abstract that describes herb use in a pregnant population and at what information is available in the literature regarding safe use of herbal medicine in pregnancy.

Nordeng and Haven interviewed 400 Norwegian women within three days of giving birth about their use of herbal medicine during their pregnancies.<sup>4</sup> More than one-third of the women reported using herbs (36%) and most used more than one product (1.7 on average). Use of herbal medicine was lowest in the first trimester and highest in the third trimester. The most commonly used herbs and their indications were echinacea (23%, for cold), iron-rich herbs (12%, for low iron), ginger (10%, for nausea), chamomile (9%, for calming effect), and cranberry (8%, for urinary tract infections). Almost half (46.5%) of the women using herbs during pregnancy were recommended to do so by friends and family. Another 23% tried herbs on their own initiative and an additional 20% relied on information from books or other media. Only 12% received information from

health care personnel; this was 2% less than the number (14%) who relied on an herbal store for advice.

The Norwegian survey appears comparable to a survey of pregnant women at an American academic medical center.<sup>5</sup> In the U.S. survey, only 13% used herbs and again the most common herb was echinacea, closely followed by ginger and a pregnancy tea. What does the literature have to say about the safe use of herbs in pregnancy?

Although a number of safety studies in pregnancy have been conducted in animals, there is almost no literature published on humans. Two bioavailability studies and a handful of clinical trials are all that has been published to date. Herbal constituents have been found in both breast milk<sup>8</sup> and placental blood.<sup>9</sup> One woman used 900 mg of a standardized St. John's wort preparation; only hyperforin was found in her breast milk, in low levels. When the infant's serum was examined, neither hyperforin nor hypericin were detectable.

Observational studies have been done on groups of pregnant women who already were found to be taking common herbal supplements. Since randomized trials in pregnant women are unlikely where there is a potential for adverse effects, observational trials will give us our most reliable evidence for safety or risk. The Toronto-based Motherisk Program, a group that assesses risk during pregnancy from both herbs and drugs, has published a prospective controlled study on the use of echinacea in pregnancy.<sup>10</sup> They enrolled 206 women who reported echinacea use to a call-in service. These women were matched with a similar cohort who had not used echinacea, and both groups were followed until delivery. No difference in pregnancy outcomes or fetal malformation was reported between groups. This very experienced group concluded that there was no evidence for teratogenic risk of using echinacea even during the first trimester. One of the few randomized trials conducted on herbal use in pregnancy examined the safety and effectiveness of raspberry leaf tea to shorten labor.<sup>11</sup> The study also collected safety data; no adverse effects on pregnancy outcome or fetal development were noted.

Given the scarcity of data in the conventional literature, medical practitioners should avail themselves of the expertise of herbal practitioners and midwives who have experience in using common herbal substances during pregnancy. One of the most accessible references for authoritative information on safety is the *Botanical Safety Handbook*.<sup>12</sup> This reference, prepared by a group of senior herbalists, lists a wide array of herbs and rates their safety for use in pregnancy and lactation. Representing the midwife's perspective, Cindy Belew has written a well-organized article about herbal use in pregnancy.<sup>13</sup>

It is especially useful for health care practitioners as it provides a general review of herbal principles and practice as well as specific information on safety.

Herbal use is popular in pregnancy, just as it is in the general population. Patients tend to prefer herbal remedies over medications for common conditions, perceiving herbs to be safer. Research in this area is beginning to provide some useful data, such as the apparent safety of echinacea during pregnancy, but clearly much more work remains to be done. As health care providers, we have to be ready to counsel our patients in advance of definitive research. The fact that so few patients include health care providers as sources of information regarding herbal use in pregnancy creates a potentially risky situation for them. We need to actively question our patients about use of herbs and dietary substances during pregnancy. To be prepared for these discussions and credible to our patients, we must educate ourselves using all available information. Since conventional sources are limited, we should reach out to our alterative colleagues, who have significant clinical experience in these areas. In this way we can help our patients achieve the best possible outcome from their pregnancies. ❖

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## CE Objectives

After reading *Alternative Therapies in Women's Health*, the health care professional will be able to:

- evaluate alternative medicine and complementary therapies for women's health concerns;
- identify risks and interactions associated with alternative therapies;
- discuss alternative medicine options with patients; and
- offer guidance to patients based on latest science and clinical studies regarding alternative and complementary therapies.

## CE/CME Instructions

Physicians and nurses participate in this continuing medical education/continuing education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. 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, you must complete the evaluation form provided and return it in the reply envelope provided at the end of the semester to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you.

## CE / CME Questions

- Turmeric is believed to have which pharmacologic effects?**
  - anti-inflammatory effects
  - anti-infectious effects
  - immune-enhancing effects
  - All of the above
- Turmeric has been found to inhibit the growth of malignant cells:**
  - in vivo.
  - in vitro.
  - both in vivo and in vitro.
  - neither in vivo nor in vitro.
- A Canadian observational study found there was no evidence for teratogenic risk for pregnant women using what herb during the first trimester?**
  - Echinacea
  - Ginger
  - Chamomile
  - Cranberry

Answers: 44. d, 45. c, 46. a.

### NCCAM's Research Centers Program Expands

The National Center for Complementary and Alternative Medicine (NCCAM) in Bethesda, MD, has announced six major awards to expand the scope and impact of its research centers portfolio.

NCCAM funds Centers of Excellence for Research on CAM and Developmental Centers for Research on CAM. The Centers of Excellence provide five years of support for experienced researchers at some of the nation's leading universities. These researchers apply technologies to identify the potential benefits and underlying mechanisms of CAM practices. The Developmental Centers provide three years of support to build research programs in some of the nation's major CAM institutions through partnerships with established research institutions. Following are details of the six recipients of these grants and their first-year funding totals:

#### Centers of Excellence for Research on CAM

- Center on Mindfulness-Based Stress Reduction, Stress Arousal, and Immune Response in Early HIV; \$1,198,000

*Principal Investigator:* Susan Folkman, PhD

*Institution:* Osher Center for Integrative Medicine, University of California, San Francisco

This center will investigate the use of mindfulness-based stress reduction, an approach in which meditation is used to help reduce stress and better manage emotions, in people with early stage HIV. The center will examine the effects of meditation on the immune system and determine whether it can help slow disease progression and delay the need for antiretroviral treatment.

- Alternative Therapies for Alcohol and Drug Abuse; \$1,071,000

*Principal Investigator:* Yue-Wei Lee, PhD

*Institution:* McLean Hospital/Harvard Medical School, Belmont, MA (co-funded with the National Institute on Alcohol Abuse and Alcoholism)

Center investigators will evaluate whether certain traditional Chinese medicines and an electrical acupuncture technique can be used to prevent addiction relapse and craving for alcohol and drugs. They also will seek to determine the physiological mechanisms by which these Chinese medical treatments affect addictive behavior.

- Translational Research Center for CAM Therapy of Asthma; \$1,200,000

*Principal Investigator:* David Peden, MD

*Institution:* University of North Carolina, Chapel Hill

The center's goal is to conduct basic and clinical research to identify antioxidant CAM therapies for asthma. The researchers will investigate whether these treatments can minimize airway inflammation in response to common triggers of asthma, such as ozone or inhaled allergens.

#### Developmental Centers for Research on CAM

- Trametes Versicolor (mushroom)-Induced Immunopotentiality; \$777,000

*Principal Investigator:* Joel Slaton, MD

*Partner Institutions:* Center for Spirituality and Healing, University of Minnesota, Minneapolis; and Bastyr University, Kenmore, WA

This center will conduct laboratory, translational, and clinical research exploring the biological basis of the effects of mushroom extracts on the immune system's response to tumors and the feasibility of using the extracts for cancer therapy and reduction of radiation therapy side effects.

- Complementary/Alternative Medicine: Expectancy and Outcome; \$840,000

*Principal Investigator:* Barry Oken, MD

*Partner Institutions:* Oregon Health and Science University; National College of Naturopathic Medicine; Oregon College of Oriental Medicine; and Western States Chiropractic College, Portland, OR.

This center will focus on defining and understanding "placebo effects," particularly patient expectation and other factors related to patient-provider interactions that produce desired biological effects. Investigators will study placebo effects to develop strategies to maximize their benefit, improve clinical trial design, and gain insight into mechanisms underlying mind-body medicine.

- Mechanisms of Osteopathic Manipulative Medicine; \$620,000

*Principal Investigator:* Michael Smith, PhD

*Partner Institutions:* University of North Texas Health Science Center's Texas College of Osteopathic Medicine, Fort Worth, TX; and Arizona College of Osteopathic Medicine, Glendale, AZ.

This center will conduct laboratory, animal, and patient studies of the effects of osteopathic manipulation on the musculoskeletal system, lymphatic fluid flow, and reduction of pain from back and neck strain. Researchers will also study the potential beneficial effects of improved lymph flow. ❖

## In Future Issues:

**Garlic for Cardiovascular Disease**

**Mistletoe for Breast Cancer**

# ALTERNATIVE THERAPIES IN WOMEN'S HEALTH

*Science-based Information for Clinicians*

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Research for Berlex and Health Decisions, Inc.

**Susan D. Reed, MD, MPH**

Consultant for Pfizer