

One of the newer and more intriguing products in the nutrition section of supermarkets and health food stores today is shark cartilage pills. What spurred this creation, and why? Over the last few years, the media (and opportunistic vitamin companies) have picked up on the research of I. William Lane, Ph.D., who studied and publicized the beneficial effects of shark cartilage on stage III and IV cancer patients in Cuba. He reports in his book *Sharks Don't Get Cancer* that nearly 3 years after being treated with shark cartilage, 14 out of 29 terminal cancer patients were completely well and cancer-free (1). This fantastic result was reported on "60 Minutes," and the frenzy for shark cartilage began. The public took the news story of Dr. Lane's findings as scientific proof even though the results were not supported by peer review. In fact, Dr. Lane's data has been called "incomplete and unimpressive" by the National Cancer Institute(2). But the astounding results were enough - before long shark cartilage grew from a nutrition novelty to a cure for cancer in the public's eye. Some experts find considerable problems with shark cartilage as cancer treatment and are especially perturbed by the public's reaction to this new 'therapy.' The purpose of this paper is to identify the scientific basis of shark cartilage as a cancer treatment, assess the public's and experts' response to shark cartilage, and consider the current status of research on the subject.

How can shark cartilage prevent tumor growth?

The idea that cartilage might prevent tumor growth is grounded in the fact that cartilage is an avascular tissue. Scientists realized that there must be some factor that inhibits blood vessel formation (angiogenesis) and that this factor may also be used to inhibit the blood supply to growing tumors. Without a blood supply, the tumor would become necrotic and cancer would be eradicated, theoretically. Since the signal to inhibit blood vessel growth in cartilage must be present during cartilage formation in the beginning of life, the first studies used neonatal cartilage to show its antiangiogenic properties. One of the earliest studies was performed in 1975 using cartilage from a neonatal rabbit scapula along with a rabbit cornea tumor assay. The study showed that the cartilage implant decreased the rate of capillary growth, induced by tumor, by an average of 75%, and they also reported complete prevention of vascularization in 28% of the tumors (3). The following year, a partially purified cartilage factor which displayed antiangiogenic properties was isolated from neonatal bovine cartilage (4). In 1990, a protein derived from bovine scapular cartilage was purified that inhibits angiogenesis in vivo and capillary endothelial cell proliferation in vitro in three separate bioassays. This protein, named cartilage-derived inhibitor (CDI), was shown to be an inhibitor of mammalian collagenase, also important in angiogenesis (5). Since cartilage was shown to be such a powerful antiangiogenic agent, some researchers began to look for other sources of cartilage - and what better animal than the shark, whose skeleton is composed completely of cartilage and not bone.

The first study that looked at shark cartilage's antiangiogenic properties was reported in 1983. MIT researchers Lee and Langer implanted pellets of cartilage extract along with pieces of tumor into rabbit corneas and found little capillary growth (6). This is the study that Dr. Lane cites as sparking his interest in the subject. More recently, a study using proliferation of endothelium as a hallmark of angiogenesis showed that shark cartilage

reduced endothelial cell proliferation by 32%. When it was used in combination with another antiangiogenic agent, tumor necrosis factor-alpha, there was a 44% reduction in endothelial cell proliferation (7). The isolation and identification of the active components in shark cartilage is continuing.

### Public and Expert Response to the Shark Cartilage Treatment

At present, the FDA classifies shark cartilage as a dietary food supplement. As such, shark cartilage is not regulated and can be purchased as pills on the vitamin shelves at your local nutrition or grocery store, or even through infomercials and on the Internet. Shark cartilage has become a \$50 million a year industry, and according to various estimates between 25,000 and 100,000 people are now using one of dozens of brands of shark cartilage (8).

There are two ways to administer shark cartilage in cancer patients: orally and rectally. Clinical researcher Charles Simone, M.D., recommends a retention enema of two 35 gram doses of powdered shark cartilage daily for advanced cancer patients. The advantages of rectal administration include: elimination of the offensive taste and odor of orally administered shark cartilage, maximal protein content absorption without digestive enzyme breakdown, and elimination of upset stomach and gastric discomfort produced by oral administration. Not surprisingly, the main problem with retention enemas is patient adherence (9). Dr. Lane's recommendation for oral administration has been a dosage level of one gram of shark cartilage for each kilogram of body weight. As there are no toxic side effects of shark cartilage, the dosage can be doubled for use in advanced cancer patients (10). Often, a blended fruit concoction is added to make a better tasting "shark cartilage shake."

The experts, however, say there are problems with shark cartilage therapy. Judah Folkman, a Harvard researcher who has studied antiangiogenesis for 25 years, sees a problem with the ingested cartilage pills. "The proteins are present in such tiny quantities that even if they could survive [acid breakdown in the stomach] and get into the bloodstream, you would have to eat pounds of it a day to get enough activity." (8) Other authorities find problems with the health fad status of shark cartilage. John Renner, M.D., a member of the American Cancer Society Subcommittee on Questionable Methods, is concerned that the ongoing sensationalism over shark cartilage is eclipsing more promising therapies as well as depleting the shark population. (2)

### Current research using shark cartilage for cancer

Despite the many detractors who dismiss him as a quack or charlatan, Dr. Lane has been rewarded for his tireless effort to promote the benefits of his shark cartilage product, Benefin. His vindication lies in the FDA's granting full Investigational New Drug permission for Phase II clinical trials on non-responsive prostate cancer, in Detroit, and on Kaposi's Sarcoma, in Santa Fe. These trials are ongoing and have been joined recently by another Phase II clinical trial - that of Stage IV breast cancer cases (11).

In addition to these national studies, Dr. Lane's continues to endorse studies outside of the United States. Studies in some foreign countries have the advantage of not needing to conform to the rigorous research standards of the U.S., even though Dr. Lane reports that these studies still follow FDA protocols. Four trials have begun in Chile. In three of the studies, advanced nonresponsive uterine/cervical cancer, breast cancer, and ovarian cancer are being treated orally with Benefin. The other study examines its effectiveness for treating advanced nonresponsive brain cancer in children. In China, seven clinical trials have been scheduled. These will include studies of liver, bone, uterine/cervical, breast, and brain cancer. Finally, various cancers are being treated with shark cartilage in clinics in Japan. (1)

The newfound popularity of using shark cartilage to treat cancer has been fed by media hype based on Dr. Lane's questionable research. While there is a strong scientific case for neonatal cartilage as an antiangiogenic factor in rabbit corneal tumors, the leap to using shark cartilage to cure cancer is one not supported at this time by the medical establishment. Like any new treatment, many rigorous studies must be carried out to determine the efficacy of shark cartilage in the treatment of cancer. Researchers are attempting to isolate the antiangiogenic protein from shark cartilage in hopes that a synthetic analog might one day be used. But in the meantime, shark cartilage continues to be regarded by some as a "miracle" cure for cancer and the many products keep the shark cartilage connoisseurs, and its critics, circling

## REFERENCES

1 Lane, I. William. "Shark Cartilage Therapy - A Personal History of its Development." Interview in Shark Cartilage Exchange - - Shark Cartilage and Cancer. <http://www.realife.com/cancer.html> . 2-7.

2 Matthew, James. "Media Feeds Frenzy Over Shark Cartilage as Cancer Treatment." Journal of the National Cancer Institute. Aug 4,1993. 85(15): 1990-1.

3 Brem H, Folkman J. "Inhibition of tumor angiogenesis mediated by cartilage." Journal of Experimental Medicine. Feb 1 1975. 141(2):427-39.

4 Langer R, Brem H, Falterman K, Klein M, Folkman J. "Isolations of a cartilage factor that inhibits tumor neovascularization." Science. July 2, 1976. 193(4247):70-2.

5 Moses MA, Sudhalter J, Langer R. "Identification of an inhibitor of neovascularization from cartilage." Science. June 15, 1990. 248(4961):140810.

6 Lee, A., Langer, R. "Shark Cartilage Contains Inhibitors of Tumor Angiogenesis." Science. Sept 16,1983. 221(4616) 1185-7.

7 McGuire, TR, Kazakoff, PW, Hoie EB, Feinhold MA. "Antiproliferative activity of shark cartilage with and without tumor necrosis factor-alpha in human umbilical endothelium." Pharmacotherapy. Mar-Apr 1996. 16(2):237-44.

8 Dold, Catherine. "Shark- Therapy: Sharks Endangered by Global Market for Cartilage, Promoted as Cancer Cure)." Discover. Apr 1996. 14(4): 50-7.

9 "Shark Cartilage and Cancer" Shark Cartilage Exchange - - Shark Cartilage and Cancer. <http://www.reallife.com/cancer.html> . 8-9.

10 Passwater, Richard A. "Shark Cartilage and Cancer Revisited: A Follow-up onterview with I. William Lane." <http://www.solgar.com/nutrition-library/articles/lane-interview2.html>.

11 Lane, 1. William. Shark Cartilage Update. <http://www.lanelabs.com/UPDATES/v3n2.html> . III (2) 1996.1-5.