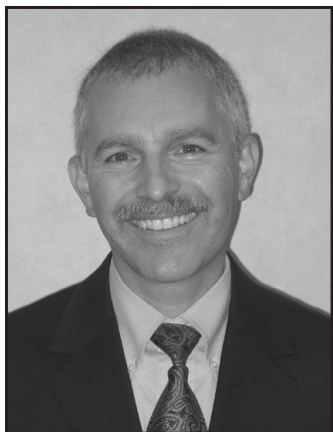


Chemoprevention of Colorectal Cancer



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Previous articles have addressed screening strategies for colon cancer, geared toward early detection and removal of precancerous polyps. An ideal complement to this strategy however is chemoprevention - the use of chemicals to prevent, halt, or even reverse the recurrence of polyps and therefore the development of colon cancer.

While none of the agents discussed below are FDA-approved specifically for the indication of chemoprevention, there is compelling data to support the "off-label" use of some of these for that purpose.

Dietary fiber increases short-chain fatty acids and reduces exposure of the colon lining to cancer-causing chemicals in food. Evidence of benefit in colon cancer prevention is observational, and phase 2 trials question fiber's chemopreventive role, while recognizing its many other benefits.

Hormone replacement (estrogens) reduce bile acids and inhibit insulin-like growth hormone. Although analysis of the literature suggests protection, safety concerns such as stroke limit its widespread recommendation.

Calcium carbonate and vitamin D inhibit cancer growth and bind bile and fatty acids. Folate and methionine provide methyl groups for DNA synthesis. Indeed, case control and prospective studies show chemopreventive benefit, and these supplements can be recommended.

Ursodiol (bear bile) reduces protein kinase, stabilizes cell membranes, and reduces cancer-

causing by-products. Not only has this been shown to reduce growth of pre-cancerous polyps (adenomas), but Urso works to prevent cancer in the settings of ulcerative colitis and primary sclerosing cholangitis.

NSAID's (commonly used for arthritis and analgesia) inhibit COX, and stimulate PPAR (peroxisome proliferator-activated receptor). While the mechanism of chemoprevention has been well studied, appropriate doses have not and casual over-use of these drugs can cause significant problems (ulcer development, bleeding, kidney disease).

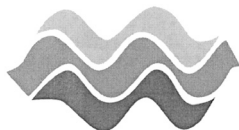
Statin drugs (used typically to lower cholesterol) suppress cell growth, metastasis, and growth of blood vessels into tumors. Chemopreventive data is observational, inconclusive, and results of studies have been mixed. While statins may not have positive chemoprevention action for colon cancer, their promise may instead be in cancers of the esophagus, pancreas, and prostate.

Antioxidants (carotenoids, retinoids, ascorbic acid, selenium, tocopherol). These substances neutralize free radicals, reduce DNA damage, and stimulate the immune system. Often touted as cancer-fighters, their benefit in chemoprevention is observational. Retrospective and prospective studies have been inconclusive, and Phase 2 studies have proved contradictory. High doses of these substances may have undesirable effects, and one study even showed increased risk of colorectal cancer in patients taking them.

Clinicians are only beginning to understand the effects of environmental factors and genetics on colon cancer. Clearly, however chemoprevention holds promise as the American population continues to age and is at higher risk for cancer. We at Anne Arundel Gastroenterology Associates look forward to further addressing your questions about prevention of colorectal and other gastrointestinal cancers.

Next Week's Feature...

John L. Newman, M.D., FACG
**"Colon Cancer Prevention
Campaign Month"**



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