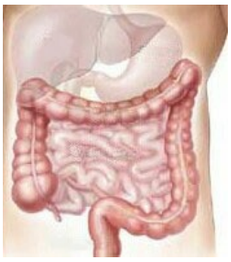
COLORECTAL CANCER RESEARCH

Month Ending January 15, 2010



The following colorectal cancer research update extends from December 19 – January 15, 2010 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Heart Drugs Shown To Fight Colon Cancer (Dec. 18/09)

Swedish scientists have reported that a group of drugs used to treat heart failure shows promise for fighting colon cancer. Cardiac glycosides are a family of naturally-derived drugs used to treat congestive heart failure and abnormal heart rhythms. Scientists have suspected for some time, based on previous research, that these heart drugs may have promise for fighting many different types of cancer. Despite this, knowledge on effects in colon cancer or combination effects with other anti-cancer drugs is lacking. But scientists know little about their potential anticancer effects and have not tested these substances against colon cancer. As part of a larger study to screen and identify natural substances with activity against colon cancer, the scientists picked several cardiac glycosides for further study. They tested five of these heart drugs against laboratory cultures of human colon cancer cells and found that they were all effective, to varying degrees, at killing the cancer cells. The sensitivity, however, was rather low when compared to that of other cancer cell types reported previously. Several of the drugs also showed increased anticancer activity when combined with certain drugs used for standard chemotherapy. The findings suggest that these heart drugs may affect colon cancer outcome when used alone or in combination with conventional chemotherapy drugs.

Felth, Jenny, et al., Cytotoxic Effects of Cardiac glycosides in colon cancer cells, alone and in combination with standard chemotherapeutic drugs. J of Natural Products. 2009, 72 (11), pp. 1969-1974

2. The Association Between Glutathione-S-Transferase and Colorectal Cancer (Nov. 16/09)

Glutathione-S-Transferase is a family of enzymes (proteins) involved in metabolism and in making toxic compounds less harmful to the body. In the past, this family of enzymes has been linked to increased risk of developing colorectal cancer. In this Korean research article, a large scale, case-control study was performed to evaluate the association between this family of enzymes and colorectal cancer, while also examining whether smoking, alcohol consumption and age modify the association. Researchers found that the family of enzymes were not associated with increased risk of colorectal cancer in Koreans. And, smoking, alcohol consumption and age did not modify the association. Researchers suggest that more large-scale studies are required to confirm this finding.

Piao, JM, et al., Glutathione-S-transferase (GSTM1 and GSTT1) and the risk of gastrointestinal cancer in a Korean population. World J of Gastroenterology. 2009; 15(45): pp. 5716-5721

3. Preoperative and Postoperative Chemo For Resectable Liver Mets (Dec. 2209)

The liver is the primary metastatic site in patients with colorectal cancer, and the only hope for a cure or prolonged survival in patients with liver metastases is provided by surgical resection. Advances obtained in non-resectable metastatic disease using new chemotherapeutic agents raise important questions about the use of neoadjuvant and adjuvant chemotherapy in patients with resectable liver metastases. Two major randomized studies have yielded positive results. First, a combined intra-arterial plus systemic fluoropyrimidine-based chemotherapy regimen (i.e. Hepatic Arterial Infusion) demonstrated a relapse-free survival benefit when compared to systemic 5-fluorouracil–leucovorin therapy alone. This approach is still restricted to specialized centres, however, due to technical limitations and locoregional toxicities. Secondly, another trial demonstrated the superiority of preoperative FOLFOX-4 chemotherapy in comparison to surgery alone. Oxaliplatin and irinotecan can induce substantial liver damage, especially steatohepatitis (fatty inflammation of the liver) and vascular lesions, but the impact of these lesions on postoperative morbidity and survival remain unclear. Ongoing and planned trials will assess the addition of anti-angiogenic (ie avastin) and anti-epidermal growth factor receptor agents (ie. erbitux) to chemotherapy regimens.

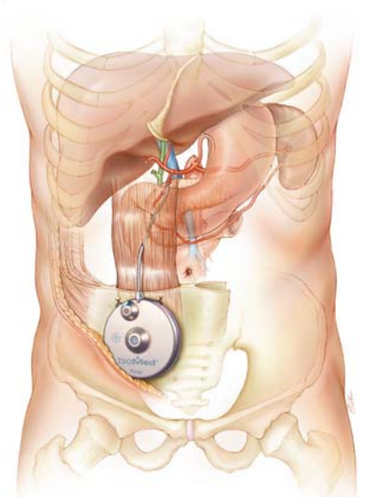


Figure Showing Placement of **Hepatic Arterial Infusion Pump** To Allow for Chemotherapy Medication to be Delivered Directly into the Liver. The placement of a pump into the hepatic artery after liver resection has also allowed for additional chemotherapy to be delivered after surgery for up to six months.

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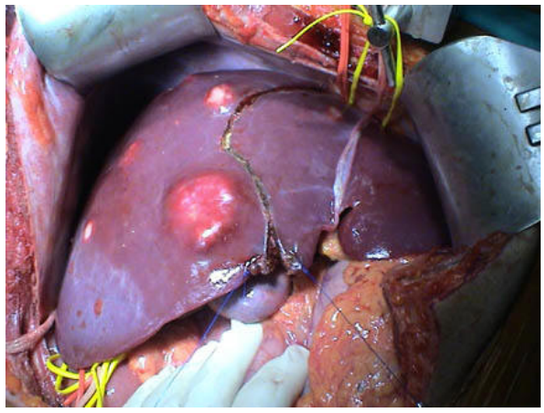
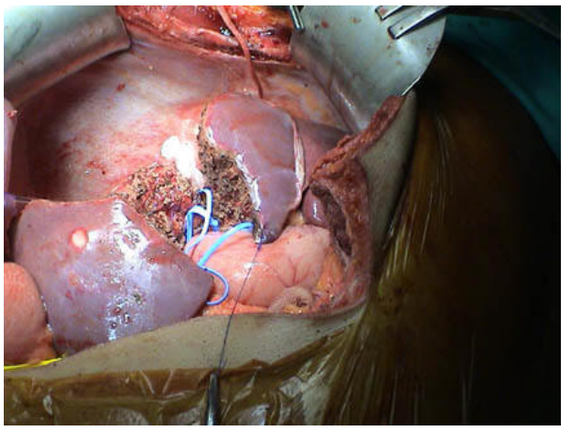
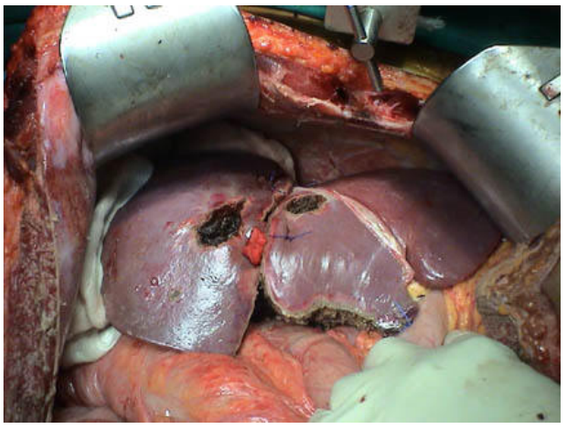


(i) **Figure Showing Colorectal Liver Metastases**



(ii) **Figure Showing Extent of Liver Resection**



(iii) **Figure Showing Liver After Complete Resection**

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Hebbar, M, et al., Integration of neoadjuvant and adjuvant chemotherapy in patients with resectable liver metastases from colorectal cancer. Cancer Treat Rev. 2009 December. 35(8): pp. 668-675

4. Kras Mutations & Prediction of Lung Mets (Jan. 3/10)

KRAS mutations in colorectal cancer primary tumors can predict resistance to anti-Epidermal Growth Factor Receptor (EGFR) monoclonal antibody therapy (such as erbitux or vectibix) in patients with metastatic colorectal cancer. In this study, KRAS mutations were retrospectively studied in 110 patients

with metastatic colorectal tumors. These studies were performed using tissue samples from both the primary tumor and their related metastases (93 liver, 84%; 17 lung, 16%). All patients received adjuvant (post surgical) 5-Fluorouracil-based chemotherapy after resection of metastases. None received anti-EGFR therapy. Mutations in KRAS were observed in 37 (34%) of primary tumors and in 40 (36%) of related metastases. Patients with primary tumors possessing KRAS mutations had a shorter disease-free survival period after metastasis resection (12.0 vs. 18.0 months) than those who did not. A higher percentage of KRAS mutations was detected in primary tumors of patients with lung metastases than in patients with liver metastases (59% vs. 32%). To further evaluate this finding, researchers analyzed 120 additional patients with unresectable metastatic colorectal cancer who previously had their primary tumors evaluated for KRAS mutational status. Separately, the analysis of these 120 patients showed a tendency towards a higher degree of KRAS mutations in primary tumors of patients with lung metastases. Taken together the group of 230 patients showed that KRAS was mutated significantly more often in the primary tumors of patients with **lung metastases** (57% vs. 35%). The results suggest a role for KRAS mutations in the tendency of primary colorectal tumors to metastasize to the lung.

Cejas P, et al. KRAS Mutations in Primary Colorectal Cancer Tumors and Related Metastases: A Potential Role in Prediction of Lung Metastasis. PLoS ONE 4(12): e8199. doi:10.1371

5. The Effectiveness of Folfox Therapy Not Linked to DNA Mismatch Repair (Jan. 5/10)

This study looked at the possibility that oxaliplatin might overcome the resistance to 5-FU treatment in a small group of people with colon cancer whose cancer comes from changes in the genes that repair damaged DNA, also known as Mismatch Repair, (about 15% of colorectal cancers.). The researchers found no difference in survival benefits between groups of patients who had these gene changes (deficient mismatch repair) or those who did not. That led them to believe that adding oxaliplatin to 5-FU might be a better treatment for those patients than 5-FU alone. Colon cancers that are caused by defects in genes that repair damaged DNA don't respond well to 5-FU treatment after surgery. However, a new analysis of patients treated with FOLFOX (oxaliplatin, leucovorin, and 5-FU) found no differences between patients with deficient mismatch repair tumours (tumours that have lost their ability to repair changes in DNA) and those with normal gene expression. In this small study of 135 patients, the research team found that adding oxaliplatin to 5-FU and leucovorin may overcome resistance to chemotherapy in mismatch repair deficient and microsatellite instable (MSI) colon cancer. South Korean researchers analyzed tumors from patients with stage II, III, or IV colorectal cancer, all of whom had surgery that completely removed all visible signs of cancer. The 14 patients with stage IV cancer had liver metastases only, which were successfully removed. They studied two genes related to deficient DNA repair — MLH1 and MSH2. They also determined microsatellite instability (MSI), and stained tumors for the expression of p53 protein. [**Microsatellite Instability** is a change that occurs in the DNA of certain cells (such as tumor cells) in which the number of repeats of microsatellites (short, repeated sequences of DNA) is different than the number of repeats that was in the DNA when it was inherited. The cause of microsatellite instability may be a defect in the ability to repair mistakes made when DNA is copied in the cell.] [**p53 Protein** is a tumor suppressor gene that normally inhibits the growth of tumors. This gene is altered in many types of cancer such as colorectal.] Researchers found that:

- Approximately 1 in 10 tumors were MSI-high (MSI-H); 9 out of 10 were MSI-low or microsatellite stable (MSI-L/S).
- Similarly, almost 10% showed deficient mismatch repair gene expression (MMR-D).
- There was almost complete agreement (94.7%) between the MSI-high and deficient mismatch repair specimens.

Comparing results to disease-free and overall survival, the study showed:

- There was no difference between patients with deficient and intact DNA mismatch repair for either disease-free or overall survival.
- p53 expression made no difference in either disease-free or overall survival.
- With respect to microsatellite instability — either high or low/stable — there was no difference in disease-free or overall survival.

Researchers, therefore, concluded that the MMR status or p53 positivity was not significantly associated with outcomes to FOLFOX as adjuvant chemotherapy in colon cancer patients with complete resection. Adding oxaliplatin in adjuvant chemotherapy may overcome negative impact of 5-FU on colon cancers with MSI-H/MMR-D.

Kim, Seung Tae, et al., Clinical Impact of microsatellite instability in colon cancer following adjuvant folfox therapy. Cancer Chemotherapy and Pharmacology. Online first edition. December 24, 2009. DOI: 10.1007/s00280-009-1206-3

6. Kras and Braf Mutations in CRC Survival (Jan. 5/10)

According to this study, for stage II and III colon cancer, a tumor mutation in the KRAS gene does not impact either relapse-free survival or overall survival. BRAF mutations, which are less common, don't help with prognosis for relapse-free survival, but do provide information about overall survival in some tumors. Patients with BRAF mutations and microsatellite-low or stable tumors had poorer overall

survival than those without mutations. As colon cancer develops, changes in genes accumulate that affect cell division and cell death. When cells no longer divide or die normally, tumors get larger and some cells may break off and move to new and dangerous sites. In earlier studies, changes in the KRAS and BRAF genes have been able to predict whether or not advanced colorectal cancer would respond to drugs that target epidermal growth factor receptors (EGFR). Patients with tumors that have mutated KRAS or BRAF don't benefit from either Erbitux (cetuximab) or Vectibix (panitumumab). But it has been unclear whether mutations in these two genes can provide information about whether early stage II or III colon cancer would recur or what the mutations meant for eventual survival. Using over 1,400 tumor specimens collected during a large, randomized trial of chemotherapy for stage II and III colon cancer, researchers were able to analyze KRAS and BRAF mutations and their impact on both relapse-free and overall survival. The scientists also looked at microsatellite instability (MSI) and coordinated it with the KRAS and BRAF results. They had good long-term information about patient relapse and survival. About 1 in 3 tumors (37%) had a KRAS mutation, similar to the percentages found in other studies in metastatic colorectal cancer. 7.9% had a BRAF mutation, and the two mutations were mutually exclusive. Neither KRAS nor BRAF mutations differed between stages II or III.

KRAS mutations

- Were significantly more frequent in low-grade tumors and right-sided tumors.
- Were borderline more common in microsatellite-low and microsatellite-stable tumors.
- **Did not predict** relapse-free survival or overall survival.

BRAF mutations

- Were more frequent in right-sided tumors, high-grade tumors, and tumors that were MSI-high.
- Were more frequent in patients over 60 and in women.
- **Did not predict** relapse-free survival.
- **Did predict poorer overall survival**, particularly in patients with MSI-low or MSI-stable tumors.

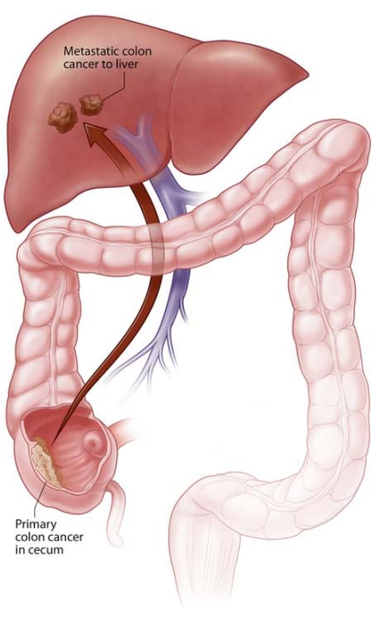
Researchers concluded that in stage II-III colon cancer, the *KRAS* mutation status does not have major prognostic value whereas the *BRAF* mutation is prognostic for overall survival in MS-L/S tumors.

Roth, Arnaud D., et all., prognostic Role of Kras and Braf in stage II and III resected colon cancer: results of the translational study on the PETACC-3, EORTC 40993, SAKK 60-00 Trial. J Clinical Oncology. Published online ahead of print, December 14, 2009. DOI: 10.1200/JCO.2009.23.3452

SURGICAL THERAPIES

7. Synchronous Liver and Colon Resection (Dec. 17/09)

The surgical strategy for the treatment of colorectal cancer and synchronous (occurring at the same time) liver metastases was examined in this study. The aim of the study was to investigate the effects of colon resection on liver function and regeneration in rats. 96 rats were block-randomized into six groups: Group I had a laparotomy performed. Group II had 1 cm colon resected and anastomosed (rejoined). Group III and V had 40% or 70 % of the liver resected, respectively. Additionally Group IV and VI had 1 cm colon resected and anastomosed (rejoined), respectively. Remnant liver function was evaluated and liver regeneration was calculated. The total number of complications was significantly higher in Group VI than Group I, III, IV, and V. Body weight was significantly lower in rats that had simultaneous colonic and liver resection performed. Hepatic regeneration rate was significantly higher in the simultaneous colectomy group. Researchers concluded that in rats, morbidity seems to be related to the extent of hepatic resection. In rats undergoing liver resection, simultaneous colectomy induced a higher degree of hepatic regeneration rate.



Metastatic colon cancer that has spread to the liver

Source:
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Sasanuma, Hideki, et al., . Increased liver regeneration rate and decreased liver function after synchronous liver and colon resection in rats. Annals of Surgical Innovation and Research 2009, 3:16

8. Testing of Lymph Nodes During Colon Surgery (Dec. 29/09)

Past studies have indicated that too few colon cancer lymph nodes are being tested during colon cancer surgery (colectomy). Some of the possible causes are surgeons who are removing too few or the pathologist not examining those lymph nodes that have been removed during surgery. There may very well be other possible causes. This study examined 430 colon cancer patients whose lymph nodes were removed during surgery in one large hospital in a period just over four years from 2003 through 2007. Researchers found no difference among 18 surgeons nor any difference that could be attributed to 10 pathologists or 3 pathology assistants. Instead, the age of the patient, the site of the tumour, the stage of the cancer, and the year the surgery was performed contributed to inadequate lymph node counts. Researchers concluded that the origin of a low lymph node count appeared multifactorial. Inadequate lymph node retrieval for colon cancer resections cannot uniformly be attributed to any one factor, such as the surgeon.

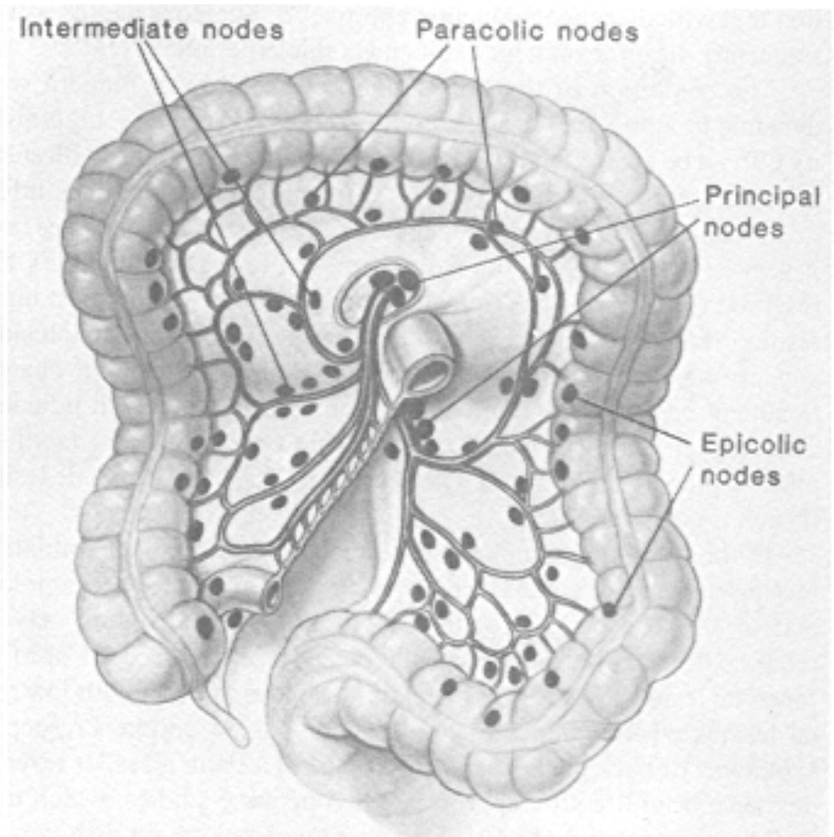

Diagram Showing Lymph Nodes Associated With Colon Surgery: The epicolic, paracolic, intermediate, and principal lymph node groups accompanying the vessels of the colon.

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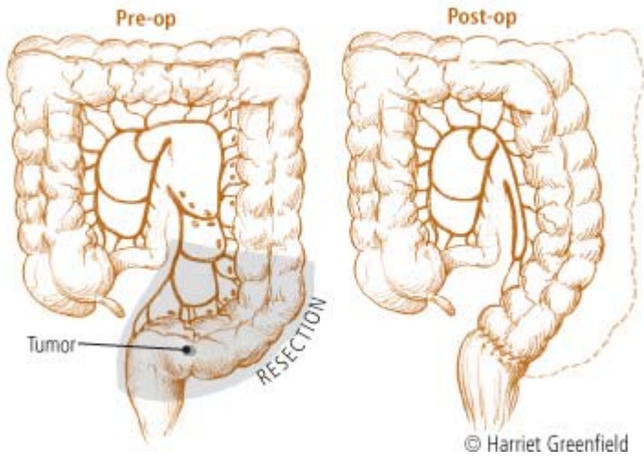

Diagram Showing Resection of Sigmoid Colon With Associated Lymph Nodes

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Jakub, James W., et al., Colon Cancer and Low Lymph Node Count. Archives Surg. 2009; 144(12): pp. 1115-1120

RADIATION / INTERVENTIONAL RADIOLOGY

9. Addressing Radiation-Induced Side Effects When Treating Colorectal Cancer (Dec. 4/09)

Radiation therapy uses high energy rays for killing cancer cells. In fact, it affects the cancer cells lying only in the affected area. Two types of radiation therapies, namely the internal radiation and external radiation, are used for treating colorectal cancer. Although radiation therapy has been mostly successful in the treatment of colorectal cancer, there are many side effects to this technique. These side effects usually depend on the part of the body and the dose of radiation given to the patient. Some common side effects of radiation for colorectal cancer treatment are vomiting, hair loss, extreme tiredness, bleeding, easy bruising and increased susceptibility to different infections. Women undertaking radiation therapy may experience symptoms like vomiting, nausea, bloody stools, urinary discomfort and diarrhea. The skin where radiation is given may even become tender, dry or red. Radiation therapy may also cause alopecia (hair loss) in the area, where treatment is carried out. Many women have experienced the side effect of having low white blood cell counts when they have undergone radiation therapy for colorectal cancer. However, this side effect of having low levels of WBC due to radiation is comparatively rare. These cells prevent bleeding and fight the body's infections. Radiation therapy can even affect the ability to have children (the same is true for males). Some of the other possible side effects resulting from radiation therapy may include discomfort or pressure in the excretory region, burning sensation during urination, fatigue, skin irritation, abdominal cramping, frequent bowel movements and nausea. However, these side effects are temporary, as they tend to resolve after the termination of radiation therapy for colorectal cancer. There are measures for controlling side effects of radiation therapy. Although these side effects vary with different patients, they can be controlled by using different medications and inflicting changes in the diet. Try to give plenty of rest to the body during this treatment, as one is more likely to become fatigued and feel tired. Do not wear tight clothes and avoid scrubbing, rubbing and putting adhesive tapes on the skin where treatment is performed. Take special care to protect the treated skin from direct sunlight. Since the skin becomes very sensitive during this time, cover it with a dark cloth if possible before going out.

If seeking more information on colorectal cancer treatment-induced side effects, please visit the section entitled "Side Effects" on the Colorectal Cancer Association of Canada's website at www.colorectal-cancer.ca

http://www.latestcancernews.com/side-effects-of-radiation-for-colorectal-cancer

SCREENING

10. ColoMarker Tests for Colon Cancer (Dec. 17/09)

Medical researchers with EDP Biotech Corporation (EDP) have captured national attention with their revolutionary new technology for a simple blood test to detect early-stage colon cancer. Following the

success of its pre-clinical trials for the ColoMarker assay, EDP has filed a patent on the biomarker, CA11-19, and all aspects of its use. Via an inexpensive blood test, ColoMarker will detect colon cancer in its earliest, most curable stages. When colon cancer is detected in its early stages, more than 90% of patients will survive. If not detected until the later stages, fewer than 10% will survive. ColoMarker detects colon cancer in these early, highly curable stages. According to American Cancer Society statistics, fewer than 20% of Americans over the age of 50 who should be screened for colon cancer, actually are. With the use of ColoMarker, a simple and inexpensive blood test, the number of people being screened would likely increase dramatically, leading to a decline in deaths due to colon cancer. In pre-clinical trials, ColoMarker successfully detected the early stages (I, II, and III) of colon cancer. In tests of 2,370 blood samples, ColoMarker showed an accuracy rate of >99% for detecting colon cancer in these early stages. ColoMarker could lead to a radical shift in the way colon cancer is detected. National researchers who study colorectal cancer are closely monitoring emerging technologies such as ColoMarker. Their findings are encouraging; last month the American Cancer Society, the National Cancer Institute, the Centers for Disease Control and Prevention and the North American Association of Central Cancer Registries released an optimistic report about the expected decline in deaths from colon cancer due to anticipated improvements in early screening methods. EDP Biotech is now moving forward expeditiously to get ColoMarker through the Food and Drug Administration clearance process.

http://www.examiner.com/x-7160-Sacramento-Nutrition-Examiner~y2009m12d18-ColoMarker-simple-blood-test-for-early-colon-cancer-detection-in-preclinical-trials?cid=exrss-Sacramento-Nutrition-Examiner

11. Post Cancer Surveillance Is Very Important (Dec. 23/09)

Admittedly, one of the biggest challenges of being a cancer survivor is coping with the fear of a recurrence. Unfortunately, this fear can lead to a "denial" attitude. Once treatment is completed, patients do not wish to be reminded of the ordeal they had with cancer. This, in turn, may lead some people to skip follow-up appointments with doctors and avoid tests that may detect a recurrence early. This has not been deemed to be a healthy coping strategy - as with a first time cancer diagnosis, the sooner you know you have cancer again, the more options you are likely to have for treating and managing it. In this study, researchers suggest that for colon cancer survivors, close follow-up for about 10 years after initial diagnosis is important for maintaining good health and catching any recurrences early. The study suggested this 10 year follow-up time is especially important for female colon cancer survivors, those who had right-sided cancers, and in people who were less than 60 years old when first diagnosed with colon cancer. This research also clarifies that the 5-year mark (5 years after first diagnosis) is important for determining who is likely to develop cancer again. But keeping close tabs on colon cancer survivors for up to 10 years will result in the best chances of catching any recurrences early for all survivors. If patients are tempted to ignore the cancer clinic when they call about follow-up appointments, it may help to know that they are not alone. Feeling seriously distressed after a diagnosis and treatment is common. Working with your health care team to access the resources needed to cope will help maintain the courage to follow up after treatment has ended.

Ringland, CL., et al., Second primary colorectal cancers (SPCRCs): experiences from a large Australian Cancer Registry. Annals of Oncology. Advance Access 2010. 21(1): pp. 92-97.

12. Lack of Colorectal Cancer Screening & The Elderly (Dec. 29/09)

Lack of colorectal cancer screening leaves elderly patients at risk for emergency surgery when a growing cancer blocks or perforates the colon. About a third (30%) of 292 emergency colorectal surgeries in a large university hospital were due to either colon obstruction or perforation. 15% of all patients older than 65 who had emergency colorectal surgery died, and 35% had at least one serious complication. Researchers concluded: *These procedures frequently involve locally advanced colorectal cancer, emphasizing the need for improved colorectal cancer screening.*

McGillicuddy, Edward, et al., Factors predicting morbidity and mortality in emergency colorectal procedures in elderly patients. Archives of Surg. 2009; 144(12): pp. 1157-1162

13. Colonoscopy May Miss Right-Sided Colon Cancers (Jan. 3/10)

This study concluded that while colonoscopy is effective in preventing cancers and advanced polyps in the lower part of the colon and rectum, it is less successful in stopping them in the right side or upper colon. German researchers examined 3300 colonoscopies and found a substantial reduction in large polyps or cancers in the left side of the colon and rectum among patients who had had a colonoscopy in the past ten years compared to those who hadn't had one. However, in the upper part of the colon, risk for an advanced polyp or cancer was the same whether or not the patient had a previous colonoscopy. Overall, colonoscopy reduced the risk of a cancer or an advanced adenoma by 50%. Doctors found an *advanced colorectal neoplasm,* defined as cancer or an advanced adenoma, in about 1 in 10 people who had not had a previous colonoscopy (11.4%). If the person had a colonoscopy in the past ten years, fewer advanced neoplasms were found (6.1%), but location in the colon was of great significance. The right side of the colon ***(proximal)*** was defined as the cecum, ascending colon, and transverse colon. The left side (***distal)*** *consisted of* the descending colon, sigmoid colon, and rectum. If an individual had a colonoscopy in the previous ten years, the risk of finding a large polyp or cancer in the left side was about a third of that of someone who hadn't had an exam. However, there was no reduction in the risk of right

sided advanced neoplasms. Cancer was found in 41 of 2,701 patients who hadn't had colonoscopy (1.5%) compared to only 1 person in the 586 who had one. (0.2%). Researchers concluded: Prevalence of left-sided advanced colorectal neoplasms, but not right-sided advanced neoplasms, was strongly reduced within a 10-year period after colonoscopy.

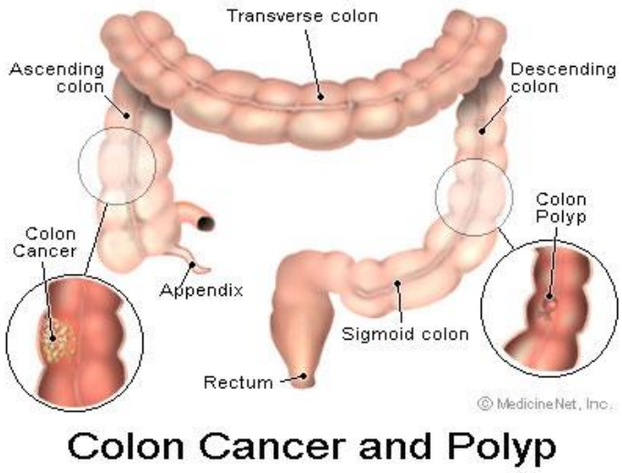

Diagram Showing Right-Sided Colon Cancer Able to Be Missed in Colonoscopy

Source: http://images.google.ca/imgres?imgurl=http://blogs.phillyburbs.com/news/bcct/wp-content/blogs.dir/2/files/2008/Sept/Wednesday/colon_cancer.jpg&imgrefurl=http://blogs.phillyburbs.com/news/bcct/study-colorectal-cancer-screenings-should-start-at-age-50/&usg=__MiR7TLgmPqu7Ls92IIqNGI_rwWc=&h=310&w=393&sz=22&hl=en&start=1&sig2=b2s0YnBye-Ypzwwzx-ZGmA&um=1&tbnid=owzLLhW2lqDqNM:&tbnh=98&tbnw=124&prev=/images%3Fq%3Dright%2Bsided%2Bcolon%2Bcancer%26hl%3Den%26lr%3D%26sa%3DN%26um%3D1&ei=DVRPS8KhL8bk8Ab92ZicCg

Brenner, Hermann, et al., protection from right- and left-sided colorectal neoplasms after colonoscopy: population-based study. J of National Cancer Institute. Published online Jan. 2, 2010. doi: 10.1093/jnci/dip436

14. Subsequent Colorectal Cancer May Develop Despite Continued Screening (Jan. 6/10)

A new study examines the occurrence of interval colorectal cancer despite regular colonoscopy and highlights the importance of close follow-up for patients who have a history of advanced adenomas, which are precancerous polyps. In this study, researchers studied the rate of interval colorectal cancer in patients participating in the Polyp Prevention Trial Continued Follow-up Study and found that 9 cases of colorectal cancer were diagnosed. Of patients in whom colorectal cancer developed, 78% had a history of advanced adenoma. The majority of the cancers detected were early stage (78% were stage I or II) and therefore highly curable. Colonoscopy is recommended as the primary screening method for colorectal cancer and is the final common pathway for all other recommended screening tests. It is considered the "gold standard" for colorectal cancer screening because of the ability to diagnose and remove polyps (growths) before they become cancer. Despite regular colonoscopy, interval colorectal cancer may occur. Researchers set out to examine the rate at which these interval cancers appear. The results showed that nine patients developed colorectal cancer despite undergoing a mean of more than three colonoscopies. The majority of patients in the study in whom colorectal cancer developed had a previous advanced adenoma. The results confirm the need for continued colonoscopy surveillance in at-risk patients because of the ongoing risk of colorectal cancer, especially among those with a history of advanced adenoma. And, researchers stress that a polyp, especially if it is an advanced adenoma, be completely removed, since cancer may develop subsequently at that site if residual tissue remains.

http://www.sciencedaily.com/releases/2010/01/100106193442.htm

PSYCHO-SOCIAL

15. Spiritual Support Aids Cancer Patients (Dec. 17/09)

When faced with a life-threatening disease, many patients find support and solace in their faith or spirituality. New research now confirms that having your medical care team acknowledge and support your spiritual needs results in compassionate care and a better quality of life when facing terminal illness. For the study, researchers interviewed 343 incurable cancer patients around the U.S. They asked about how they were coping with their illness, how well their medical team addressed their spiritual needs, and their preferences about end-of-life treatment. The patients who reported that their spiritual needs were supported by their medical team were:

- more likely to receive hospice care

- less likely to receive aggressive medical interventions
- more likely to report better well-being at the end of life

The study authors concluded that addressing each patient's spiritual needs is an important way to ensure comfort and well-being near death.

Balboni, TA, et al., Provision of spiritual care to patients with advanced cancer: Associations with medical care and quality of life near death. J Clinical Oncology. 2009; DOI:10.1200/JCO.2009.24.8005

16. Emotional Support Aids Cancer Patients (Dec. 29/09)

This study demonstrated that when cancer patients receive emotional support in the three months after their diagnosis, they were much more likely to look on their cancer experience as an opportunity for positive growth many years later. For those cancer patients who received reassurance, comforting, and help with problem solving from family and friends, there was a greater tendency towards the fostering of positive outcomes from their cancer illness eight years after having been originally diagnosed. And researchers referred to these positive outcomes as “posttraumatic growth”. The findings suggest that getting support from family and friends, characterized by reassuring, comforting, and problem-solving in the period following diagnosis is an important resource that may help cancer survivors to find positive meaning in the cancer experience

Schroevers, Maya, et al., Type of social support matters for prediction of posttraumatic growth among cancer survivors. Psycho-Oncology; Vol. 19, Issue 1, pp. 46-53

17. Coping With a Cancer Diagnosis (Jan. 2/10)

Being diagnosed with cancer can bring a wide range of emotions, including grief. Grief is defined as a normal reaction to loss. With cancer, the losses may be large or small. People may grieve the loss of independence or their status as a "healthy person". People may grieve the loss of their normal role in the family or even the loss of a body part due to surgery. Regardless of the source of grief, one of the most important things to know is that there is no "one right way" to grieve. In the past, many mental health experts felt that there were emotional stages most grieving people moved through. They expected each person would move through these stages in a specific order as well. Newer studies and work with grieving people have shown this is to be not necessarily true. Mental health experts now point out that grief can include emotions as different as denial, anger, and guilt. This can lead to physical problems as well. Addressing these physical problems won't resolve the grief completely, but can help a person feel better and cope with the emotional aspects of grief more effectively. According to the Mayo Clinic, there are several positive steps that may help a person better cope with grief:

- Express feelings and seek support. Family, friends, support groups, a religious community, or grief counselor can provide support in times of crisis. If you've been diagnosed with cancer, seeking support early is critical.

- Avoid making major life decisions. When grieving, you may not think as clearly as you normally would. Options that seem like a good idea now may not be right for you in the future. To avoid making any major decisions you may later regret, seek help for coping with your grief first. Focus on the big life decisions when you are in a better place emotionally.

- Take care of yourself. Get plenty of rest, eat right, and get regular, moderate exercise if you can do so. If you have been diagnosed with cancer, consult with your doctor about engaging in an exercise program.

- Give it time. Moving through and beyond grief may take months or even years in some cases. If you feel that your grief is so severe that you cannot function in your daily life, talk to your doctor. He or she can explain options such as counseling or anti-anxiety and antidepressant medications. These approaches can be used to get through a particularly difficult period.

Grief is a normal response to a cancer diagnosis. Don't feel badly if you're not grieving in a way that people expect or want. Just be sure to take care of your emotional and physical needs. It's OK to work through grief at your own pace and in your own way.

http://bookstore.mayoclinic.com/

OTHER

18. Advances Associated With The Molecular Basis of Colorectal Cancer (Dec. 17/09)

This study highlighted some of the key advances associated with the molecular basis of colorectal cancer. Researchers are trying to better understand the molecular basis of individual susceptibility to colorectal cancer and to determine factors that initiate the development of the tumour, drive its progression, and determine its responsiveness or resistance to antitumour agents. The key advances are summarized as follows:

- Discoveries in DNA sequencing technology have made it possible to sequence the entire genome of a human cancer. Colorectal cancer provided the first example of the power of this technology. Sequencing of 18,000 (nearly all) of the known human genes in 35 colon cancers identified 140 as candidate cancer genes that were mutated in at least two colon cancers and that likely contributed to the cancer phenotype.
- Biological pathways that are deregulated in colon cancer have been identified, and could now form the basis of new therapeutic agents. Although some high-frequency mutations are attractive targets for drug development, common signaling pathways downstream (further forward on the DNA molecule) from these mutations may also be tractable as therapeutic targets.
- Studies that aid in the understanding of colorectal cancer on a molecular level have provided important tools for genetic testing for high-risk familial forms of the disease, predictive markers for selecting patients for certain classes of drug therapies and molecular diagnostics for the noninvasive detection of early cancers.
- Recent progress in molecular assays (analysis) for the early detection of colorectal cancer indicates that understanding the genes and pathways that control the earliest steps of the disease, and individual susceptibility, can contribute to clinical management in the near term. For example, patients whose colon cancers have mutations in either RAS or BRAF genes are known not to benefit from treatment with the anti-colon cancer agent Cetuximab or Panitumumab.
- Moreover, patients with inherited mutations in tumor-suppressor genes, such as APC, MLH1, and MSH2 have a very high risk of colorectal cancer and require early and frequent surveillance for colon cancer and often prophylactic surgery.
- Last, the development of molecular diagnostics for the early detection of colorectal cancer is emerging as an important translation of colon-cancer genetics into clinical practice. One example is the development of stool DNA tests to detect cancer-associated aberrant (deviant) DNA methylation (the replacement of a hydrogen atom for a methyl group on DNA) as a method for early detection of patients with colorectal cancer or advanced adenomas. Stool DNA testing for colorectal cancer has been added to the cancer-screening guidelines of the American Cancer Society.

Markowitz, Sanford D., et al., Molecular Basis of Colorectal Cancer. New England J of Medicine, 2009; 361: pp. 2449-2460

19. MSH6 Mutation Increases Risk of Colorectal Cancer (Dec. 29/09)

People with a mutation in the MSH6 gene, part of the Lynch syndrome, have a greatly increased risk of developing colorectal, endometrial, and other related cancers. Lynch syndrome, also known as hereditary nonpolyposis colon cancer (HNPCC), is an increased cancer risk, inherited directly from parent to child. Changes in the genes that repair damaged DNA increase the chances that cells can grow out of control and develop into cancer. The cancers can occur in old age, with an increasing risk from age 70 to 80. About 4 in every 1000 colorectal cancers are due to an inherited mutation in the MSH6 gene. It accounts for approximately 10-20% of Lynch syndrome mutations. By the time they are 80 years old, men have eight times the risk of developing colorectal cancer and women have 26 times the risk of endometrial cancer — cancer that begins in the lining of the uterus. In this study, a research team identified 113 families with inherited MSH6 mutations in five countries, including 3,104 relatives. They estimated the risk that they would have been diagnosed with a Lynch-related cancer by the time they were 70 and by the age of 80. They also compared the risk of a cancer diagnosis in Lynch carriers to the general population.

- Men had a 22% risk of colorectal cancer by age 70 which rose to 44% by age 80.
- Women had a 10% risk of colorectal cancer by 70 which was 20% by 80.
- Women had a 26% risk of endometrial cancer by 70, 44% by 80.

For any Lynch-related cancer

- Men had a 24% risk by 70 with a 47% risk by 80.
- Women had a 40% risk by 70 and a 65% risk by 80.

Compared to other people without the Lynch-related MSH6 gene:

- Men had 8 times the risk of getting colorectal cancer in their lifetime.
- Women had 26 times the risk of endometrial cancer and 6 times the risk of any Lynch-related cancer.

Baglietto, Laura, et al., Risks of Lynch Syndrome Cancers for MSH6 Mutation Carriers. J of the National Cancer Institute. Advance Access Published online on December 22, 2009. doi: 10.1093/jnci/djp473

20. Management of Recurrent Rectal Cancer (Jan. 3/10)

This study presents a concise review on the evaluation and management of locally recurrent rectal cancer, which despite marked reduction in the rate of recurrent rectal cancer remains an important problem. The review discusses the diagnosis, evaluation, and management of recurrent rectal cancer. The researchers identify that despite improvements in both the neoadjuvant and surgical management of rectal cancer, local recurrence is still an important problem, with documented recurrence rates of 4-8%. They point out that the recurrence requires a team of specialists and that accurate detection and diagnosis followed by chemoradiotherapy and surgical resection may result in 5-year survival rates of up to 35%. The article concludes by emphasizing the need for a multimodality approach to the successful management of recurrent rectal cancer which could lead to either successful palliation or oftentimes a cure.

Bouchard, Philippe, et al., Management of Recurrent Rectal Cancer. Annals of Surgical Oncology. Published online ahead of print. December 30, 2009. doi: 10.1245/s10434-009-0861-2

21. Colon Cancer Patients Fare Better With Close Family History (Jan. 13/10)

According to this study, colon cancer patients whose first degree relatives also had colon cancer, have a significantly better prognosis. Even after all risk factors were taken into consideration, they had less chance of cancer recurring and less chance of dying than people without a close family history. However, the same did not apply to rectal cancer. Researchers in Sweden questioned 318 consecutive colorectal cancer patients about their family cancer history. They found 31 (10%) had at least one first-degree relative who also had colorectal cancer — a parent, sister or brother, or child. They then followed all of the patients for the next six years, watching for recurrences and deaths. Two patients met the criteria for Lynch syndrome and were not included in the study. They found a 63% reduction in risk for recurrence among patients who also had a family member with colorectal cancer and a 75% reduction in the risk of dying. This reduced risk could not be explained by other factors including the patient's age or sex, the cancer stage, tumor differentiation or invasion of nearby blood vessels. Researchers concluded that family history for colorectal cancer in a first-degree relative is an individual prognostic factor in patients with colon cancer and could not be explained by known clinico-pathological factors. The value of family history is therefore not only valuable when identifying families with hereditary colorectal cancer, but also valuable as it relates to the prognosis of the patients.

Birgisson, Helgi, et al., the correlation between a family history of colorectal cancer and survival of patients with colorectal cancer. Familial Cancer. Vol. 8, No. 4, December 2009; doi: 10.1007/s10689-009-9286-0

NUTRITION & HEALTHY LIFESTYLE

22. Tumor Recurrence Minimized With Exercise (Dec. 17/10)

There is a growing body of evidence that supports physical activity significantly reducing the risk of tumor recurrence. The study included 668 men who had been treated for stage I, stage II or stage III colon cancer that had not spread (nonmetastatic cancer) in the body. Every two years, the men were sent questionnaires that asked them about any new cancer and disease diagnoses, as well as their physical activity. A metabolic equivalent task (MET) score was matched to each type of physical activity, with exercises that burned more energy receiving higher MET scores. During the study period, which ended in January 2006, 258 of the participants died, including 88 who died from colon cancer. The results show that men who were physically active after diagnosis of nonmetastatic colorectal cancer experienced a significantly decreased risk of colorectal cancer-specific death, as well as death from any cause. This benefit was independent of age, disease stage, body mass index and tumor location and from the pre-diagnosis physical activity. The data demonstrates that physical activity will most certainly help in the fight against colon cancer. The more physically active, the greater the protection. Men with the highest activity levels (equal to brisk walking about 12.3 hours per week), relative to those with the lowest, had a 53% lower rate of death from colorectal cancer and a 41% lower rate of death overall during the study.

Meyerhardt, Jeffrey, et al., Physical Activity and male colorectal cancer survival. Archives of Internal Medicine. 2009; 169(22): pp. 2102-2108

23. Salt and Cancer (Dec. 18/09)

Sodium intake as a whole salt equivalent may not increase the risk of cancer but may increase that of cardiovascular disease (CVD); and in contrast, salted food intake may increase the risk of cancer, according to this study. During 1995 to 1998, a validated food-frequency questionnaire was administered to 77,500 men and women aged 45 to 74 years. By the end of 2004, 4476 cases of cancer and 2066 cases of CVD were identified. Higher consumption of sodium was associated with a higher

risk of CVD but not with the risk of total cancer: Higher consumption of salted fish roe (fish eggs) was associated with higher risk of total cancer, and higher consumption of cooking and table salt was associated with higher risk of CVD. Similar results were seen for the risk of gastric or **colorectal cancer** and stroke. The findings support the notion that sodium and salted foods have differential influences on the development of cancer and CVD.

Takachi, Ribeka, et al., Consumption of sodium and salted foods in relation to cancer and cardiovascular disease: the Japan Public Health Center – based prospective study. American J Clinical Nutrition. December 16, 2009. doi: 10.3945/ajcn.2009.28587

24. Folic Acid, Vitamin B12 and Cancer (Dec. 24/09)

This study analyzed the results of two Norwegian trials among patients with heart disease, where there was a statistically insignificant increase in cancer incidence in the groups assigned to folic acid treatment. The researchers examined whether folic acid treatment was associated with cancer outcomes and all-cause mortality after extended follow-up. The authors were quoted as saying, "Because there is no folic acid fortification of foods in Norway, this study population was well suited for such an investigation." "Experimental evidence suggests that folate deficiency may promote initial stages of carcinogenesis, whereas high doses of folic acid may enhance growth of cancer cells," the authors wrote. Since 1998, many countries, including the United States and Canada, have implemented mandatory folic acid fortification of flour and grain products to reduce the risk of neural-tube birth defects. Recently, concerns have emerged about the safety of folic acid, in particular with respect to cancer risk. The two clinical trials included 6,837 patients with heart disease who were treated with B vitamins or placebo between 1998 and 2005, and were followed up through the end of 2007. The researchers found that after a median 39 months of treatment and an additional 38 months of post-trial follow-up, 288 participants who did not receive folic acid plus vitamin B12 versus 341 participants who received such treatment were diagnosed with cancer, representing a 21% increased risk. A total of 100 patients who did not receive folic acid plus vitamin B12 versus 136 who received such treatment died from cancer, a 38% increased risk. A total of 16.1% of patients who received folic acid plus vitamin B12 vs. 13.8% who did not receive such treatment died from any cause. "Results were mainly driven by increased lung cancer incidence in participants who received folic acid plus vitamin B12. Vitamin B6 treatment was not associated with any significant effects," the authors wrote. "Our results need confirmation in other populations and underline the call for safety monitoring following the widespread consumption of folic acid from dietary supplements and fortified foods."

Ebbing, Marta, et al., Cancer Incidence and Mortality After Treatment With Folic Acid and Vitamin B12. J of the American Medical Association. Vol. 302, No. 19, November 2009. pp. 2119-2126

25. Proanthocyanidins Can Reduce Colorectal Cancer Risk (Dec. 23//09)

According to this study, people who eat more proanthocyanidin-rich foods seem to have lower risk of many chronic diseases, including colorectal cancer. Researchers in Italy recently added more evidence that proanthocyanidins may keep colorectal cancer at bay. For the study, the diet habits of 1,953 people with colorectal cancer and 4,154 people without colorectal cancer were studied. Researchers looked for links between the amount of proanthocyanidins in the diet and colorectal cancer risk. Compared with people who eat a diet with the lowest levels of proanthocyanidins, those who eat the most have up to 31% lower likelihood of being diagnosed with colorectal cancer. Many common foods contain these healthful nutrients. The researchers note that for anyone concerned about colorectal cancer, a diet rich in proanthocyanidins is a good choice. Should you wish to get more proanthocyanidins into your diet, think purple and red. Many foods that are deep purple and red in color are loaded with these healthful, disease-fighting nutrients. The best sources of proanthocyanidins include:

- Apples
- blueberries
- blackberries
- red and purple grapes (go for those with seeds and eat the seeds for extra proanthocyanidins)
- red wine
- cranberries
- plums
- black currants
- bilberries

There are a few other foods that aren't red or purple, but still pack a powerful proanthocyanidin punch. In addition to the purples and reds, try to include these proanthocyanidin-rich foods:

- dark chocolate (at least 70% cocoa)
- green and black tea,
- cinnamon (dried spice),
- hazelnuts, pistachios, pecans, and almonds ,

- red and kidney beans

Rossi, Marta, et al., Proanthocyanidins and the risk of colorectal cancer in Italy. Cancer Causes and Control. Online edition. Doi: 10.1007/s10552-009-9455-3

26. High Fat Diet and Colon Inflammation (Jan. 2/10)

Colorectal cancer has been linked to an increased prevalence of the Western diet: one high in fat and low in fiber, vitamin D and calcium. In this study a team of scientists have shown what happens to colon tissue when mice are fed such a diet: an inflammatory response that could be the trigger for carcinogenic processes. According to the researchers, there is convincing evidence that increased intake of red meat, processed meat and alcohol can increase risk of colorectal cancer, whereas greater consumption of dietary fiber, milk and calcium might decrease risk. The findings show that a Western diet induces oxidative stress and alters immune responses in the colon of mice long before tumors occur. The researchers fed experimental mice either a standard diet containing 5% fat and ample amounts of calcium and vitamin D or a Western diet containing 20% fat and adequate but marginal levels of calcium and vitamin D for three or six months. As expected, animals consuming the Western diet were heavier and had more fat tissue than those on the control diet. 41 genes were identified that were being expressed at significantly different levels between the Western diet and control animals. Most of these genes were related to metabolic processes such as lipid metabolism and glutathione metabolism, which is important for preventing damage caused by oxidation. In addition, expression of a series of genes collectively associated with immune and inflammatory responses was altered. The Western diet also increased the number of macrophages, cells associated with inflammation in the colon, as well as several proteins such as myeloperoxidase and MCP-1 and colonic oxidative stress genes associated with inflammation. Taken together, the lead investigator Holt maintained that the data suggest macrophage recruitment and oxidative stress is a potential early mechanism underlying the carcinogenic effect of the Western diet.

Erdelyi, Ildiko, et al., Western-style diets induce oxidative stress and dysregulate immune responses in the colon in a mouse model of sporadic colon cnacer. J Nutrition. Vol. 139, No. 11: pp. 2072-2078