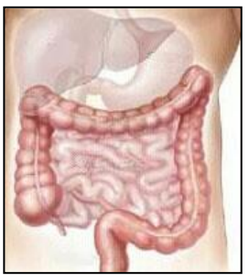
COLORECTAL CANCER RESEARCH

Month Ending March 18th, 2011



The following colorectal cancer research update extends from February 19th, 2011 – March 18th, 2011 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Colorectal Cancer Clinical Trial Testing New Monoclonal Antibody CT-011 (Feb. 20/11)

Curetech Ltd. Has completed recruitment for the Phase II (efficacy) clinical trial of its monoclonal antibody CT-011 for the treatment of metastatic colorectal cancer. The trial will include 171 patients undergoing chemotherapy (folfox) and will last 18 months. The trial details may be found by clicking on the following link: http://www.clinicaltrials.gov/ct2/show/NCT00890305?term=CT-011+colorectal+cancer&rank=1 . Centres identified as taking part include Sloan Ketterig in New York. The proposed clinical trial will be a multi-center, randomized, open label, active control study in previously **untreated** patients with **metastatic** colorectal cancer aimed to evaluate the safety, tolerability and efficacy of the monoclonal antibody, CT-011, administered at 3mg/kg in combination with FOLFOX chemotherapy (FOLFOX4 or mFOLFOX6) compared with treatment by FOLFOX alone. Approximately 171 patients are enrolled in this study. The primary endpoint will be the median progression free survival in patients treated with **CT-011** plus FOLFOX compared to that of patients treated with FOLFOX alone.

http://www.clinicaltrials.gov/ct2/show/NCT00890305?term=CT-011+colorectal+cancer&rank=1

2. Treating Colorectal Cancer That Has Spread to the Liver (Feb.20/11)

Advanced colon cancer used to be considered incurable. Many people believed that if colon cancer had spread from the colon to the liver, for example, the odds of a cure were slim. Fortunately, this is not always the case. A review of the options for treating colon cancer that has spread to the liver concludes that 25-35% of people in this category can be treated with a curative approach. This means the colon cancer is treated with the expectation of a cure, not just to slow its advance. Among the conclusions of the review are that other treatments, including chemotherapy and certain types of radiation therapy should be used, when appropriate, along with surgery to increase the number of people who can be treated with the goal of a cure. For example, if a person has colon cancer in the liver and the tumors appear too large to safely remove with surgery, chemotherapy can be used to shrink the tumors first. After chemotherapy, the shrunken tumors then are removed with surgery. Certain types of concentrated radiation therapies can be used in a similar way to shrink tumors, which can make surgery safer and more effective. Another option is that tumors are removed from the liver surgically first. This is followed by another form of treatment, such as chemotherapy, to increase the chances of killing all of the cancer cells.

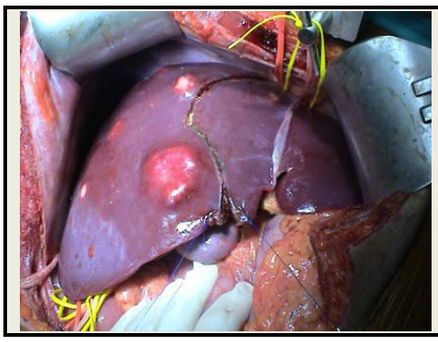


Figure 1: Showing liver mets

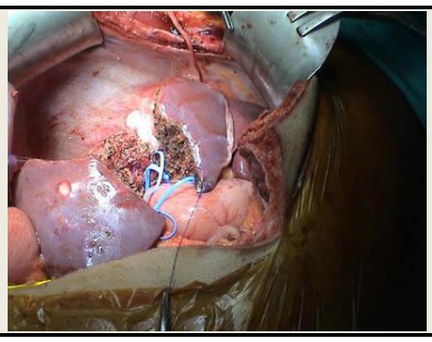


Figure 2: Showing extent of liver resection

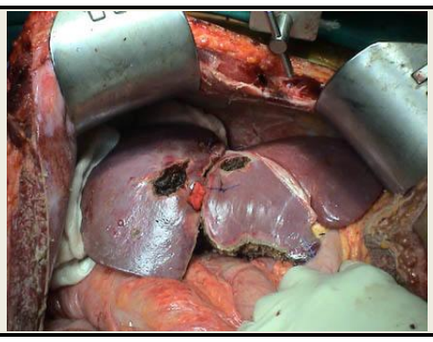


Figure 3: Showing liver after complete resection

Stein, Alexander, et al., The Role of peri-operative treatment in resectable liver metastases of colorectal cancer. Therapeutic Advances in Medical Oncology. Nov. 2010, Vol. 2, No. 6: pp. 389-398

3. Sulindac, Atorvastatin and Probiotic Dietary Fiber for Colorectal Cancer Chemoprevention (Feb. 21/11)

Sulindac (a nonsteroidal ant inflammatory drug - NSAID - used for the management of mild to moderate pain, fever, and inflammation), **atorvastatin** (an oral drug that lowers the level of cholesterol in the blood) or prebiotic dietary fiber may reduce colorectal cancer (CRC) risk. However, there is currently very little clinical trial data to support their use. In this study, researchers conducted a randomized, phase II chemoprevention trial involving patients age ≥ 40 years, with previously resected colon cancer or multiple/advanced colorectal adenomas. Intervention assignments were: (A) atorvastatin 20 mg qd; (B) sulindac 150 mg bid; (C) oligofructose-enriched inulin 6 gm bid; or (D) control (maltodextrin) 6 gm bid, for 6 months. Percent change in rectal polyps within this population of patients was the primary endpoint. Among 85 eligible randomized patients, 76 (86%) completed the trial per protocol. Data from this multi-center, phase II trial do not provide convincing evidence of CRC risk reduction from six month interventions with atorvastatin, sulindac or prebiotic dietary fiber, although statistical power was limited by the relatively small number of patients enrolled in the study.

Limburg, Paul, et al., Randomized Phase ii trial of sulindac, atorvastatin, and prebiotic dietary fiber for colorectal cancer chemoprevention. Cancer Prev Res; 4(2): pp. 259-269

4. Brain Mets Originating from Colorectal Cancer (Feb. 23/11)

Brain metastases (BM) occur in approximately 20-40% of cancer patients. The present study investigated the clinical outcomes of patients with BM from colorectal cancer (CRC) to assess the benefit of systemic chemotherapy (CT) administered after surgical or radiotherapeutic control of BM and to identify independent prognostic factors associated with survival after BM. Between August 2001 and July 2009, 118 patients with symptomatic BM from CRC received either cranial irradiation or craniotomy at two large cancer centers in South Korea. Median time from diagnosis of metastatic CRC to detection of BM was 12.2 months. Thirteen patients (11%) exhibited brain involvement at initial presentation. Median survival after BM development was 4.1 months. Forty-six patients (40%) had been treated previously with the chemotherapeutic agents fluoropyrimidine, oxaliplatin, and irinotecan. Patients who received chemotherapy after BM exhibited significantly improved survival compared with those who did not (12.4 versus 3.1 months). Data revealed that chemotherapy intervention after presentation with BM was **significantly associated** with survival after BM. Although BM is a late-stage phenomenon in CRC, approximately two-thirds of patients were still unexposed to irinotecan or oxaliplatin at the development of BM in this study. Thus, researchers maintain that additional chemotherapeutic intervention after BM associated with CRC may be beneficial for selected patients.

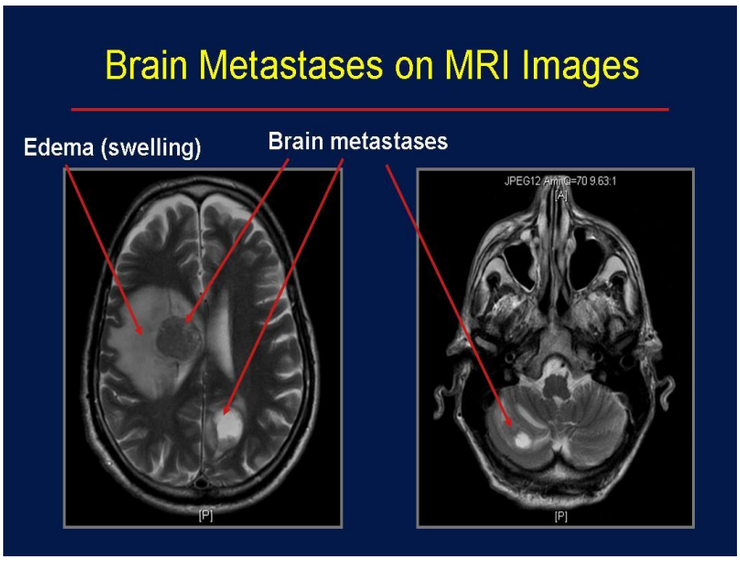


Figure 4: Showing brain mets originating from colorectal cancer.

Baek, Ji Yeon, et al., Characteristics and prognosis of patients with colorectal cancer-associated brain metastases in the era of modern systemic chemotherapy. J of Neuro-Oncology. Online edition. DOI: 10.1007/s11060-011-0539

5. New Trial Testing Agent in the Recurrence of Colorectal Cancer (Feb. 25/11)

Researchers at the National Surgical Adjuvant Breast and Bowel Project (NSABP) are conducting a clinical trial exploring whether a statin drug can reduce the risk of new polyps, colon cancer recurrence, or a new primary colon cancer. In the P-5 Clinical Trial (http://www.cancer.gov/clinicaltrials/search/view?cdrid=658554&protocolsearchid=8767923&version=patient), stage I and II colon cancer patients will be randomly assigned to take either rosuvastatin (Crestor®) or an inert placebo for five years. Studies of statins and colorectal cancer risk are controversial and some conflict. However, a study that looked back at colon cancer patients in Israel and matched them to similar people who didn't have colon cancer found that a larger percentage of patients who didn't have colon cancer had taken statins for more than 5 years. About half as many colon cancer patients had taken statins (6.1%) as people who didn't have cancer (11.6%). Even after adjusting for other risk factors for colorectal cancer, including taking aspirin regularly, statin use reduced colon cancer risk by about 45%. In addition, scientists looking at cell processes have found that statins block a protein that is important in cell growth. Blocking its action may prevent colon cancer from spreading or polyps from developing. Stage I and II colon cancer patients are eligible for the trial who:

- have finished their planned treatment — surgery or adjuvant chemotherapy
- are no more than 1 year past their treatment
- have had a complete colonoscopy in the past six months and all polyps removed
- if they are taking aspirin regularly agree to continue it during the five years of the trial
- have not taken a statin within a month of entering the trial

The following patients would be excluded from the study:

- Patients who are regularly taking NSAIDS, except for aspirin

- Patients with familial adenomatous polyposis (FAP)
- Patients with Lynch syndrome (HNPCC or hereditary non-polyposis colon cancer)
- Have high cholesterol levels that might require them to take a statin.

The study title is ***Phase III Randomized Study of Adjuvant Rosuvastatin in Patients With Resected Stage I or II Colon Cancer.*** The two groups of patients would consist of the following:

- Arm I: Patients receive oral rosuvastatin once a day for five years.
- Arm II: Patients receive an oral placebo once a day for five years.

Patients on the trial will have physical exams every six months, a colonoscopy within 6 months of starting the trial, and colonoscopies at 1, 3, and 5 years to look for new polyps. The study is double-blinded — neither patients nor their doctors will know if they are getting rosuvastatin or a placebo. Some study patients will also be asked about their quality of life and tissue samples will be analyzed for biomarkers.

http://www.cancer.gov/clinicaltrials/search/view?cdrid=658554&protocolsearchid=8767923&version=patient

6. Survival of Patients with Peritoneal Mets Undergoing Chemo (Feb. 25/11)

Palliative chemotherapy (chemotherapy that is used when a cure is not attainable) improves survival in patients with metastasized colorectal cancer. However, researchers maintain that there is a lack of data regarding the effectiveness of modern chemotherapy in patients with isolated peritoneal carcinomatosis (PC) – widespread metastatic disease appearing on the peritoneum (the lining that surrounds the abdominal organs). All patients discovered to have PC at the time their primary tumour was discovered, were included in the study between 1995 and 2008. Researchers assessed the use of chemotherapy and overall survival in three time periods related to the availability of different chemotherapy regimens. Chemotherapy use gradually increased over time. Median survival (MS) for patients with PC without other metastases diagnosed in 1995–2000 was 35 weeks and 34 weeks in 2005–2008. Median Survival in patients diagnosed with PC plus other metastases was 21 weeks in 1995–2000 and 26 weeks in 2005–2008. Researchers maintain that according to the data, use of chemotherapy had a beneficial influence on survival only in 2005–2008. In the first two periods, chemotherapy treatment did not decrease the risk for death. The researchers, therefore, concluded that despite increasing usage of palliative chemotherapy and availability of new agents, population-based survival of patients with PC did not improve until very recently. Response to palliative chemotherapy in PC should be evaluated separately from other metastases.

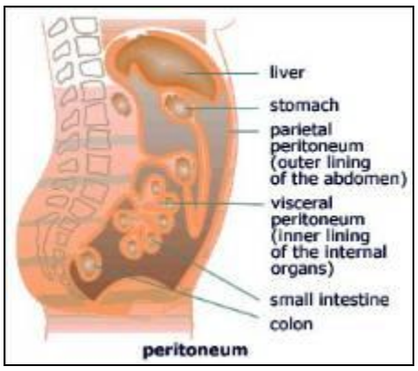


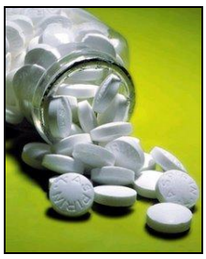
Figure 5: Diagram Illustrating the location of the peritoneum.

Klaver, YLB, et al., Population-based survival of patients with peritoneal carcinomatosis from colorectal origin in the era of increasing use of palliative chemotherapy. Annals of Oncology (2011) doi; 10.1093/annonc/mdq762 First published online: Feb. 23, 2011.

7. Aspirin Protection Against Colorectal Cancer Dependent on Inflammatory Pathways (Mar. 8/11)

The reduced risk of colorectal cancer associated with taking aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs) may be confined to individuals already at risk because of elevations in a particular inflammatory factor in the blood. The study found that higher baseline levels of a novel inflammatory marker indicated increased risk of developing colorectal tumors and also predicted who might benefit from taking aspirin or NSAIDs. These findings suggest that a blood biomarker may be helpful in deciding whether individuals should take aspirin or NSAIDs to reduce their cancer risk. They also indicate that chronic inflammatory pathways are quite complex and further studies are needed to understand which facets of the inflammatory response are most associated with the development of colorectal cancer. In recent years, considerable research has supported the importance of inflammation in the development of chronic conditions such as cardiovascular disease and several forms of cancer. Many studies have found reduced incidence of colorectal cancer among individuals who regularly take aspirin or other NSAIDs, and disorders such as colitis and inflammatory bowel disease are known to

increase the risk. To investigate whether moderately elevated levels of chronic inflammation also raise the risk of colorectal cancer, the investigators analyzed data from more than 120,000 female registered nurses since 1976, gathering comprehensive health information from its participants every two years.



The current study analyzed data from NHS participants who had provided a blood sample in 1989 or 1990 and were cancer-free at that time. After identifying 280 participants who developed colorectal cancer during the subsequent 14 years and 555 age-matched controls who did not, the research team analyzed their baseline levels of three inflammatory factors -- C-reactive protein (CRP), interleukin-6 (IL-6) and soluble tumor necrosis factor receptor-2 (sTNFR-2). Although no association was seen between levels of CRP or IL-6 and risk of developing colorectal cancer, participants with the highest levels of **sTNFR-2 had a 60% greater risk than did those with the lowest levels of the factor**. In addition, the reduced risk of developing colorectal tumors associated with regularly taking aspirin or NSAIDs was primarily seen among participants with high baseline sTNFR-2 levels. The results suggest that, even though chronic inflammation may increase colorectal cancer risk, not all blood markers of inflammation are markers of that risk. The most common blood biomarkers of inflammation -- CRP and IL-6 -- do not appear to be relevant, while **sTNFR-2 does**. A better understanding of the significance of these markers will help to identify individuals most likely to benefit from chemoprevention using aspirin or NSAIDs.

Chan, Andrew T, et al., . Inflammatory Markers Are Associated With Risk of Colorectal Cancer and Chemopreventive Response to Anti-Inflammatory Drugs*. Gastroenterology*, 2011; 140 (3): 799 DOI: 10.1053/j.gastro.2010.11.041

8. Analyzing Biomarkers KRAS, BRAF, PTEN, IGF1R, EGFR intron 1CA in Primary Tumors and Paired Mets to Determine Benefit From Erbitux (Mar.9/11)

The aim of this study was to determine the expression of molecular markers in metastatic colorectal cancer (mCRC) and the similarity between primary tumor and metastasis. Researchers also aimed to determine the relationship between molecular markers and clinical outcomes of cetuximab-containing chemotherapy, also more commonly known as erbitux.

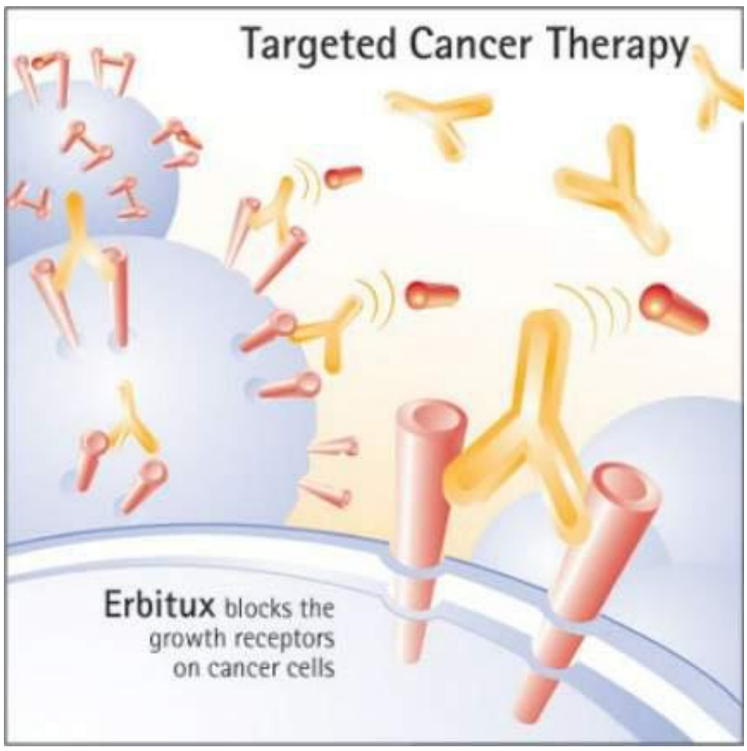


Figure 6: How the drug Erbitux targets colorectal cancer cells. Erbitux is a monoclonal antibody (MAb) that is specific for the epidermal growth factor receptor (EGFR). Erbitux is an approved treatment for metastatic colorectal cancer in KRAS wild type patients. Over-expression of EGFR is common in many solid tumours, such as colorectal. EGFR protects malignant tumour cells from the toxic effects of chemotherapy and radiotherapy, making these treatments less effective. Erbitux binds to the extracellular domain of EGFR on the tumour cell, thereby inhibiting receptor-associated tyrosine kinase. This inhibition blocks the intracellular pathways associated with tumour cell proliferation, so preventing tumour growth and dissemination as well as inducing cell death (apoptosis). By interfering with cell signalling pathways involved in cell proliferation, inhibition of EGFR-associated tyrosine kinase represents a novel approach to the treatment of solid tumours.

Seventy-five mCRC patients who received cetuximab-containing chemotherapy between 2000 and 2008 were enrolled in this study. Biomarker status such as EGFR, p-EGFR, PTEN, IGF-1R, KRAS, BRAF, and PI3 KCA were determined. The positive expression of EGFR, p-EGFR, PTEN, and IGF-1R was determined in 45 (64.3%), 9 (14.8%), 35 (50.7%), and 10 patients (16.1%), respectively. KRAS mutation and BRAF mutation were detected in 19 patients (27.5%) and 5 patients (7.0%), respectively. Among tested biomarkers, only the EGFR intron 1 CA and BRAF mutation showed similarity between primary tumor and paired metastasis. Skin rash was a strong predictive marker for response rate, Progression Free Survival (PFS), and Overall Survival (OS). In KRAS mutant tumors, PTEN expression was associated with a longer PFS. BRAF mutation was related to poor outcome in KRAS wild-type tumors. Researchers concluded that BRAF mutations and EGFR intron 1 CA were similar between primary tumors and paired metastases. In KRAS mutant tumors, PTEN expression was a predictive marker for favorable outcomes. In KRAS wild type, BRAF mutation was a strong predictive marker for poor outcomes.

Park, Jin Hyun, et al., Analysis of kras, braf, pten, igf1r, egfr intron 1 ca status in both primary tumors and paired metastases in determining benefit from cetuximab therapy in colon cancer. Cancer Chemotherapy and Pharmacology. Doi: 10.1007/s00280-011-1586-z

9. Mismatch Repair and KRAS Mutations Affect Outcomes in Colorectal Cancer (Mar.9/11)

What is Mismatch repair: *A system within the cell for correcting errors in genetic material called DNA that works by detecting and replacing bases in the DNA that are wrongly paired (mismatched bases). The system repairs the mismatch. When there is a mismatch in the DNA, a mismatch correction enzyme (chemical protein) goes to that strand of DNA and removes a segment of the strand containing the mismatched base. The gap in the strand is then filled through the action of the enzyme DNA Polymerase.*

Figure 7: During DNA replication, mistakes can occur as DNA polymerase copies the two strands. The wrong nucleotide can be incorporated into one of the strands causing a mismatch. Normally there should be an "A" opposite a "T" and "G" opposite a "C". If a "G" is mistakenly paired with a "T", this is a potential mutation. Fortunately cells have repair mechanisms. In this case repair proteins called PMS2, MLH1, MSH6, and MSH2, help recruit an enzyme called EXO1 that chops out a segment of the mutant strand. Then a DNA polymerase can replace the missing section of the strand with a new section and the mistake is repaired.

What is KRAS Mutation*: KRAS testing, which is a test to see which version of the KRAS gene your colon cancer tumor has, is an important first step to determining if your treatment should include anti-EGFR (anti-epidermal growth factor receptor) therapy such as erbitux and vectibix. For people with metastatic colon cancer, testing for what is known as the KRAS mutation before beginning anti-epidermal growth factor receptor (EGFR) therapy is now considered "best practice." This testing will be the standard of care for people with metastatic colon cancer who are being considered for treatment with anti-EGFR medications such as erbitux or vectibix. KRAS refers to a gene that can be altered (mutated) in colon cancer cells. Studies show that if this alteration (mutation) is present (present in approximately 40% of the crc population), the anti-EGFR medications cetuximab (Erbitux) and panitumumab (Vectibix) are not as effective and should not be used.*

What is BRAF**:** Research shows that another gene mutation, called BRAF, also plays a role in determining who can benefit from anti-EGFR therapies. Studies have found that people who do not have the BRAF mutation (a mutation in the BRAF gene - identified as BRAF Wild Type) or the KRAS mutation (identified as KRAS wild type) in their colon cancer cells benefit the most from anti-egfr therapies.

This study concluded that mismatch repair tests and KRAS mutational analysis provide useful risk stratification to guide chemotherapy use in patients with colorectal cancer. Investigators used data from 3239 predominantly **stage II colorectal cancer patients** to investigate the prognostic and predictive value of defective DNA mismatch repair (dMMR) and KRAS and BRAF mutations on tumor recurrence and chemotherapy outcomes. Recurrence risk of dMMR tumors (11%) was about half that for patients with MMR-proficient tumors (26%); this difference was most notable for patients with right-sided stage II colon cancers (8% versus 21%, respectively). The prognostic value of MMR status didn't differ according to the presence or absence of chemotherapy. The study does not support the previous view that MMR deficient patients do not respond to adjuvant chemotherapy. However, researchers maintain that further very large studies are needed to definitively confirm this. KRAS mutations were associated with significantly higher risks of recurrence (28%) compared with KRAS wild-type tumors (21%), and the increased risk wasn't significantly different in the presence or absence of chemotherapy. The increased risk of recurrence was more pronounced in rectal cancer than in colon cancer. BRAF mutations weren't significantly associated with the risk of recurrence. Researchers concluded that routine MMR testing is warranted because you can get an indication of HNPCC (hereditary nonpolyposis colorectal cancer) and be referred to a clinical geneticist; plus these patients have a significantly better outcome and not using adjuvant (postoperative0 chemotherapy should be considered. Researchers added, "From previous work we have undertaken, they need more careful follow up as they may have a higher risk of new cancers." "Routine KRAS testing may be warranted as testing for this mutation would be needed if the patients relapsed and anti-EGFR antibodies, such as erbitux or vectibix, were being considered, and the mutation

does confer an increased risk of relapse." "The most important ways to improve outcomes in bowel cancer are effective population-based screening and optimal surgery. "Only after these do we need to look at personalized medicine such as we are investigating here. However, if you are unlucky enough to need adjuvant therapy then there are now routine tests to help decide your future pattern of treatment."

Quirke, Philip, et al., Value of Mismatch Repair, KRAS, and BRAF Mutations in Predicting Recurrence and Benefits From Chemotherapy in Colorectal Cancer. J of Clinical Onc. Published online before print March 7, 2011, doi: 10.1200/JCO.2010.30.1366 JCO March 7, 2011 JCO.2010.30.1366

10. Comparing Capecitabine Plus Oxaliplatin with 5FU and Folinic Acid As Adjuvant Therapy for Stage III Colon Cancer (Mar.9/11)

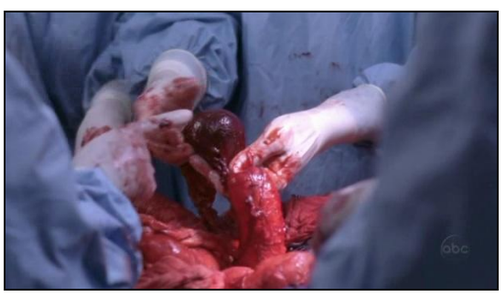
This multicenter, randomized trial compared capecitabine plus oxaliplatin (XELOX) with bolus fluorouracil (5FU) and folinic acid (FA) as adjuvant therapy for patients with stage III colon cancer. Patients who had undergone curative resection for Stage III colon cancer were randomly assigned to XELOX or a standard bolus FU/FA adjuvant regimen (Mayo Clinic for 24 weeks or Roswell Park for 32 weeks). Researchers were measuring disease-free survival (DFS – time before disease got worse) as a primary end point. The patient population consisted of1,886 patients; 944 patients were randomly assigned to XELOX and 942 to FU/FA (Mayo Clinic, n = 664; Roswell Park, n = 278). After 57 months of follow-up for the primary analysis, 295 patients (**31.3%)** in the XELOX group had relapsed, developed a new primary colon cancer, or died compared with 353 patients (**37.5%)** in the FU/FA group. The 3-year DFS rate was **70.9%** with XELOX and **66.5%** with FU/FA. The 5-year OS for XELOX and FU/FA were **77.6% and 74.2%,** respectively. Follow-up is ongoing. Researchers concluded that the addition of oxaliplatin to capecitabine improves DFS in patients with stage III colon cancer and that XELOX is an additional adjuvant treatment option for these patients.

Maroun, Jean, et al., Capecitabine plus oxaliplatin compared with fluorouracil and folinic acid as adjuvant therapy for stage iii colon cancer. J of Clin Oncol. Published online before print March 7, 2011, doi: 10.1200/JCO.2010.33.6297 JCO

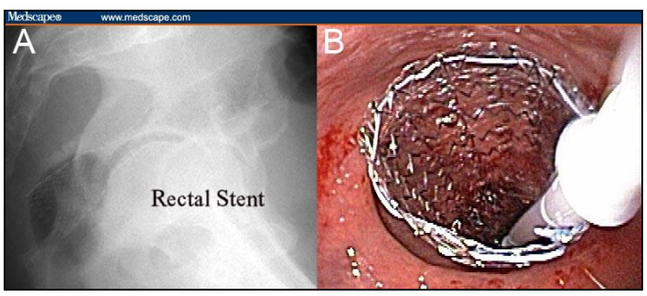
SURGICAL THERAPIES

11. Colonic Stenting vs. Emergency Surgery for a Colon Obstruction (Mar.14/11)

According to the results of this study, colonic stenting does not offer a decisive advantage over emergency surgery in patients with acute obstructive left-sided colorectal cancer, and may pose safety concerns. Researchers investigated whether colonic stenting has better health outcomes than emergency surgery in 98 patients with acute obstructive left-sided colorectal cancer. Between 2007 and 2009, 47 patients were randomly assigned to receive colonic stenting as a bridge prior to elective surgery and 51 were assigned to emergency surgery. The investigators found <u>increased 30-day morbidity</u> in the **<u>colonic stenting group</u>**. The study was suspended Sept. 18, 2009, following advice of the data safety monitoring committee. At the final follow-up there was no difference in overall mortality, 30-day mortality, morbidity, and stoma rates between the two treatment groups. The most common serious adverse events were perforations (six in stent group versus none in emergency surgery group), abscess (three versus none), anastomotic leakage (five versus one), pneumonia (three versus one), and wound infection (one versus three). Researchers concluded that colonic stenting has no decisive clinical advantages to emergency surgery. It could be used as an alternative treatment in as yet undefined subsets of patients, although with caution because of concerns about tumor spread caused by perforations.



<u>Figure 8:</u> Showing surgical removal of colonic obstruction



<u>Figure 9</u>: Insertion of colonic stent to manage colonic obstruction

Van Hooft, Jeanin, et al., Colonic stenting versus emergency surgery for acute left-sided malignant colonic obstruction: a multicentre randomized trial. The Lancet Oncology. Early online publication, 12 March 2011. Doi: 10.1016/S1470-2045(11)70035-3

RADIATION / INTERVENTIONAL RADIOLOGY

12. The Role of PET/CT in Abdominal Wall Mets (Feb.20/11)

Metastasis (spread) to the abdominal wall including port sites after laparoscopic surgery for colorectal cancer is rare. Resection of metastatic lesions may lead to greater survival benefit if the abdominal wall

metastasis is the only manifestation of recurrent disease. This study reports that a 57-year-old man, who underwent laparoscopic surgery for advanced colon cancer of the cecum 6 years prior, developed a nodule in the surgical wound at the lower right abdomen. Although tumor markers (such as CEA) were within normal limits, the metastasis to the abdominal wall and abdominal cavity from the previous cecal cancer was suspected. An abdominal computed tomography (CT) scan did not provide evidence of metastasis. 18F-fluorodeoxyglucose positron emission/computed tomography (18F-FDG PET/CT) was therefore performed, which demonstrated increased 18F-fluorodeoxyglucose uptake (maximum standardized uptake value: 3.1) in the small abdominal wall nodule alone. Examination of the resected nodule from a pathologist confirmed the diagnosis of metastatic colon cancer. Researchers concluded that this case suggests an important role of 18F-FDG PET/CT in early diagnosis and decision-making regarding therapy for recurrent disease in cases where a firm diagnosis of recurrent colorectal cancer is difficult to make.

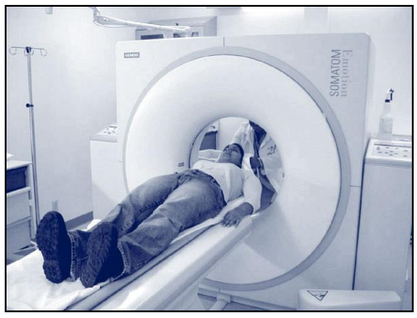


Figure 10: Patient undergoing CT scan.

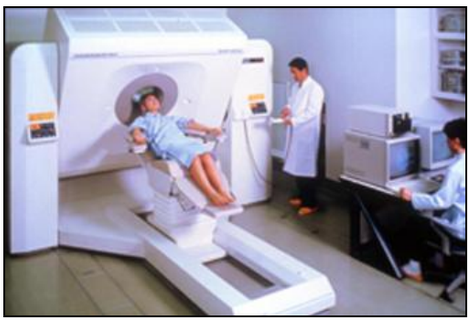


Figure 11: Patient undergoing PET scan.

The positron emission tomography (PET) scanner is a nuclear medicine imaging technology that allows detailed diagnostic measurement of physiological and biochemical bodily processes. This technology can be used to detect and evaluate different types of cancer; or to examine brain function, blood flow or heart disease. During a computerized tomography (CT) scan, a thin x-ray beam rotates around an area of the body, generating a 3-D image of the internal structural differences.

Funahashi, Kimihiko, et al., A role of 18F-fluorodeoxyglucose positron emission/computed tomography in a strategy for abdominal wall metastasis of colorectal mucinous adenocarcinoma developed after laparoscopic surgery. World J of Surg Oncology. 2011, 9:28

13. Using Stereotactic Body Radiation Therapy for Spinal Mets (Feb.20/11)

According to the results of this study, stereotactic body radiotherapy for previously irradiated, progressive spinal metastases may be a viable option in selected patients.

***Stereotactic body radiation therapy (SBRT**), is a type of radiation therapy that uses a very high dose of radiation delivered to a precise area. The procedure uses special positioning and radiology techniques to spare normal tissue, so that a higher dose of radiation can be used. It is also used for a shorter period of time than traditional radiation therapy.*

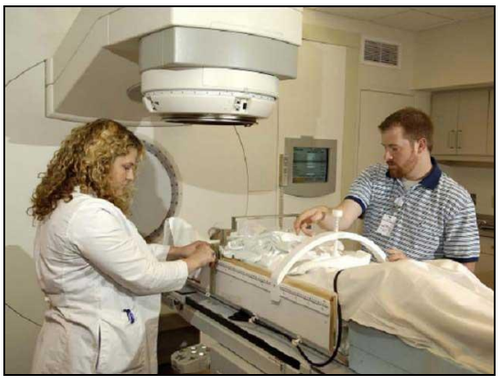


Figure 12: Photo illustrating SBRT.

A total of 59 patients with 63 tumors of the spine were re-irradiated with stereotactic body radiotherapy between 2003 and 2009. Spinal magnetic resonance imaging (MRI) was performed both before treatment initiation and at regular follow-up intervals. The average follow-up was 17.6 months. 1-year radiographic local control and overall survival for all patients were both 76%. Of the tumors that progressed after stereotactic body radiotherapy, 13 (81%) of 16 patients had tumors that were within 5 mm of the spinal cord, and 6 of them eventually developed spinal cord compression. Toxicity was most commonly grade 1 or 2 fatigue. Two patients experienced mild to moderate radiation injury (lumbar plexopathy) while still able to perform their daily activities and pain free. The researchers concluded that re-irradiation for progressive spinal metastases with stereotactic body radiotherapy results in good local control and limited toxicity. Initial surgery should be considered for tumors within 5 mm of the spinal cord.

Shiu, AS, et al., Prospective Evaluation of spinal reirradiation by using stereotactic body radiation therapy. Cancer. 2011, Feb. Epub ahead of print.

14. Improved Access to Colorectal Cancer Screening & Treatment in the Waterloo Region
(Feb. 21/11)

Asa Leobel is among over a thousand area patients who have already benefited from a regional approach to detect and treat colorectal cancer faster. The Waterloo Wellington Regional Cancer Program and area hospitals have sped up access to treatment after a positive screening test result is returned. After a year in operation, the regional colonoscopy network has screened over 1,100 patients and detected 21 patients with cancer much earlier than before. The RCN offers faster colorectal cancer screening through a coordinated booking service across Waterloo and Wellington for those with a positive fecal occult blood test or a family history of colorectal cancer. The average RCN wait time is three to four weeks, compared to three to 12 months through traditional referral methods. Early detection of colorectal cancer has an estimated 90 per cent cure rate. Mr. Leobel, a 63 year old resident of Guelph took an at-home FOBT last year, with the result coming back positive. A follow-up colonoscopy through the RCN revealed colon cancer. A specially-trained nurse navigator walked him through the next steps of his diagnosis. Mr. Leobel had surgery in December and has been told his prospects are very good. "My family doctor urged me to do an FOBT. I didn't think it was important because I didn't have any symptoms, but thankfully, at the end of the day I am glad I did it. I am blessed not only that my cancer was discovered, but that it was discovered in the early stages when it's most treatable," said Mr. Leobel. GRH's Grand River Regional Cancer Centre coordinates the RCN. Through the centralized referral office located at GRRCC, patients throughout the region are screened and prepared for a colonoscopy via a telephone consultation. In partnership with surrounding regional hospitals including St. Mary's, Cambridge Memorial, Guelph General and Louise Marshall in Mount Forest, patients are booked into the next available appointment closer to home. "If we detect colon cancer early, we can effectively treat it with minimal complications. Catching it later means poorer outcomes, and a much worse quality of life due to a range of complications," said Dr. Craig McFadyen, the regional vice president for Cancer Care Ontario and a cancer surgeon at Kitchener's Grand River Hospital. For patients with cancer, the program offers the help of a gastrointestinal nurse navigator. The nurse navigator provides support and guidance to newly-diagnosed colorectal cancer patients and helps to speed up required testing needed to proceed with treatment. "I had tremendous relief when the nurse navigator contacted me and provided an explanation around my diagnosis and treatment. She made a big impact under the level of stress I was experiencing after finding out I had cancer," said Mr. Leobel.

http://www.abbanetwork.com/health/over-a-thousand-area-patients-benefit-from-improved-access-to-colorectal/

15. Adenomas Associated with Increased Risk for Colorectal Cancer (Feb. 21/11)

According to this study, there has been increased attention paid toward quality measures for colonoscopy, particularly adenoma detection rates, which can serve as predictors for interval colorectal cancer.

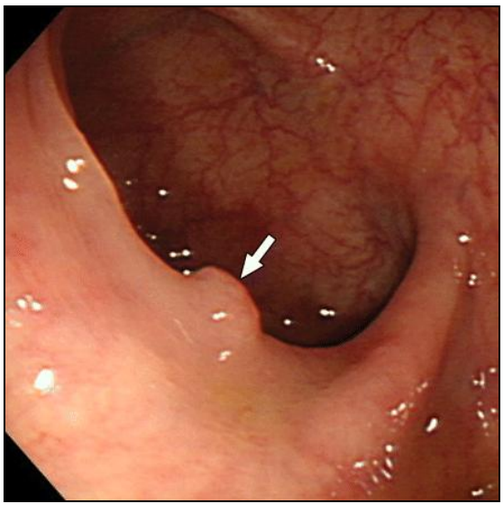


Figure 13: Colonic adenoma.

In the study, researchers studied more than 45,000 patients. During a follow-up, 32 endoscopists detected 42 interval colorectal cancer cases. The median adenoma detection rate was 12.2%. After analyzing the results, researchers suggest the patient's age and endoscopist's adenoma detection rates serve as independent predictors of interval colorectal cancer. This study highlights the need for additional studies to determine what adenoma detection rate is appropriate as benchmark for quality colonoscopy outcomes.

Kaminski, MF, et al., Association of adenoma detection rate with the risk of interval colorectal cancer. Gastro. Vol. 140, Issue 2: pp. 724-726

16. Screening Test that Might Replace Colonoscopy (Feb. 22/11)

This study speaks to the potential of using genetic biomarkers to predict colon cancer caused by inflammation. Researchers found biomarkers in mouse feces that predicted inflammation-associated colon cancer. This is the same type of cancer associated with some common inflammatory bowel diseases such as ulcerative colitis and Crohn's Disease. The team found that the bacterium that leads to inflammation-associated colon cancer in mice first results in inflammation that can be detected by screening feces for genetic material called messenger RNA. The lead investigator believes this discovery could lead to tests for similar genes that are present in humans with early inflammation-associated colon cancer. The assumption was that the gene expression couldn't be detected in fecal matter because RNA breaks down very rapidly. Historically, this was something that a lot of scientists hadn't considered. But technology has evolved, and scientists now have the means of preserving RNA much better than they did 15 years ago. Many people put off colonoscopies longer than they should because of the invasiveness and unpleasant nature of the exam. For this study, the team also used a high-powered MRI machine. While effective, this technique was not as sensitive as the fecal biomarkers in predicting cancer, and it requires extensive expertise and very expensive equipment.

http://www.medicalnewstoday.com/articles/216781.php

17. DNA Test May Detect Early Colorectal Cancer (Mar.3/11)

Scientists have discovered for the first time that DNA methylation patterns - a key process in cell development - could accurately detect early colorectal cancer. Researchers from Cancer Research UK's Cambridge Research Institute analyzed 261 tumour samples taken from patients who had either benign bowel polyps or had developed bowel cancer. They revealed that the **DNA methylation** patterns of two genes called SFRP2 and IGF2 identified and distinguished between tumours and benign polyps - with an accuracy of more than 90%. DNA methylation is essential for life. In healthy cells a compound called a **methyl group** is tagged to DNA where it acts as a 'red light', preventing certain genes from producing proteins. But this process can go wrong in cancer cells. DNA methylation can also contribute to the cause and development of cancer by blocking important 'protective genes'. Lead author maintains that the molecular signals, which tell genes whether to make proteins or not, can become jumbled in cancer cells. They have identified several places where this signal becomes damaged and shown this is linked to colon cancer development. The majority of colon cancers develop from benign polyps that turn cancerous - and this crucial research deepens the understanding of the molecular changes behind this development. This first step in detecting molecular 'flags' for colon cancer, could, one day, lead to a simple test to search DNA for the early signs of the disease. The scientists also measured levels of an enzyme called DNMT3B, which helps add methyl groups to DNA. They found levels of the enzyme in tumour samples increased from lower amounts present at the polyp stage to higher levels in colon cancer. The increase in enzyme levels corresponded with the increased amount of DNA methylation - and provided an explanation for these changes. This important research opens the way to improve detection of colon cancer as early as possible when it is easier to treat successfully.

Ibrahim, Ashraf, et al., Sequential DNA methylation changes are associated with DNMT3B overexpression in colorectal neoplastic progression. Gut. doi:10.1136/gut.2010.223602

PSYCHOSOCIAL

18. Cancer Patients' Partners Become Ill As Well (Mar.3/11)

According to the results of this study, people who are married to or cohabitating with a cancer patient suffer more illness in the year following their spouse or partner's cancer diagnosis, according to a recent study. The finding comes from a new thesis by cancer nurse Katarina Sjövall from Lund University, Sweden. Katarina Sjövall has studied partners of individuals with colorectal cancer, lung cancer, breast cancer or prostate cancer. The study shows that the number of diagnosed diseases among partners increased by 25% after the cancer diagnosis. Having a close relative with cancer entails worry and anxiety and an increased workload that places a strain on one's health. The most significant increase was in diagnoses of mental illnesses such as depression. However, there was also a significant increase in cardiovascular disease, musculoskeletal diseases and abdominal diseases. The highest increase was in cardiovascular disease among spouses and partners of those with lung cancer, which increased by almost 50%. The increase in diagnosed diseases led to increased use of health services, primarily in-patient care. Among the partners who worked, the number of days of sick leave also increased. The worst affected were spouses and partners of lung cancer patients, who had over 70% more days off sick than the general population in the year following their partner's diagnosis. While women in general are responsible for a larger proportion of healthcare costs than men in Sweden, the reverse was true in this case. Healthcare costs increased most for men under 64 who had a partner with cancer. One possible explanation could be that the men feel less comfortable taking on a caring role as the partner of a cancer patient and that they therefore suffer more stress cites the lead investigator. In one of her studies, Ms Sjövall interviewed patients with colorectal cancer and their partners. The patients sometimes spoke of feeling that their physical and psychological experiences were not acknowledged by the health service. Neither did their partners always feel as involved as they would like to be. The interviews showed that the cancer patients sometimes chose not to tell those closest to them what they were going through out of consideration for them. However, this considerate attitude could have the opposite effect, according to Sjövall. When it comes to the health service, Ms Sjövall finds that care at the end of life is good at also

helping the relatives and making them feel involved in what is happening. At earlier stages, however, there may be wide variations in approach and opportunities to offer support to relatives. Another part of the study looks at the cancer patients' sick leave in the year prior to the cancer diagnosis. Individuals with colon cancer and lung cancer had twice as many days off sick as the control group even in the year before their diagnosis. One reason could be that both forms of cancer have a lot to do with lifestyle. Therefore, individuals with colon cancer often also have diabetes, and individuals with lung cancer often have cardiovascular disease. The sick leave may have been due to these other diseases -- but it could also have been due to early symptoms of the cancer. This makes one wish there were better ways to make a diagnosis based on very early cancer symptoms. The title of the thesis is *Living with cancer. Impact on cancer patient and partner* and will be defended on 4 March.

Lund University. "Cancer patients' partners become ill themselves, Swedish study shows." Science Daily 3 March 2011. 16 March 2011 <http://www.sciencedaily.com /releases/2011/03/110303072845.htm>.

OTHER

19. Celiac Disease Not a Risk Factor for Colorectal Cancer (Feb.28/11)

Celiac disease has long been linked to an increased risk of gastrointestinal problems including lymphoma and small bowel malignancy. Despite the connections to other GI problems, there has not been a conclusive link between celiac disease and colorectal cancer, the most common form of GI cancer in the world today. In this study, a team of doctors investigated the connection. The aim of their study was to compare the prevalence of colorectal adenomas in patients with celiac disease against those without celiac disease or gluten tolerance problems. In order to monitor participants over a 44 month period, the research team analyzed colonoscopy results from a total of 180 patients from both groups of participants. In their research, adenomas were present in 13% of celiac disease patients and 17% of the general participants without celiac conditions. Once compared to the number of participants and factoring in age, gender and endoscopist, the team was able to reach a conclusion in their study. Their conclusion was that there was no evidence to support a connection between an increased risk for colorectal cancer on the part of celiac disease.

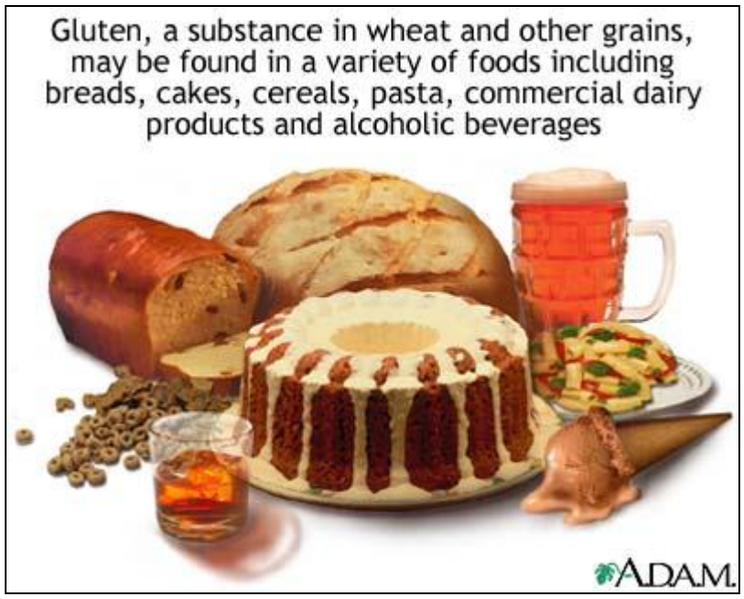


Figure 14: Celiac Disease is a disease of the immune system and in this disease the body rejects certain kinds of foods or is allergic to certain foods. This disease is also known as Gluten-sensitive enteropathy and for a person who has this disease, any food which contains gluten will spark a reaction damaging the intestines. This disease is also known as celiac sprue and Nontropical sprue. Gluten is abundant in medications, food containing high quantity of vitamins and the gum present in postal stamps. Close contact with any of these could give impetus to the disease. The symptoms may differ from person to person; however, the usual ones are diarrhea, depression and pain in the abdomen.

Lebwohl, B, et al., Risk of colorectal adenomas in patients with celiac disease. Alimentary Pharmacology & Therapeutics. Vol. 32, Issue 8: pp. 1037-1043

20. Tumor Burden Can Predict Colorectal Cancer Outcomes (Mar.3/11)

In patients with node-negative colorectal cancer (stage II), the occult (hidden) molecular tumor burden in the lymph nodes is an independent predictor of the time to recurrence and disease-free survival, according to the results of this study. Researchers investigated the link between occult nodal metastases, measured via the molecular tumor marker **guanylyl cyclase C (GUCY2C**), and prognosis in node-negative colorectal cancer patients. Lymph nodes of 291 node-negative patients were examined by histopathology, and occult tumor burden was measured by quantifying GUCY2C. Patients were followed for a median time period of 24 months, with time to recurrence as the primary end point and disease-free survival as the secondary end point. The researchers found that the occult tumor burden independently predicted prognosis. With increasing molecular tumor burden, the time to recurrence and disease-free

survival decreased. Of the 176 patients with a low tumor burden, all but four remained disease-free. Of the 90 patients with an intermediate tumor burden, 30 had recurrent cancer; whereas, among the 25 patients with a high tumor burden, 17 developed recurrent cancer. Researchers demonstrate for the first time that occult tumor burden assessed across the regional lymph node network is a powerful independent prognostic marker of time to recurrence and disease-free survival in node-negative colorectal cancer patients. This approach can improve prognostic risk stratification and chemotherapeutic allocation in these patients.

Hyslop, Terry, et al., Occult tumor burden predicts disease recurrence in lymph node-negative colorectal cancer. Clin Can Research. Published OnlineFirst February 9, 2011; doi: 10.1158/1078-0432.CCR-10-3113

21. Hepatitis B Infection May Lower Liver Metastasis in Colorectal Cancer (Mar.9/11)

A research team from China evaluated the effect of hepatitis B virus (HBV) infection on liver metastasis of colorectal cancer. The study showed that HBV infection decreases the risk of liver metastasis in patients with colorectal cancer and elevates the surgical resection rate of liver metastatic lesions**.** Metastatic liver disease more frequently develops metachronous (after initial diagnosis of primary tumor) metastasis following treatment of CRC. It was reported that hepatitis B virus (HBV) infection finally reduces the risk of intrahepatic metastasis in hepatocellular carcinoma (HCC – primary liver cancer) patients with a higher survival rate and therefore can be considered an important prognostic factor for HCC patients. Rare reports are available on the relation between HBV infection and hepatic metastasis of colorectal cancer which is why this study addresses this question. The authors designed a study to observe the relation between HBV infection and liver metastasis of colorectal cancer. The results showed a decrease in the percentage of metastases in the Hepatitis B virus infected group (**14.2%)** with respect to the control group (**28.2%).** In contrast, the number of patients that developed extrahepatic metastases (metastases outside the liver) was significantly higher than the control group, without any significant difference in the overall survival rate. Finally, the authors suggested that HBV infection in colorectal cancer patients could be used as a prognostic factor in terms of hepatic metastasis formation.

Qiu HB, Zhang et al., HBV infection decreases risk of liver metastasis in patients with colorectal cancer: A cohort study. World J Gastroenterol 2011; 17(6): 804-808

NUTRITION & HEALTHY LIFESTYLE

22. Raspberries & Purple Fruits Can Ward Off Cancer (Feb. 19/11)

Researchers continue to uncover the critical link between a diet packed with natural plant based phytonutrients and cancer prevention. Research conducted at the University of Illinois show that a diet supplemented with **black raspberries** lowered the incidence of colorectal cancer by **45%**. The study authors conclude that the high polyphenol content of the raspberries are likely to influence digestive gene targets and may be of benefit to other digestive cancer lines as well. A second study demonstrated that there are over 2000 genes that are responsible for regulating digestive health. These genetic targets are down regulated with a diet of processed foods, hydrogenated fats and sugar to favor the initiation and development of cancer. Supplementing with a concentration of freeze-dried black raspberries was shown to return 462 of those genes to a normal state. The study author concluded, *"We have clearly shown that berries, which contain a variety of anticancer compounds, have a genome-wide effect on the expression of genes involved in cancer development"*. Researchers have shown that the active compound found in black raspberries inhibits tumor development by suppressing the activity of a protein needed for the disease to progress. Further, black raspberries reduce levels of dangerous systemic inflammation that lower tumor formation by 50%.

http://technorati.com/lifestyle/article/choose-raspberries-and-purple-fruits-to/

23. Vitamin D Can Help Prevent Colorectal Cancer Deaths (Feb. 28/11)

According to the results of this study, Vitamin D appears to have potentially significant cancer prevention effects. An innovative prospective clinical research study is now reporting its results, which appear to link Vitamin D deficiency to colorectal cancer death rates. As with previous research studies, the findings of this study strongly suggest that Vitamin D deficiency may be linked with a higher risk of death due to colorectal cancer. An interesting and unique aspect of this particular clinical research study was its evaluation of the potential impact of Vitamin D deficiency on the well-known increased risk of death due to colorectal cancer that has been observed in African-Americans when compared to Caucasian patients. As our bodies create active Vitamin D from exposure of our skin to sunlight, and as people with darkly pigmented skin are more prone to developing Vitamin D deficiency, when compared to lightly-pigmented people, the authors of this study sought to assess the potential colorectal cancer risk impact of Vitamin D deficiency on patient volunteers with darkly pigmented skin. In this large public health study, which was conducted between 1988 and 1994, blood levels of Vitamin D were measured in study volunteers. Patients with a Vitamin D level of less than 20 ng/dL were considered to be deficient in Vitamin D. As previous public health studies have also shown, the results of this study indicated that African-Americans are twice as likely to die of colorectal cancer when compared to Caucasians. When blood levels of Vitamin D were considered, specifically, the *increased risk of dying from colorectal cancer* observed in African-American patients, *decreased by 40%* among those African-Americans who had normal levels of Vitamin D in their blood. (These results, therefore, suggest that at least 40 percent of the increased risk of dying from colorectal cancer in African-American persons is likely to be caused by Vitamin D deficiency.)

When patients of all races were considered in terms of Vitamin D deficiency as a risk factor for death due to colorectal cancer, *patient volunteers with a blood level of Vitamin D less than 20 ng/dL were more than twice as likely (i.e., a 211% increase in risk) to die of colorectal cancer* during the course of this prospective research study, when compared with patients who had normal Vitamin D levels. In summary, this large prospectively conducted public health study found, as have previous studies, a significant association between Vitamin D deficiency and the risk of dying from colorectal cancer. (Previous Vitamin D studies have also identified a 25 to 40% reduction in the incidence of colorectal cancer, and death due to colorectal cancer, in study volunteers with blood Vitamin D levels in the 30 to 40 ng/dL range.) While not all clinical research studies have shown this level of colorectal cancer risk reduction associated with normal blood levels of Vitamin D, this particular study joins a growing list of clinical studies that appear to show a significant reduction in colorectal cancer risk associated with adequate levels of Vitamin D in the blood.

http://ezinearticles.com/?Vitamin-D-and-Death-Due-to-Colorectal-Cancer&id=6009869

24. More Vitamin D Needed to Reduce Colorectal Cancer Risk (Feb. 23/11)

Researchers have reported that markedly higher intake of vitamin D is needed to reach blood levels that can prevent or markedly cut the incidence of breast cancer, colorectal cancer and several other major diseases than had been originally thought. They found that daily intakes of vitamin D by adults in the range of 4000-8000 IU are needed to maintain blood levels of vitamin D metabolites in the range needed to reduce by about half the risk of several diseases -- including colon cancer. They were surprised to find that the intakes required to maintain vitamin D status for disease prevention were so high -- much higher than the minimal intake of vitamin D of 400 IU/day that was needed to defeat rickets in the 20th century. The study reports on a survey of several thousand volunteers who were taking vitamin D supplements in the dosage range from 1000 to 10,000 IU/day. Blood studies were conducted to determine the level of 25-vitamin D -- the form in which almost all vitamin D circulates in the blood. Most scientists who are actively working with vitamin D now believe that 40 to 60 ng/ml is the appropriate target concentration of 25-vitamin D in the blood for preventing the major vitamin D-deficiency related diseases. Researchers maintain that now that the results of this study are in, it will become common for almost every adult to take 4000 IU/day.

Heaney, Robert, et al., Vitamin D Supplement Doses and Serum 25-hydroxyvitamin D in the range associated with cancer prevention. Anticancer Research. Vol. 31, No. 2 (2011)

25. Turmeric Can Fight Colon Cancer and Inflammation (Mar.4/11)

Turmeric, a bright yellow spice from south Asia belonging to the ginger family, is the main ingredient in curries - and ancient wisdom has suggested that it may be very good for one's health. Taking this wisdom to the laboratory, Tel Aviv University researchers have discovered that turmeric's active ingredient called curcumin amplifies the therapeutic activity of highly toxic anti-inflammatory drugs used to fight colon cancer when used at high doses. The researchers have found that curcumin can fight cancer when used in combination with a popular anti-inflammatory drug, alleviating the inflammatory response caused when cancer takes root in the body. A treatment based on this finding has already had promising results in human clinical trials. Although more testing will be needed before a possible new drug treatment is developed, one could combine curcumin with a lower dose of a cancer anti-inflammatory drug, to better fight colon cancer. Research in the last few decades has shown that cancer is linked to inflammation. Several lines of evidence demonstrate that chronic inflammation in the stomach can cause gastric cancer and that inflammation in the liver from hepatitis can lead to liver cancer. Researchers found that Celecoxib, a popular anti-inflammatory drug commonly used to treat arthritis, also inhibits proliferation of colon cancer in laboratory settings. Curcumin increases the anti-cancer and anti-inflammatory effects of Celecoxib while reducing its dose, thus reducing its toxic side-effects. Researchers maintain that curcumin has the promise of being an important life-extending therapy, particularly for non-curable pancreatic cancer, suggested by the very promising results the researchers achieved for 20 pancreatic cancer patients. Previous experiments conducted by the research team show that curcumin inhibits an enzyme known as **COX-2** (cyclooxygenase-2), believed to cause inflammation. The team's research demonstrates that curcumin neutralizes oxygen free radicals, which are believed to play an important role in carcinogenesis (the development of cancer). These effects may be the basis for drug treatment of both inflammation and cancer through the combination of curcumin and Celecoxib. And it may also help return previously shelved potent anticancer drugs - taken out of use due to high toxicity - back to the market under lower dosage indications.

http://tag.sagepub.com/

26. Good Cholesterol May Help Prevent Colon Cancer (Mar. 8/11)

According to the results of this study, high levels of "good" cholesterol (high density lipoprotein – HDL) may reduce the risk of colon cancer.. If other studies confirm this finding, people with low levels of high-density lipoprotein (HDL) cholesterol may "be advised to change their lifestyle to reduce their risk of colon cancer. Cutting "bad" (LDL) cholesterol and increasing "good" (HDL) cholesterol already are known to reduce the risk for heart disease, and this new study provides another reason to pay attention to blood cholesterol numbers. For the study, the researchers compared 1,238 people with colorectal and cancer to 1,238 healthy people. Of those with cancer, 779 had colon cancer and 459 had rectal cancer. The researchers reviewed the results of blood samples and dietary-lifestyle questionnaires provided by

participants enrolled in the study, a long-term look at the effect of diet on cancer in 10 countries. The investigators found that those with the highest levels of HDL cholesterol and another blood fat called apolipoprotein A (apoA) had the **least** chance of developing colon cancer, but no impact was seen on rectal cancer. This association is independent of some other markers in the blood that are related to the development of cancer. Those markers include inflammation, insulin resistance and oxygen free radicals. For each 16.6 milligrams per deciliter (mg/dL) increase in HDL and 32 mg/dL increase in apoA, the risk of colon cancer was cut by **22% and 18%,** respectively. But for a subset of patients followed for more than two years, only high HDL levels were linked with a lower risk of colon cancer. The researchers speculate that HDL's anti-inflammatory properties may explain the finding, but say further research is needed to tease out the specific cause. They also acknowledged that the short follow-up period -- just 3.8 years -- is a limitation to their study. Depending on the results of such investigations, HDL levels may someday be a useful tool in moderating a patient's colon cancer risk, the authors stated. Currently, the best recommendation to reduce one's risk [of colon cancer] is to stop smoking, increase physical activity, reduce obesity and abdominal fatness and limit intakes of alcohol and red and processed meats.

http://www.nlm.nih.gov/medlineplus/news/fullstory_109599.html

27. More on Vitamin D Fighting Colorectal Cancer (Mar.11/11)

A new meta-analysis (a compilation of studies) suggests that taking vitamin D supplements can cut risk of colorectal cancer. The researchers searched studies on vitamin D and colorectal cancer published prior to 2010 in the medical database Pubmed. Only original, peer-reviewed studies were included in the analysis. Ten studies showed that each additional 100 IU of dietary vitamin D per day within the range of 39 to 719 IU per day was associated with a 5% reduction in the risk of colorectal cancer. Six studies showed each additional 100 IU of serum vitamin D per liter within the range of 200 to 1800 IU/L was associated with 4% reduced risk of colorectal cancer. Supplementation of vitamin D at the range of 0 to 600 IU per day, total vitamin D intake ranging 79 to 732 IU per day and 25-hydroxyvitamin D status were inversely associated with colon cancer risk. The findings suggest that vitamin D protects against colorectal cancer.

Touvier, Mathilde, et al., Meta analyses of vitamin D intake, 25-hydroxyvitamin D status, vitamin D receptor polymorphisms and colorectal cancer risk. Cancer Epidemiology, Biomarkers & Prevention. Published online first March 4, 2011; doi: 10.1158/1055-9965.EPI-1041

28. High Protein Diets and The Colon (Mar. 1711)

The high-protein, low-carbohydrate diets many people turn to for weight loss might have potentially harmful long-term effects on the colon, according to the results of a small study. In a study of 17 obese men, UK researchers found that a protein-heavy, low-carb diet created certain changes in the colon that could, over time, contribute to colon cancer risk. The study looked only at short-term shifts in certain compounds that are byproducts of metabolism, and not actual disease risk. So it does not show whether high-protein diets really raise the risk of any colon diseases. But the findings raise that possibility according to researchers. The concern raised by the study is that the risk of colorectal cancer might be raised by long-term adherence to diets that are high in protein and low in carbohydrate, especially fiber. Diets relatively high in protein and lower in carbs have been shown to help heavy people shed pounds. And, researchers point out, obesity is thought to be a risk factor for a number of diseases, including colon cancer. People should not be discouraged from losing weight, as this offers important health benefits, researchers maintain. However, they added, they should make sure that any weight loss plan they follow includes adequate amounts of fiber. People should also be aware that a high protein intake over months to years might have ill effects in the colon. The findings are based on 17 obese men who each followed three short-term diets: a one-week menu plan designed to maintain their weight; a four-week high-protein diet with moderate amounts of carbohydrates; and a four-week high-protein diet low in carbs.

- The first diet, which allowed about 360 grams of carbs per day, typically offered cereal, eggs and toast for breakfast; a sandwich and salad for lunch; and chicken, fish or soy, along with pasta, for dinner.
- The low-carb diet -- which allowed just 22 grams of carbs each day -- generally consisted of eggs-and-bacon breakfasts, and lunches and dinners heavy in meat, poultry and fish, along with some vegetables and cheese.
- The moderate-carbohydrate diet allowed 181 grams of carbs each day. Both high-protein diets contained just less than 140 grams of protein per day.

At the end of each diet period, the research team analyzed fecal samples from the men to look at levels of certain metabolic byproducts. On average, the study found, when the men were on the high-protein diets, they had higher levels of substances known as N-nitroso compounds, and certain other metabolites that have been linked to cancer. And when they were on the high-protein, low-carb diet, they had lowered concentrations of fiber-derived compounds thought to be protective against cancer. Exactly what those changes might mean for a person's long-term health is not clear. But researchers maintain that the findings suggest that people should be cautious about consuming too much protein and too little fiber over a prolonged period. People seeking to lose weigh should be sure to get enough fiber in their diets. In general, experts recommend that adults get about 28 grams of fiber per day -- though it's not known whether that's enough for someone on a high-protein weight-loss diet.