

Carciknow News

the voice of Carcinogenesis foundation

Colon Cancer– Need for global awareness

March 2009

Editorial

Every year more than 940,000 cases of colon cancer occur worldwide and nearly 500,000 die from it each year. It is the second leading cause of cancer death among men and women in the US. Colorectal cancers are the most preventable of all cancers. Early detection of precancerous lesions is the key for prevention.

To make people aware about colon cancer, the US Senate passed a resolution in 1999 making March National Colorectal Cancer Awareness Month. The goals of this initiative are to generate widespread awareness about colorectal

cancer and to encourage people to learn more about prevention of the disease through regular screening and a healthy lifestyle.

In developing countries, more and more people are embracing western lifestyles, including smoking, high-fat diets, fast food and less physical activity. According to 2008 World Cancer Report published by the World Health Organization, the total number of cases of cancer in the developing world between 2000 and 2020 is expected to increase by 73 per cent. As developing countries become urbanized, patterns of cancer, including those most strongly associated with diet, tend to shift towards

those of economically developed countries.

Populations in these countries are expected to grow by 38 percent by 2030. And, these countries will have a high number of older people as populations age, increasing the number of cancers in these countries. While these statistics are of serious concern, there are opportunities to make a difference. Carcinogenesis Foundation calls for declaration of March as a global colon cancer awareness month by the World Health Organization. Let us initiate a global carcinoprevention drive.

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Special points of interest:

- COLON CANCER AWARENESS MONTH
- PHYSICAL ACTIVITY FOR CARCINOPREVENTION
- BENEFICIAL BUGS FOR HEALTHY COLON

Forthcoming Event of CF Frontiers in Carcinogenesis and Carcinoprevention Research on April 24, 2009. For further details please visit http://carcinogenesis.com/downloads/carcinogenesis_conf.pdf

Inside this issue:

GENE'S EYE VIEW OF CO-	2
VIRUS STRICKEN CHICKEN	2
VARIOUS COLON CANCERS	2
ERROR THAT SPELLS	3
PROBIOTICS AND COLON	3
CANCER FROM HISTORY	3
EARLY DETECTION – PHYSICAL ACTIVITY	4

Major Milestones in Carcinogenesis Research

1914 Chromosomal Mutations in Cancer.

1918 Confirmation that Coal tars produces skin cancer.

1933 Benz[a]pyrene was shown to produce skin cancers in mouse.

1941 Two-stage carcinogenesis theory was proposed by Berenblum.

1950 Connection between tobacco exposure and lung cancer was demonstrated.

1963 Chemical carcinogens were shown to transform

cells to cancerous cell in vitro
1968 Connection between DNA repair and cancer was proposed.

1971 Two-hit theory of carcinogenesis was proposed in retinoblastoma by Alfred Knudson .

Cancerous Transformation of cells:

The conversion of normal cells into tumor cells involves changes in the activity of a number of distinct different genes and proteins in a cell. Although scientists have been able to transform normal mouse cells into tumor-forming cells by introducing several cooperating cancer-causing genes into these cells, human cells have been resistant to such transformation for a long time. Researchers led by Dr. Robert A. Weinberg of the Whitehead Institute for Biomedical Research have made the first genetically defined human cancer cells in 1999.



Colorectal cancers are the most preventable of all cancers and in fact curable in many cases if detected in pre-cancerous stages.

Gene's Eye View of Colon Cancer

Colorectal cancer is probably the type of cancer for which the most is known about the genes affected by cancer-causing mutations (changes in genes), their normal functions and their carcinogenic effects when mutated. Mutations in two classes of genes, tumor-suppressor genes and proto-oncogenes (normal gene that can become cancer gene), are thought to impart a proliferative advantage to cells and contribute to development of

the malignant phenotype. Inactivating mutations of both copies (alleles) of the adenomatous polyposis coli (APC) gene - a tumor-suppressor gene on chromosome 5 - mark one of the earliest events in colorectal carcinogenesis. Germline mutation of the APC gene and subsequent somatic mutation of the second APC allele cause the inherited familial adenomatous polyposis syndrome. This syndrome is characterized by

the presence of hundreds to thousands of colonic adenomatous polyps. If these polyps are left untreated, colorectal cancer develops. In addition, mutation of the tumor-suppressor gene p53 on chromosome 17 appears to be a late phenomenon in colorectal carcinogenesis. This mutation may allow the growing tumor with multiple genetic alterations to evade cell cycle arrest and apoptosis.

Virus stricken chicken in the forefront of cancer research

Peyton Rous discovered in 1910 the first avian tumor, which originated in a hen, that could be transplanted to others. Rous would inoculate part of the tumor into the breast and peritoneal of hens to transfer and propagate the tumor. A year later he used cell-free filtrates of the tumor to induce tumor growth, and the agent in this filtrate was shown to be a virus, the Rous

sarcoma virus (RSV).

Robert Huebner and George Todaro proposed that there is a class of viruses that plays an important role in the development of tumours in animals. They believed that the C-type retrovirus could be transmitted from animal to progeny animal and that the activation results in oncogene (cancer gene) expression and

cell transformation. Their work led to identifying the first retroviral oncogenes.



Peyton Rous

Colon and Colon Cancer types

The colon and rectum are parts of the digestive system. After food is chewed and swallowed, it is sent to the small intestine, also known as the small bowel. The wall of the colon and rectum is made up of several layers of tissue. Colorectal cancer starts in the innermost layer and can grow through some or all of the other layers. Of the several types of colon cancers, adeno-

matous polyps are polyps that have potential to turn into cancer.

More than 95 per cent of colorectal cancers are adenocarcinomas. These are cancers that start in cells that form glands that make mucus to lubricate the inside of the colon and rectum.

Other less common types of tumors may also develop in the colon and rectum. Carci-

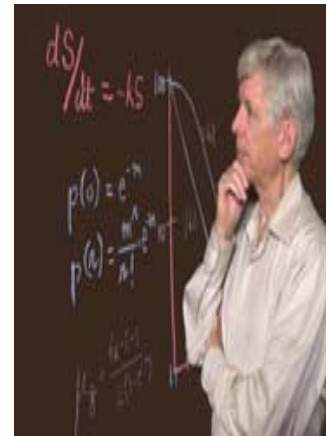
noid tumors develop from specialized hormone-producing cells of the intestine. Gastrointestinal stromal tumors (GISTs) develop from specialized cells in the wall of the colon. Inflammation of the colon is major risk factor for developing colon cancer in patients with Crohn's and colitis diseases.

Errors that Spell Disaster

Genes mastermind the production of proteins that run various cellular functions. A minute fault in genes can trigger a cascade of events leading to physiological anomalies, sometimes with deadly outcome like cancer. In the early 70s, while studying cases of retinoblastoma, Alfred G. Knudson stumbled upon error in the activity of genes, chief miscreants in the development of cancer. Knudson came across two faults or 'mutations' in genes.

One mutation could be inherited, while the other would be acquired later, or two mutations would be somatic in sporadic tumors, famously known as two-hit hypothesis. Knudson's 'two-hit' theory explained the relationship between the hereditary and non-hereditary forms of a cancer and predicted the existence of tumour-suppressor genes that can suppress cancer cell growth. Knudson's powerful insights into the development of cancer hold

implications for both treatment and prevention. Tumor-suppressor genes, in particular, are important targets for prevention research, since they normally put brakes on cellular growth, and this is a topic of his current research. Defects in tumor-suppressor genes permit abnormal, cancerous growth, so devising ways to remedy such flaws or replace the gene's missing product through medication are of interest to researchers.



Alfred Knudson ponders

Probiotics and colon health

Probiotics, which means "for life" are defined by WHO as "Live microorganisms which when administered in adequate amounts confer a health benefit on the host". By lowering the pH in yogurt, lactic acid bacteria may create fewer opportunities for spoilage organisms to grow. Such bacteria may prevent gastrointestinal infections when taken through diet.

Strains of the genera Lactobacillus and Bifidobacterium are the most widely used probiotic bacteria. Known to assist body's gut-flora, probiotics strengthen the immune system to combat allergies, stress, and exposure to toxic substances. Russian scientist Dr. Eli Metchnikoff first suggested that useful microbes could replace harmful microbes of gut flora. Taking cue from certain long-lived

rural Europeans, Metchnikoff who himself consumed sour milk fermented with bacteria proposed that consumption of fermented milk would "seed" the intestine with harmless lactic-acid bacteria decreasing the intestinal pH and suppressing the growth of proteolytic bacteria. Cancer researchers are also interested in studying the carcinopreventive properties of probiotics.

Cumin for digestive health

Cumin was originally cultivated in Iran and Mediterranean region is it is mostly grown in Iran, Uzbekistan, Tajikistan, Turkey, Morocco, Egypt, India, Syria, Mexico, and Chile. Cumin was well known in ancient Greece and Rome and was mentioned in the Bible.

Cumin seeds have traditionally been noted to be of benefit to the digestive system, and scientific research is beginning to support the age-old notion. Research has shown that cumin may stimulate the secretion of pancreatic enzymes, compounds necessary for proper digestion and nutrient assimilation.

Cumin is a potent free radical scavenger and has abilities to enhance the activities liver's detoxification enzymes thus making it a potential carcinopreventive agent.

Cancer: From the Pages of History

Hippocrates, the father of medicine, believed that the body contained 4 humors (body fluids) - blood, phlegm, yellow bile, and black bile. An excess of black bile collecting in various body sites was thought to cause cancer. This theory of cancer was passed on by the Romans and was embraced by the influential

doctor Galen's medical teaching, which remained the unchallenged standard through the Middle Ages for over 1300 years.

In 1838, German pathologist Johannes Muller demonstrated that cancer is made up of cells and not lymph, but he was of the opinion that cancer cells did not arise from nor-

mal cells. Muller proposed that cancer cells arose from budding elements (blastema) between normal tissues. His student, Rudolph Virchow (1821-1902), the famous German pathologist, determined that all cells, including cancer cells, are derived from other cells.

Research-Awareness-Care-Education



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Carcinogenesis Foundation's Mission

The mission and activities of Carcinogenesis Foundation can be summarized by an acronym PRIME (Prevention-Research-Innovation-Medicine-Education). Prevention is the best medicine for any disease, especially cancer. CF believes that innovative research and development of medicinal agents coupled with education will be the key to the global vision of eradicating cancer incidence. The Foundation will catalyze and support innovations in carcinogenesis research and education.

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Indian spice for carcino-prevention

Several laboratory based studies have consistently shown that curcumin, a compound from Turmeric possesses anti-cancer activity.

*Turmeric is a spice common to India and the surrounding regions and is derived from the rhizome of *Curcuma longa*. The overwhelming evidence from laboratory and animal based studies suggests that curcumin may prove to be useful for the chemoprevention of colon cancer in humans.*

Early detection and Physical Activity can Prevent Colon cancer

Regular screening or testing is one of the most powerful weapons in preventing colorectal cancer. From the time the first abnormal cells start to grow, it usually takes about 10 to 15 years for them to develop into colorectal cancer. Screening can make early detection of some polyps or growths before they turn malignant.

People who have no identified risk factors (other than age) should begin regular screening at age 50. Those who have a family history or other risk factors for colorectal polyps or cancer, such as inflammatory bowel disease, should be screened at more frequent

intervals.

Genetic tests can help determine if members of certain families have inherited a high risk for developing colorectal cancer due to syndromes such as familial adenomatous polyposis (FAP) or hereditary non-polyposis colorectal cancer (HNPCC).

Recommendations from WHO for cancer prevention

Resorting to physical activity, people can lower their risk of developing cancers. The primary goal should be to perform physical activity on most days of the week. More

vigorous activity, such as fast walking, may give some additional benefits for cancer prevention.

Overall consumption of salt preserved foods and salt should be moderate.

Minimize exposure to aflatoxin in foods.

Have a diet which includes at least 400 g per day of total fruits and vegetables.

Consume moderate amounts of preserved meat (e.g. sausages, salami, bacon, ham).