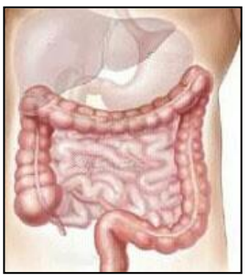
COLORECTAL CANCER RESEARCH UPDATES

Month Ending August 17th, 2012



The following colorectal cancer research update extends from June 23rd, 2012 – August 17th, 2012 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Early Detection of Resistance to Colorectal Cancer Drugs Helpful (Jun.22/12)

Mutations in a gene called KRAS are causally associated with acquired resistance to targeted therapies for colorectal cancers (CRC), according to new findings from EU-funded researchers from Italy and their research colleagues in the United States. The team explains that patients often develop resistance to colorectal cancer drugs that target epidermal growth factor receptors (EGFRs), such as Erbitux and Vectibix. The team shows in cell-line models that KRAS mutations can cause resistance to an anti-EGFR therapy called cetuximab (Erbitux). These mutations can either be acquired during treatment or may have pre-existed in a small fraction of tumour cells before treatment. Emergence of secondary resistance to anti EGFR therapies (disease progression) in colorectal cancers is presently established by radiological evaluation. In the paper the team describes for the first time that KRAS gene alterations are a mechanism of acquired resistance to anti EGFR therapies in CRCs and occur in approximately 50% of patients. The findings in this latest study come at the same time as a second team of researchers publish results demonstrating that resistance mutations in KRAS and other genes are highly likely to be present in a subpopulation of tumour cells before treatment. In this complementary study researchers from Austria, China and the United States show that these mutations can be detected months before there is clinical evidence of treatment failure, which could provide a signal to start alternative treatments. Both studies show that DNA from these mutations can be detected in liquid biopsies several months before radiographic evidence of disease progression is observable. The hope now is that scientists will be able to build on these results by using combination therapy to anticipate and counter resistance before patients relapse. Both study groups demonstrate that these mutations can be detected in plasma using an approach called 'liquid biopsy'. This means that it is now possible to monitor the evolution of the tumour in response to therapy using a blood draw to detect early mutations that drive acquired resistance. The concept of liquid biopsy is an important step forward in the field. It was already known that the measurement of circulating tumour free DNA in the blood of patients could be used to monitor tumour burden. Their work shows that molecular determinants of acquired resistance can be detected several months before the clinical manifestation of relapse. What they have discovered is 'not a novel way to detect colon cancer' rather they have found a strategy to non-invasively detect early relapse from therapy in colorectal cancer patients.

Misale, S., et al. Nature, 2012. doi:10.1038/nature11156

Diaz, L.A., et al. Nature, 2012. doi:10.1038/nature11219

2. Depression Drug May Help Oxaliplatin-Induced Neuropathy (Jun. 27/12)

The antidepressant drug Duloxetine (Cymbalta®) was shown in a recent study to provide pain relief to people suffering from peripheral neuropathy caused by chemotherapy. Chemotherapy drugs such as oxaliplatin (Eloxatin®, used in the FOLFOX regimen for colorectal cancer) can damage “peripheral” nerve cells (those beyond the brain and spinal cord), causing pain, tingling, and numbness especially in feet and/or hands. This side effect, called chemotherapy-induced peripheral neuropathy (CIPN), can worsen over time and last long after the chemotherapy has stopped. Duloxetine (Cymbalta®) is an antidepressant medication also FDA-approved to ease pain caused by diabetic neuropathy, perhaps because it raises brain levels of the neurotransmitters serotonin and norepinephrine that help keep pain sensations from reaching the brain. Researchers wanted to test whether duloxetine could similarly ease neuropathy pain caused by chemotherapy. In results presented at this year’s ASCO annual conference in a symposium called “*Cancer: Getting on Your Nerves*,” lead researcher Ellen Lavoie Smith, PhD, APRN, of the University of Michigan, noted that the phase III trial was “…the first placebo-controlled randomized trial to show that any drug is effective in minimizing CIPN.” The trial enrolled 231 patients with significant neuropathy pain who had received chemotherapy. (About 60% had received oxaliplatin). Results showed the following:

- 59% reported less pain while taking duloxetine, (vs. 38% taking a placebo).
- 30% of those taking duloxetine reported no change in pain. (vs. 34% of those taking the placebo).
- 11% of patients reported increased pain while taking duloxetine (vs. 28% while taking the placebo).
- The most common drug side effect was fatigue.

During the ASCO seminar discussing this study, other experts mentioned that another neurotransmitter-enhancing drug (venlafaxine, or Effexor®), showed similar results in a less rigorous trial. Early trials are showing some promise using a topical gel (baclofen/amitriptyline/ketamine), and an electrostimulation device on the skin.

J Clin Oncol 30, 2012 (suppl; abstr CRA9013)

http://fightcolorectalcancer.org/research_news/2012/06/depression_drug_may_ease_peripheral_neuropathy_pain

3. Treating Liver Metastases with Irinotecan + Oxaliplatin + 5FU (Jun.20/12)

Hard-hitting new treatment for colorectal cancer tumors that have turned up in the liver has shown good results according to this study. Doctors designing the study tested several concepts at once, adding more drugs to current treatment, focused on aggressive use of surgery when possible, and injected the chemotherapy directly into the liver for maximum delivery. In their presentation, at the American Society of Clinical Oncology, a research team based in France concluded that the triple therapy of Camptosar (irinotecan), Adrucil (5-fluorouracil) and Eloxatin (oxaliplatin) was a safe and effective option for patients with colorectal cancer metastasis in the liver, even in patients that had not responded to previous chemotherapy. The study showed that the combination of these three drugs shrunk the liver tumors enough to make surgical removal an option in 15 of the 48 patients. The specialized treatment combination included chemotherapy injected directly to the hepatic artery (Hepatic Arterial Infusion – HAI) to increase exposure of the liver to the drugs, and this study describes one of the few drug trials for metastasis that involves surgery as a key part of the treatment. By following a cycle of chemotherapy with surgery, which is referred to as neoadjuvant chemotherapy, the surgery is made easier since the tumors are smaller. More importantly, undetectable tiny areas of metastasis are likely to be destroyed, and it is less likely that any cancer remains afterwards. The response was fairly good considering the challenges of treating these advanced cancers. Of the 48 patients, 21 showed response to the treatment, and three patients had no detectable tumors under imaging at the end of the trial. Overall, the triple chemotherapy treatment showed an ability to reduce the size of the tumors in 41 of the 48 patients in the trial. Follow up after treatment continued for 47 months, with researchers documenting an average (the median) of 14 months until the cancer growth began anew, and the one year survival included 45 out of the 48 patients. Impressively, one patient in the trial had complete remission of her 25 different liver tumors and is no longer under treatment, and still had no signs of cancer 17 months later. Former studies using Eloxatin in colorectal cancers have shown overall longer times before tumor growth, high response rates, and few side effects. Common side effects that were documented during the trial included lowered amounts of immune cells, reversible nerve damage, fatigue, nausea, vomiting, and diarrhea which are symptoms consistent with the use of platinum-based chemotherapy drugs.

ASCO 2012 Abstract 3547, "First European phase II trial of intravenous (iv) cetuximab (Cet) and hepatic artery infusion (HAI) of irinotecan, 5-fluorouracil and oxaliplatin in patients with unresectable liver metastases from wt KRAS colorectal cancer"

NIH/National Cancer Institute, "New drug regimen shows clear benefit for treating advanced colorectal cancer"

http://www.dailyrx.com/liver-metastasis-treatment-irinotecan-5-fluorouracil-and-oxaliplatin-phase-ii-trial

4. Take Home Messages from ASCO 2012 (June 5/12)

Dr. Axel Grothey has identified the following 2012 ASCO Annual Meeting abstracts as the most important in colorectal cancer:

Abstract LBA3500
Bevacizumab (Bev) with or without erlotinib as maintenance therapy, following induction first-line chemotherapy plus Bev, in patients with metastatic colorectal cancer (mCRC): Efficacy and safety results of the international GERCOR DREAM phase III trial. Presented by Christophe Tournigand, MD.

- **Take-home message:** Results of this intergroup study showed an increase in maintenance progression-free survival with bevacizumab (Avastin) plus erlotinib over bevacizumab alone; but, with an increase in diarrhea and skin toxicity, suggesting a possible role for dual targeting of VEGF and EGFR in mCRC after all.

Abstract 3502
Phase III CORRECT trial of regorafenib in metastatic colorectal cancer (mCRC). Presented by Eric van Cutsem, MD PhD.

- **Take-home message:** Results of this study comparing the oral multikinase inhibitor regorafenib with placebo in patients with chemorefractory mCRC showed significantly increased overall survival (OS) with regorafenib, from 5.0 to 6.6 months (HR, .77; P = .0052). OS and progression-free survival (PFS) benefits were seen across all pre-specified subgroups, and KRAS status was not predictive of outcomes. Overall, toxicities with regorafenib were manageable.

Abstract CRA3503
Bevacizumab (BEV) plus chemotherapy (CT) continued beyond first progression in patients with metastatic colorectal cancer (mCRC) previously treated with BEV plus CT: Results of a randomized phase III intergroup study (TML study). Presented by Dirk Arnold, MD.

- **Take-home message:** Patients with mCRC progressing on standard first-line therapy (chemotherapy + bevacizumab) were randomized to standard second-line chemotherapy plus bevacizumab or chemotherapy alone. Median OS was significantly higher in the bevacizumab group (11.2 months vs 9.8 months). Median PFS was 5.7 months vs 4.1 months. Results confirm that bevacizumab is beneficial in this setting, providing a new second-line treatment option for patients with mCRC.

Bevacizumab therapy given beyond progression represents a new treatment approach, which is also currently being tested in other tumor types.

Abstract 3505
Effects of prior bevacizumab (B) use on outcomes from the VELOUR study: A phase III study of aflibercept (Afl) and FOLFIRI in patients (pts) with metastatic colorectal cancer (mCRC) after failure of an oxaliplatin regimen. Presented by Carmen Joseph Allegra, MD.

- **Take-home message:** In the pivotal VELOUR study, aflibercept (Zaltrap), when added to FOLFIRI, improved survival by approximately 2 months compared with FOLFIRI alone in patients with oxaliplatin-refractory mCRC. In this pre-specified subgroup analysis of VELOUR evaluating the consistency of aflibercept-associated benefit based on previous exposure to bevacizumab, no significant difference in OS or PFS was seen between patients receiving or not receiving aflibercept, regardless of whether bevacizumab was given earlier. Toxicity with aflibercept was not increased in bevacizumab-treated patients.

Abstract 3506
FOLFOX4 (12 cycles) versus sequential dose-dense FOLFOX7 (6 cycles) followed by FOLFIRI (6 cycles) in patients with initially resectable metastatic colorectal cancer: A GERCOR randomized phase III study (MIROX). Presented by Mohammed Hebbar, MD PhD.

- **Take-home message:** In this study comparing FOLFOX-based regimens in colorectal cancer patients with resected liver metastases, sequential FOLFOX7 followed by FOLFIRI was not superior to standard FOLFOX4.

Abstract 3508
EORTC liver metastases intergroup randomized phase III study 40983: Long-term survival results. Presented by Bernard Nordlinger, MD.

- **Take-home message:** Previous results from the EORTC 40983 study comparing perioperative FOLFOX4 chemotherapy vs surgery alone in patients with liver metastases from colorectal cancer showed an absolute PFS benefit of 8.1% favoring perioperative chemotherapy at 3 years (36.2 % vs 28.1%). In the long-term follow-up results at 5 years, perioperative chemotherapy improved OS by 4.1% (52.4% vs 48.3%) compared with surgery alone. The results were not statistically significant, conceivably due to the small sample size of the trial.

http://www.oncologystat.com/conferences/conference_coverage/Take_Home_Messages_From_ASCO_2012_Colorectal_Cancer.html;jsessionid=40801931CA1440E2978DFACAE6DEF627

5. KRAS Mutation on Codon 13 Shows Better Response to Therapy (Jul.6/12)

This retrospective analysis of data from the CRYSTAL and OPUS trials demonstrated that patients with metastatic colorectal cancer with KRAS G13D mutations had better outcomes than those with other KRAS mutations in response to cetuximab (erbitux) plus chemotherapy. Monoclonal antibodies that target epidermal growth factor receptor (EGFR), such as cetuximab (erbitux) and panitumumab (vectibix), generally do not show efficacy among patients with metastatic colorectal cancer with mutations in the KRAS locus. The most common KRAS mutational subtypes occur at codons 12 (G12D or G12V) and 13 (G13D). A previous study demonstrated that only G12V mutations were significantly associated with poor outcomes of treatment with anti-EGFR monoclonal antibodies, whereas other studies suggest that KRAS codon-13 mutations were associated with better outcomes than other KRAS mutations. The present study was a retrospective analysis that evaluated responses of patients with KRAS G13D, G12V, and other KRAS mutations using updated data from two large studies, the Cetuximab Combined With Irinotecan in First-Line Chemotherapy for Metastatic Colorectal Cancer (CRYSTAL) and Oxaliplatin and Cetuximab in First-Line Treatment in Metastatic Colorectal Cancer (OPUS) studies. In both studies, addition of cetuximab to first-line infusional fluorouracil, leucovorin, and irinotecan (FOLFIRI) or fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) improved outcomes in patients without the KRAS mutation, but not in those with KRAS mutations. Patients were included if they had previously untreated metastatic colorectal cancer and were enrolled in CRYSTAL or OPUS. KRAS mutation status was evaluated using DNA extracted from tumor tissue that was formalin-fixed and paraffin-embedded, or from slides used to evaluate EGFR expression. A total of 1,535 patients were randomly assigned in both studies, of whom 1,378 were evaluable for KRAS mutation analysis in tumor tissue. A total of 845 (61%) had KRAS wild-type tumors, and 533 (39%) had KRAS-mutant tumors. Among patients with KRAS-mutant tumors, 83 (16%) had G13D, 125 (23%) had G12V, and 325 (61%) had other KRAS mutations. Study results shows that patients with KRAS G13D mutations had better outcomes than those with other KRAS mutations in response to cetuximab plus chemotherapy.

Tejpar, S, et al., Association of KRAS G13D tumor mutations with outcome in patients with metastatic colorectal cancer treated with first-line chemotherapy with or without cetuximab. J Clin Oncol. 2012. Epub Ahead of print.

6. FDA Approves Erbitux Plus Folfiri for Metastatic Colorectal Cancer (Jul.7/12)

The FDA has approved cetuximab (Erbitux) in combination with the irinotecan, 5-fluorouracil, leucovorin (FOLFIRI) regimen as a first-line treatment for patients with metastatic colorectal cancer (mCRC) who express the epidermal growth factor receptor (EGFR) and who are also ***KRAS* wild-type**, meaning they test negative for the *KRAS* mutation. Approved concurrently was a diagnostic test designed to help identify patients who will benefit from the combined therapies. Cetuximab, a chimeric monoclonal antibody and EGFR inhibitor, has been approved to treat mCRC since 2004, but the previous approval was only for patients who were refractory or intolerant to irinotecan-based therapy. It is estimated that between 30% and 50% of patients with colorectal cancer have the *KRAS* mutation. While not every patient without the *KRAS* mutation will respond to an anti-EGFR therapy, this newly approved combination could still potentially increase survival in thousands of colorectal cancer patients. Positive data from the CRYSTAL, CA225025, and EMR 62 202-047 (OPUS) trials suggested a statistically significant benefit to mCRC patients. In 2011, an updated analysis of overall survival among participants in the CRYSTAL trial was published in the *Journal of Clinical Oncology*. In that analysis, 1,198 patients in the intent-to-treat (ITT) population were randomly assigned to receive either cetuximab plus FOLFIRI (n=599) or FOLFIRI alone (n=599). Wild-type *KRAS* patients receiving cetuximab plus FOLFIRI had a *significantly improved period of progression-free survival (PFS) with a median PFS of 9.9 months compared to 8.4 months in patients who received FOLFIRI alone*. Wild-type *KRAS* patients in the cetuximab plus FOLFIRI arm of the study also experienced significantly improved overall survival (OS), with a median OS of 23.5 months compared to 20.0 months in the FOLFIRI alone arm.

http://www.onclive.com/web-exclusives/FDA-Approves-Cetuximab-Plus-FOLFIRI-Regimen-for-Metastatic-Colorectal-Cancer/

Van Cutsem E, Köhne CH, Láng I, et al. Cetuximab plus irinotecan, fluorouracil, and leucovorin as first-line treatment for metastatic colorectal cancer: updated analysis of overall survival according to tumor KRAS and BRAF mutation status.* J Clin Oncol. *2011;29(15):2011-2019..

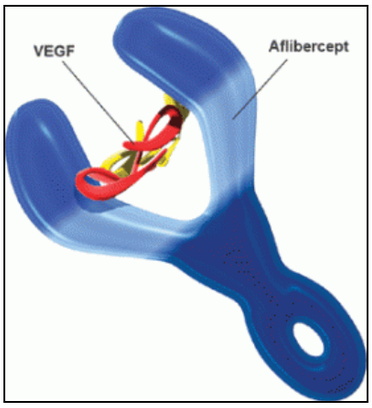
7. Biological Agents in the Resection of Colorectal Liver Metastases (CLM) (Jul.24/12)

Surgically resecting liver metastases from colorectal cancer offers the only potentially curative option. Chemotherapy-induced downsizing of colorectal liver metastases (CLMs) increases the proportion of patients with resectable metastases. Several recent studies have reported that adding a biological agent such as cetuximab (erbitux), panitumumab (vectibix) or bevacizumab (avastin) to chemotherapy could further increase response and resectability rates. This overview discusses the reported resection rates for biological agents combined with chemotherapy and the difficulties of cross-trial comparisons, the pre-, peri- and postoperative roles of biological agents, particularly with regards to comparisons of surgical complications, and ongoing clinical trials in which the resectability of CLMs is a predefined end point. Currently, targeted therapies combined with chemotherapy probably increase the resection rate of CLMs, although this has been shown in only one phase III randomized study and it is difficult to draw definitive conclusions about the relative efficacy and safety of the different available biological agents in terms of converting unresectable CLMs to resectable lesions. Available data for each of them are discussed. More data from phase III trials are expected to confirm the utility of the different biological agents in converting patients with unresectable CLMs to a resectable status.

Nordlinger, B, et al., The role of biological agents in the resection of colorectal liver metastases. Clin Oncol. 2012 August 1; 24(6): 432-442

8. Zaltrap (Aflibercept) Approved by FDA (Aug.3/12)

The FDA in the U.S. has approved the angiogenesis inhibitor aflibercept (Zaltrap) for patients with previously treated metastatic colorectal cancer. The approval stipulates use of aflibercept in combination with FOLFIRI chemotherapy (5-FU, irinotecan, and leucovorin) in patients whose disease has progressed on or exhibited resistance to oxaliplatin (Eloxatin)-based chemotherapy. This approval demonstrates the benefits of adding a biological agent, Zaltrap, to a commonly used chemotherapy drug regimen, FOLFIRI. An improvement in median survival time was noted with the addition of Zaltrap to FOLFIRI, accompanied by an improvement in response rate and a delay in tumor progression and growth. In April, the FDA designated aflibercept for priority review, meaning that preliminary data suggest a drug has therapeutic potential for a condition that does not have adequate treatment or might represent a significant advance over currently available therapy. The priority review designation was based primarily on results of the phase III VELOUR trial, wherein 1,226 patients with metastatic colorectal cancer were randomized to FOLFIRI plus placebo or aflibercept. As reported last year at the combined European oncology meeting, the addition of aflibercept was associated with a 1-month improvement in overall survival and a 2-month increase in progression-free survival. At the 2012 American Society of Clinical Oncology meeting, investigators reported that the aflibercept-FOLFIRI regimen can be used safely in patients previously treated with bevacizumab (Avastin), also an angiogenesis inhibitor.



Like its cousin Avastin, the new drug Zaltrap is a biologic (targeted) protein that blocks the development of new blood vessels needed by a fast-growing tumor. Zaltrap disguises itself as the receptor, basically setting a trap (hence its name) that captures and blocks three different growth factors (two VEGFs and placental growth factor). Perhaps because it has a broader spectrum of action than Avastin, Zaltrap seems to cause more side effects. The FDA approval comes with a “black box” warning of rare but serious or life-threatening side effects such as severe bleeding, gastrointestinal perforation (a hole in the stomach or intestine), and delayed wound healing. But the most common side effects seen in trials were low white blood cells, diarrhea, high blood pressure, mouth sores, fatigue and muscle weakness.

http://www.medpagetoday.com/hematologyoncology/coloncancer/34046

https://mail.google.com/mail/?shva=1#inbox/1392f23ffc2ad99a

SURGICAL THERAPIES

9. Peri-operative Chemo in the Management of Resectable Colorectal Cancer Lung Metastases (Jun. 26/12)

Surgery is often advocated in patients with resectable pulmonary (lung) metastases from colorectal cancer (CRC). This study aimed to evaluate peri-operative chemotherapy in patients with metastatic CRC undergoing pulmonary resection. Patients treated for CRC who underwent pulmonary resection by a single surgeon were identified. Outcome measures included survival, peri-operative complications, radiological and histological evidence of chemotherapy-induced lung toxicities. Between 1997 and 2009, 51 eligible patients were identified undergoing a total of 72 pulmonary resections. Thirty-eight patients received peri-operative chemotherapy, of whom 9 received an additional biological agent. Five-year overall survival rate was 72% in the whole cohort - 74% and 68% in those who received peri-operative chemotherapy (CS) and those who underwent surgery alone (S) respectively. Five-year relapse free survival rate was 31% in the whole cohort - 38% and [less than or equal to]18% in CS and S groups respectively. Only 8% had disease progression during neoadjuvant chemotherapy. There were no post-operative deaths. Surgical complications occurred in only 4% of patients who received pre-operative chemotherapy. There was neither radiological nor histological evidence of lung toxicity in resected surgical specimens. The investigators concluded that peri-operative chemotherapy can be safely delivered to CRC patients undergoing pulmonary resection. Survival in this selected group of patients was favourable.

Hawkes, Eliza, et al., Perioperative chemotherapy in the management of resectable colorectal cancer pulmonary metastases. BMC Cancer 2012, 12:326

RADIOTHERAPY/INTERVENTIONAL RADIOLOGY

10. Treating 5 or More Brain Mets with Stereotactic Radiosurgery (Jun.11/12)

This study's data should help in the decision-making about stereotactic radiotherapy for patients with multiple previously radiated brain metastases, showing almost doubling of survival. This study sought to examine the outcomes of patients with five or more brain metastases treated in a single session with stereotactic radiosurgery (SRS). Sixty-four patients with brain metastases treated with SRS to five or more lesions in a single session were reviewed. Primary disease type, number of lesions, and status of primary and systemic disease at SRS were included. Investigators defined prior whole-brain radiotherapy (WBRT) as WBRT completed >1 month before SRS and concurrent WBRT as WBRT completed within 1 month before or after SRS. The median OS after SRS was 7.5 months. The number of lesions treated did not significantly influence OS (median OS, 6.6 months for eight or fewer lesions vs. 9.9 months for more than eight). Primary site type did not significantly influence median OS. Whole-brain radiotherapy before SRS compared with concurrent WBRT significantly influenced survival. No significant differences were observed when no WBRT was compared with concurrent WBRT or when the no WBRT group was compared with prior WBRT. Investigators concluded that stereotactic radiosurgery to five or more brain lesions is an effective treatment option for patients with metastatic cancer, especially for patients previously treated with WBRT

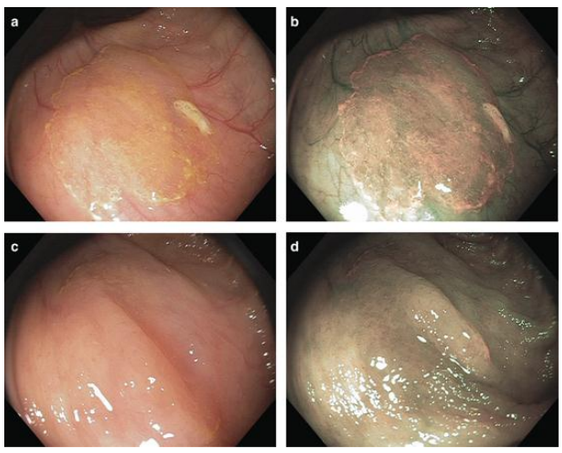
SCREENING

11. Flat Polyps May Explain Colorectal Cancer Screening Discrepancy (Jun.27/12)

In this study, poor ability to detect sessile serrated polyps (SSPs) may explain why endoscopy is more effective at reducing cancer in the distal (left side) than the proximal (right side) colon. The team of investigators found that in a population of patients aged 50-75 years, receipt of previous endoscopy was associated with a significant reduction in the overall likelihood for detecting colorectal polyps at the index procedure, which occurred between 1998 and 2007. This was true when considering polyps in the rectum/distal colon, or proximal colon and did not significantly differ between colonoscopy and sigmoidoscopy. By contrast, there was no significant association between prior endoscopy and the likelihood for detecting SSPs, possibly because these flat lesions are more difficult to detect than pedunculated or protruding advanced adenomas. "Our results support the hypothesis that the effect of endoscopy differs between advanced adenomas and SSPs," say Andrea Burnett-Hartman (Fred Hutchinson Cancer Research Center, Seattle, Washington) and co-authors. "This may have implications for proximal colon cancer prevention and may be due to the failure of endoscopy to detect/remove SSPs, or the hypothesized rapid development of SSPs." The study examined pathology reports from 213 patients with advanced adenoma (10 mm in diameter with 20% villous component or high-grade dysplasia), 172 patients with SSPs (exaggerated crypt serration, dilatation or branching, or other distortions), and 1704 patients with no findings on their index examination. Just over half of the patients (54%) had at least one previous sigmoidoscopy before the index procedure, 13% had colonoscopy, and 15% had undergone both types of examination. Writing in the *American Journal of Gastroenterology*, the team concludes: "There is now a growing awareness of the importance of SSPs, and future studies should assess whether this increased vigilance for SSPs results in better effectiveness of endoscopy for the prevention of SSPs, and more importantly, proximal colon cancer."

About Sessile Serrated Polyps:

A **sessile serrated adenoma** (abbreviated **SSA**), also known as **sessile serrated polyp** (abbreviated **SSP**), is a premalignant flat (or sessile) lesion of the colon, predominantly seen in the cecum and ascending colon (right side of the colon). SSAs are thought to lead to colorectal cancer through the (alternate) *serrated pathway*. This differs from most colorectal cancer, which arises from mutations starting with inactivation of the APC gene.



Typical endoscopic appearances of a sessile serrated adenoma in the proximal colon

Source: http://www.nature.com/ajg/journal/v105/n12/fig_tab/ajg2010330f1.html

http://www.news-medical.net/news/20120627/Flat-polyps-may-explain-colorectal-cancer-screening-discrepancy.aspx

12. Laxative Free Virtual Colonoscopy Can Detect Large Polyps (Jun.30/12)

Computed tomographic colonography (CTC), also known as virtual colonoscopy, administered without laxatives is as accurate as conventional colonoscopy in detecting clinically significant, potentially cancerous polyps, according to the results of this study. Investigators demonstrated that laxative-free CTC is a valid tool for detecting polyps that are clinically significant. Virtual colonoscopy, which has been approved by the American Cancer Society as a valid screening test for colorectal cancer, uses a CT scanner to screen for cancers and polyps in the colon non-invasively. In standard optical colonoscopy (OC), a physician inserts a six-foot-long scope into the entire colon. Currently, both methods call for patients to take a bowel-cleansing laxative before the procedure. With laxative-free CTC, patients do not have to go through bowel cleansing before the exam, but instead begin a low fiber diet two days before the test. They also ingest a tagging agent the day before the exam, which mixes with residual material in the colon and can then be identified and removed digitally when radiologists interpret the scans. The

use of laxatives is often viewed as the worse aspect of having not only a virtual colonoscopy but an optical colonoscopy. Investigators hope that this research will encourage patients who have delayed screening for colon cancer to be examined with this less invasive method. The study of 605 patients, aged 50 to 85, assessed the accuracy of laxative-free CTC in detecting lesions 6 millimeters or larger in size compared with standard optical colonoscopy. The authors found that laxative-free CTC exams detected clinically significant polyps 10 mm or larger with 91% accuracy compared to OC exams, which were 95% accurate. Statistically, there is no difference between these two numbers state researchers. Scan sensitivity using laxative-free CT colonography decreases with polyp size, as it does for regular CT colonography, she said. With polyps measuring 6 mm, sensitivity for CTC was 59%, compared with standard colonoscopy at 76%. The smaller the polyp, the less likely it is to harbor malignancy. For smaller polyps 5 mm or less, there is an extremely low risk of cancer, and these polyps may not need to be removed. For polyps between 6 and 9 mm in size, the decision about whether to remove them depends on the patient's risk factors and how many are found. Polyps 10 millimeters or larger unquestionably come out. During the study, three of the 605 subjects were found to have cancerous polyps. The cancers were identified by both the laxative-free virtual colonoscopy and the standard OC exam. The researchers also surveyed the research participants about their experiences while preparing for the examinations. They found that laxative-free virtual colonoscopy scored higher on all survey questions, and was indicated by more participants to be their exam type of choice. Researchers noted that the current study is one of the first and largest to measure the effectiveness of the new, laxative-free procedure. Because the procedure is still in the early stages of development, additional studies still need to be conducted. They predict that once radiologists are trained in reading the new images and gain experience with the exam process, laxative-free CTC exams will be available wherever virtual colonoscopies are performed.

Michael E. Zalis et al. Diagnostic Accuracy of Laxative-Free Computed Tomographic Colonography for Detection of Adenomatous Polyps in Asymptomatic Adults: A Prospective Evaluation. **Annals of Internal Medicine*, May 15, 2012***

13. Colonoscopy with Polypectomy Significantly Reduces Colorectal Cancer Incidence and Mortality in the General Population (Jun.26/12)

A study from researchers in Switzerland found that colonoscopy with polypectomy significantly reduces colorectal cancer incidence and colorectal cancer-related death in the general population. A total of 12 colorectal cancer cases were identified in the screening group of 1,912 patients and 213 cases of colorectal cancer were found in the non-screened group of 20,774 patients. One of the 12 persons of the screened individuals with a colorectal cancer and 51 of the 213 persons of the non-screened individuals with a colorectal cancer died because of their cancers. Colorectal cancer (CRC) has a very high incidence in Switzerland as well as in other European countries and is the second most frequent cause of cancer-related deaths in Europe. It is detected in approximately 413,000 people in Europe every year, half of whom die because of the disease. Therefore, a need exists for efficient strategies for prevention and early detection of CRC. Colonoscopy with the possibility of an immediate polypectomy is a recommended and preferred screening method because polyps (growths in the colon) can turn into cancer over the course of years to decades. Removing polyps during a colonoscopy prevents that polyp from becoming cancerous. In contrast to earlier CRC screening studies that used colonoscopy, this population-based closed cohort observational study aimed to obtain complete and comparable data on CRC incidence and CRC-related mortality after a single screening colonoscopy compared with no screening, while taking into account the potential differences in risk profiles between the screened and non-screened participants. Researchers found that colorectal cancer screening by colonoscopy markedly reduces not only the incidence of colorectal cancer, but also cancer-related death. They state that they are unaware of any other long-term prospective study assessing the role of colonoscopy screening for the reduction of colorectal cancer incidence and mortality in a well-defined, population-based setting under real-life conditions.

American Society for Gastrointestinal Endoscopy (2012, July 24). Colonoscopy screening markedly reduces colorectal cancer incidence and death. **Science Daily*. Retrieved August 14, 2012.***

PSYCHOSOCIAL

14. Patients and Partners Are Affected by Colorectal Cancer (Jul.11/12)

Partners of individuals with colorectal cancer, as well as the patients themselves, are at risk for psychological morbidity according to the type of treatment given, show Portuguese study results. Specifically, colorectal cancer patients treated surgically have lower levels of depression, anxiety, and traumatic stress symptoms than their counterparts treated with surgery plus either chemotherapy or radiation. And the psychological effects followed suit among the patients' partners, say the researchers. Patients who had been diagnosed for longer than a year were also at risk for traumatic stress symptoms, possibly because the threat for recurrence becomes more real as time goes on. The findings highlight a need for greater understanding of "factors that may predict cancer-specific distress," thereby enabling better clinical or psycho-educational interventions. The team evaluated the influence of treatment on quality of life, depression, anxiety, and traumatic stress symptoms using data for 141 colorectal cancer patients, of whom 35 underwent only surgical treatment (19 partners), 41 underwent surgery followed by

chemotherapy (26 partners), and 38 who underwent surgery then radiotherapy (22 partners). The researchers found significant differences in anxiety symptoms (measured using the Hospital Anxiety and Depression Scale) by patient treatment group, with surgically treated patients scoring significantly lower than surgery plus chemotherapy/radiotherapy groups at 5.97, 10.41, and 9.73, respectively. Similar-direction associations were found for depression and traumatic stress symptoms. Furthermore, partners of surgical patients also presented lower levels of anxiety and traumatic stress than partners of patients treated with the other methods analyzed. Duration of diagnosis also had an effect on anxiety and the other outcomes; patients who had been diagnosed for over a year presented significantly more global traumatic stress, intrusion, and hyper-vigilance than those who had been diagnosed less than 6 months previously or between 6 months and 1 year beforehand. Finally, as measured using the Quality of Life Scale-Cancer measure, anxiety and depression had the biggest effect on patient-reported quality of life, explaining 78.4% of variance, while traumatic stress and anxiety together predicted symptom distress, reports the research team. "Early identification of high-risk couples is critical". "Hospitals should provide interventions to help patients and partners adapt to cancer and go through the illness' stages in order to promote their quality of life".

Pereira, Graca, et al., Anxiety, depression, traumatic stress and quality of life in colorectal cancer after different treatments: A study with Portuguese patients and their partners European Journal of Oncology Nursing Vol. 16, Issue 3, Pages 227-232

OTHER

15. Online Tool Provides Genetically Specific Treatment for Colorectal Cancer (Jun.27/12)

The College of American Pathologists (CAP) has published a free online tool to provide patients with late-stage colon cancer and their doctors access to the most up-to-date information for treating their condition. The **Therapy Finder** — **Colorectal Cancer** was developed in partnership with CollabRx, an organization co-founded by a survivor of metastatic melanoma who experienced serious shortcomings in accessing information for treating his own condition. The Therapy Finder is a dynamically updated online resource that enables doctors and patients to identify diagnostic tests and clinical trials associated with therapies that target the unique genetic profiles of patients′ tumours. It allow users to input information about their disease ─ including the stage, treatment history, status of genetic mutations known to have implications for treatment, and sites of metastasis, if any. It then provides personalized therapy-related options, based on peer-reviewed medical and scientific content that may be of use to the patient and physician, such as identification of potential drugs, diagnostics, and clinical trials that may be useful in the specific form of colorectal cancer selected. The Therapy Finder – Colorectal Cancer app is a novel and much needed educational resource that provides cancer patients and physicians access to complex and highly valuable information about how tumour genetics can be used to guide through clinical trials and treatment options. This is one of the first sites which uses a cutting-edge approach for biomarker driven chemotherapy," said Dr Heinz-Josef Lenz, professor at the Keck School of Medicine, University of Southern California. "This online and freely accessible tool will support and enable patient empowerment, engagement, and participation in discussing and creating a personalized cancer treatment plan that leverages the unique aspects of a patient′s medical history and tumour genetic profile whenever possible," added Dr Wells Messersmith, a clinical advisor to the Therapy Finder – Colorectal Cancer. The Therapy Finder – Colorectal Cancer may be accessed through the following link: http://www.collabrx.com/colorectal

http://www.bj-hc.co.uk/bjhc-news/news-detail.html?news=2187&lang=en&feed=130

16. Alberta Cancer Patient Outcomes To Improve with Increased Surveillance (Jun.28/12)

Colorectal cancer patients must receive adequate follow-up care after their treatment is over to ensure any cancer recurrence is detected early, but many of those patients are currently not adhering to the recommended guidelines, say researchers. A new research project funded by the Alberta Cancer Foundation and Sanofi Canada aims to improve the chances of early diagnosis if the cancer returns and save lives across the province. "Something is clearly missing when it comes to stage 2 and 3 colorectal cancer patients in Alberta," says Dr. Jennifer Spratlin, medical oncologist at Alberta Health Service's Cross Cancer Institute and co-investigator on the project. "We know that if we follow these patients once they are discharged from their cancer care health team, we will be able to improve patient outcomes and ultimately, save lives." Prior to 2007, patients at the Cross Cancer Institute were sent home with recommendations for blood tests every three months, a CT scan at one and three years, and lifelong colonoscopies. Patients and their family doctors were also sent letters outlining the recommendations. Spratlin conducted a study to see how people were adhering to the recommendations and found that only a staggering 7.2% of patients were getting the suggested tests. Based on these findings, the Cross Cancer Institute implemented changes, including a clinic that booked appointments for patients. A follow-up study determined that as a result, adherence had risen to 49.5%, which meant half of the patients still weren't seeking adequate care. The Tom Baker Cancer Centre also added its own interventions with similar results. Healthcare leader Sanofi Canada learned of the opportunity to be involved with a colorectal cancer surveillance program, with the goal of reaching 90% adherence to follow-up guidelines and capturing recurrence when a cure is still possible. The company partnered with the Alberta Cancer Foundation with a $105,000 investment to support the research program over the next three years. The Alberta Cancer Foundation also contributed $175,000 to support data analysis at both the Cross Cancer Institute and the Tom Baker Cancer Centre, Alberta Health Services – Cancer Care's two main cancer

centres. "Improvement of patient health outcomes requires not only the best of innovative medications and diagnostic techniques, but the whole healthcare continuum," says Dr. Stanislav Glezer, VP Evidence, Value and Access at Sanofi Canada. "Contributing to more effective screening and follow-up programs is one of the ways Sanofi Canada is focusing on patients' needs." "The Alberta Cancer Foundation is the only Alberta-based foundation with a mandate to facilitate improved outcomes and quality of life for Albertans facing cancer," says Alberta Cancer Foundation CEO Myka Osinchuk. "Making sure that Albertans have access to the most effective evidence-based surveillance programs is key to improving patient outcomes." Examples of the improved surveillance program include patient education, patient journals, workshops for family physicians, advanced nurse practitioner follow up and data collection. The research team also believes this program will decrease waiting times to see an oncologist since follow-up care will be done through other routes and make room for those cancer patients needing primary care. Levels of satisfaction may also improve as patients become more engaged with their own care.

http://albertacancer.ca/page.aspx?pid=1469

17. Decreasing Cancer Risk Associated with Inflammatory Bowel Disease (Jul.9/12)

Inflammatory bowel disease is caused by chronic inflammation, which leads to damage of the intestinal epithelium (lining). Patients with inflammatory bowel disease have an elevated risk for developing colorectal cancer because of this chronic inflammation. In an effort to develop strategies to break the cycle of inflammation, researchers in Los Angeles examined two mouse models of colorectal cancer. Their work shows that inactivating a key receptor, known as epidermal growth factor receptor, increases the frequency and severity of colorectal tumors. Though epidermal growth factor has well-defined roles in promoting tumor growth, the research team now finds that epidermal growth factor receptor can ameliorate the response to chronic inflammation and reduces tumor development by fine-tuning inflammation and the generation of intestinal epithelium. Their results suggest that promoting epidermal growth factor activity in patients with inflammatory bowel disease could decrease long-term cancer risk by reducing inflammation.

Polk, Brent, et al., Epidermal growth factor receptor inhibits colitis-associated cancer in mice. J Clin Invest. Vol. 122, Issue 8, August 1, 2012

18. Risk Tool to Help GPs Detect Cancer Earlier (Jul.10/12)

GPs should use a bowel cancer risk calculator to improve early diagnosis instead of relying on individual 'red flag' symptoms, researchers have said. Independent analysis of the risk-prediction tool QCancer found it was twice as accurate at detecting bowel cancer as using individual symptoms such as abdominal pain alone. Researchers said the tool could help GPs detect and refer potential cases of bowel cancer earlier. The tool was developed by researchers at Nottingham University. It combines seven risk factors for women and nine for men to better predict the chance of a patient having bowel cancer. These include age, symptoms such as rectal bleeding and lifestyle behaviors such as alcohol consumption. Now, researchers from the Oxford University have independently verified the performance of the tool. They tested the calculator on cases of cancer found among the records of 2.1 million patients registered with GP practices in January 2000 to June 2008. Researchers compared recorded symptoms with the incidence of bowel cancer within the next two years of presentation. They found QCancer would have identified 71% of colorectal cancers in women and 74% in men. Conversely, investigation prompted by rectal bleeding alone would have identified only 34% and 40% of bowel cancers respectively. Abdominal pain by itself could have identified only 36% and 31% of cancers respectively. Study lead Dr Gary Collins of Oxford University said: 'Our research shows that the QCancer calculator clearly outperforms individual signs and symptoms as a way of predicting whether a patient has bowel cancer. 'It's great to see that the government is considering this model along with others to help spot people with cancers that might otherwise go undetected. Ultimately tests like this will be likely to improve early diagnosis of the disease so that patients have the best possible chance of survival.' Sara Hiom, director of cancer information at Cancer Research UK, said: 'This study highlights a new approach to helping GPs make better decisions about which patients to refer for further tests. Ultimately we hope risk calculators like these could contribute to swifter diagnosis of bowel cancers. Encouraging more people to take up their invitation to bowel screening is also important.' It has been suggested GPs could integrate the tool into their IT systems to form a list of high-risk patients needing investigation.

Collins, Gary, et al., Identifying patients with undetected colorectal cancer: an independent validation of QCancer (Colorectal). British J of Cancer, 107: pp. 260-265

19. High Iron Levels May Cause Colorectal Cancer (Aug.16/12)

New research has revealed that high levels of iron switches on a key pathway in people with faults in a critical anti-cancer gene (APC) that could raise the risk of bowel cancer**.** Bowel cancer is 2 to 3 times more likely to form in mice fed high amounts of iron with a faulty APC gene, compared to mice who still had a fully functioning APC gene. However, mice with the faulty gene that were fed very low amounts of iron did not develop bowel cancer at all. Bowel cancer is also known as colorectal cancer. Symptoms of this disease may go unnoticed for a long time. Fortunately if diagnosed early, it is often curable. A few symptoms include constant fatigue, unexplainable weight loss, blood or mucus in the feces, bloating, and

cramps. The APC gene is faulty in around 8 out of 10 bowel cancers but until now researchers haven't known how this causes the disease. It's clear that iron is playing a critical role in controlling the development of bowel cancer in people with a faulty APC gene. And, intriguingly, their study shows that even very high levels of iron in the diet don't cause cancer by itself, but rely on the APC gene. Results also suggest that iron could be raising the risk of bowel cancer by increasing the number of cells in the bowel with APC faults. The more of these cells in the bowel, the greater the chance that one of these will become a starting point for cancer. The finding could also suggest why red meats, and other foods high in iron, are linked to an increased risk of bowel cancer. Two proteins become turned on, when the APC gene is deleted, which results in a buildup of iron in bowel cells. When this occurs, *wnt* (a key cancer signaling pathway) is turned on, which results in cells growing out of control. Results showed that bowel cancers did not form in mice that were given no iron in their diet, and the cells with a faulty APC gene were killed. When mice that had a working APC gene were given a diet high in iron, they did not develop bowel cancers. In their bowel cells, the iron accumulation proteins were turned off and *wnt* signaling remained inactive.

Sansom, Owen, et al., Luminal Iron Levels Govern Intestinal Tumorigenesis after Apc Loss In Vivo. Cell Reports (2012). http://dx.doi.org/10.1016/j.celrep.2012.07.003

20. Regular Patient/Clinician Interaction Can Help Increase Follow-up Cancer Screening (Aug.17/12)

An analysis of colorectal cancer (CRC) patients who maintained regular contact with their clinicians (doctors, nurses, specialists) indicates those patients are more likely to follow recommendations for detecting cancer recurrence than patients who do not. In fact, researchers found CRC patients were more than twice as likely to adhere to medical follow up procedures if they had regular patient clinician information engagement (PCIE). The study team followed over 300 CRC patients since 2005. The patients in the study—roughly half male, half female; mostly white (88.5%); a mean age of 68; and most (72.5%) indicating concern about cancer recurrence—responded to surveys over the three-year span of the study. All reported whether they had received specific follow up screening tests—two or more office visits, two or more serum carcinoembryonic antigen (CEA) tests, and one colonoscopy. The study tracked how often these procedures were received in comparison to the amount of interaction patients had with their clinicians. While only 41% reported receiving all three surveillance procedures, the researchers did note that patients who had consistent PCIE were 2.8 times more likely to adhere to recommended follow up tests. In the article the research team acknowledges that several socio-demographic and clinical factors affecting whether or not someone follows advice cannot be modified. These include the patients' age, income level, race, and severity (stage) of the cancer. However, they note that understanding the impact and effects of PCIE can help health professionals develop pilot interventions to improve adherence through patient active engagement with their clinicians on cancer-related information. "We recommend that prospective studies be considered to determine if pilot programs encouraging active patient engagement with clinicians about cancer-related information would be beneficial in terms of increasing the proportion of patients receiving post-treatment surveillance testing, and ultimately in improving patient outcomes and survival," the researchers write in their conclusion.

Tan, Andy, et al., Patient-Clinician information engagement improves adherence to colorectal cancer surveillance after curative treatment: results from a longitudinal study. The Oncologist. August 2012.

NUTRITION & HEALTHY LIFESTYLE

21. Eating Fish May Reduce Colorectal Cancer Risk (Jun. 23/12)

A new study suggests that eating fish may reduce the risk for colorectal cancer. Colon cancer is cancer of the large intestine (colon), which is the lower part of the digestive system. Rectal cancer occurs on the last eight to ten inches of the colon. They are often referred to together as colorectal cancers. In the colon and rectum, the exaggerated growth of cells may cause precancerous polyps (adenomas or adenomatous polyps), which form in the lining of the intestine. Over a period of time some of these polyps may become cancerous. In the later stages of the disease, these cancerous polyps may penetrate the colon walls and metastasize (spread) to nearby lymph nodes and other organs. In a new study, researchers conducted a comprehensive literature search for studies evaluating the relationship between fish consumption and colorectal, colon or rectal cancer risk. Forty-one studies were ultimately identified for inclusion. Through analyses of the study results, the researchers found that eating fish reduced the risk of colorectal cancer by 12%. The highest reported fish consumption was linked to a 17% decreased risk, while the lowest reported fish consumption was linked to a 7% decreased risk. The authors concluded that eating fish may reduce the risk of colorectal cancer; however, further research is necessary before firm conclusions can be made. Fish is a dietary source of both docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). There is supportive evidence from multiple studies that suggests the intake of recommended amounts of DHA and EPA in the form of dietary fish or fish oil supplements lowers triglycerides; reduces the risk of death, heart attack, dangerous abnormal heart rhythms and strokes in people with known cardiovascular disease; slows the buildup of atherosclerotic plaques ("hardening of the arteries") and lowers blood pressure slightly. Several previous population studies have also reported that dietary omega-3 fatty acids or fish oil may reduce the risk of developing breast, colon or prostate cancer. Additional research is needed in this area.

Wu, S, et al., Fish consumption and colorectal cancer risk in humans: a systematic review and meta-analysis. Am J Med. 2012 June; 125(6): pp. 551-9.e5.

22. Should Patients Fast During Cancer Therapy (Jul.10/12)

The internet is full of raging debates, fervid testimonials and opinions about what you should or shouldn't eat when you're being treated for cancer. One of the most common chat topics is whether you should cut out 'sugar' to decrease the amount of "fuel" available for voracious cancer cells. If only cancer, and nutrition, were so simple. But every kind of calorie is fuel, every cell uses fuel, and cells become cancerous in many different ways. But thankfully, scientists are working hard to shed more light on the role that nutrients might play in cancer cells—and they're coming up with some tantalizing clues, according to the most recent National Cancer Institute *Cancer Bulletin* (July 10 2012). For example, researchers are asking, if cancer patients went on a total food fast before and/or after chemotherapy sessions, could that reduce side effects or even make the treatments more effective in destroying cancer cells? Dr. Valter Longo, professor of gerontology and biology at the University of Southern California (USC), has been peering into the actual cells—both normal and cancer—in both tissue cultures and in mice to see how normal and cancer cells respond to fasting, and to chemotherapy drugs after fasting for 2 or 3 days before treatment. His laboratory has found that fasting causes dramatic—and very different–changes in the cells. Normal cells essentially go into a "survival mode," turning down their genes that stimulate cell growth to target what little energy they have into a protective, maintenance and cell-repair mode. Theoretically, this might make normal cells less harmed by chemotherapy. In contrast, cancer cells seem to have mutations that prevent them from shifting into this slow-growth protective mode, so they're actually *more* sensitive to chemotherapy–especially drugs that target fast-growing cells, according to a study the USC team published in the March 2012 *Science Translational Medicine*. The cancer cells also get a double-whammy because the fasting deprives them of the fuel they need as they keep trying to grow and divide quickly. Other trials have shown that tumors in fasting mice grew slower, and much slower in mice that fasted before getting an anticancer drug. But there's been only one tiny study in humans: In 2009, ten elderly human volunteers with a variety of cancers were able to fast safely from 2 to 5 days before, and up to 2 days after, chemotherapy treatments. In cycles when they fasted, they reported fewer side effects from chemotherapy. Dr. Longo and others have started three early-phase human trials, with another two multi-center trials to begin shortly. The human trials will test whether fasting is safe, whether it might reduce chemotherapy side effects, and how—or if—it changes how well different cancer drugs work against tumors and cancer cells. The NCI Bulletin article also reported why fasting should not be tried with *oral drugs taken as pills*. Certain oral cancer drugs (such as nilotinib for leukemia and lapatinib for breast cancer) are *strongly affected* by being taken with or without food. Some drugs don't work as well, some oral drugs are vastly strengthened by the presence or absence of food in the gut when these medicines are taken. University of Chicago researchers are now studying whether fasting could be safe, or how it would change necessary doses for certain drugs.

NCI Cancer Bulletin, *July 10 2012, Vol. 9, No 14*: *"To Eat or Not to Eat: With Cancer Therapies, That Is the Question"*

http://fightcolorectalcancer.org/research_news/2012/07/to_fast_or_not_to_fast

Aging: *Dec. 2009 Vol.1 No 12, "Fasting and Cancer Treatment in Humans: A Case series report."*

23. Dietary Fiber May Cut Colorectal Cancer Risk (Jul.22/12)

A new study suggests that eating lots of fiber-rich foods can decrease the risk of colorectal cancer drastically. The results showed intake of an additional 10 grams of total dietary fiber per day was associated with a 13% reduced risk of colorectal cancer. An early analysis of data from the same EPIC study showed that dietary fiber intake was inversely associated with colorectal cancer risk. But some other large cohort studies do not support the results. The current study considered data collected from the study during a longer follow-up. During an average follow-up of 11 years, 4,517 incident cases of colorectal cancer were identified. Fiber intake was estimated at baseline. Total fiber intake was also found inversely associated with colon cancer and rectal cancer. Colorectal cancer refers to a combination of both so the findings are reasonable. The associations were not affected by factors including age, sex, or anthropometric (body measurement research), lifestyle, and dietary variables did not affect the associations, the researchers reported. With regard to the fiber source, fibers from cereals, fruits and vegetables all had the same inverse association with colon cancer. But **only fiber from cereals or grains** not that from fruit and vegetables was linked to **reduced risk** of rectal cancer.

Murphy, Neil., et al., Dietary Fibre Intake and Risks of Cancers of the Colon and Rectum in the European Prospective Investigation into Cancer and Nutrition (EPIC). PloS One. June 22, 2012. Online Access.

24. Shrinking Colon Polyps with Spice (Jul. 22/12)

The spice turmeric is a part of the ginger family and is responsible for the bright yellow coloring of some fabulous dishes, such as curry. Alongside other notable studies, Johns Hopkins is currently researching curcumin, a specific plant chemical (known as a phytochemical) in turmeric, to establish a link between this herb and the reduction of colon polyp size. Specifically, the study is looking at adults with familial adenomatous polyposis (FAP), a hereditary condition that dramatically increases the sufferer's chances

of developing colon cancer. If left untreated, certain polyps mutate into colon cancer, which is why routine screening exams, such as the colonoscopy, aim to catch them early. Several clinical trials have already found a link between curcumin and anti-inflammatory, antioxidant and anti-cancer properties in animals. Phase II trials are underway to establish the safe upper doses of this common herb in humans. Like any other drug, herbs can have side effects and interactions with prescription medications. If you are considering using herbal medicine, talk to your doctor before making any decisions or taking a dietary supplement on your own. Your doctor will be able to discuss side effects, interactions and warnings with you and help you make a safe, informed decision. According to the Linus Pauling Institute Micronutrient Research Center, there are no known adverse events while using turmeric as part of a healthy diet at this time.

http://coloncancer.about.com/b/2012/07/21/shrinking-colon-polyps-with-spice.htm

25. Study Suggests Aspirin Could Help Prevent Cancer-Related Deaths (Aug. 11/12)

According to these study results, taking a daily dose of aspirin can help fight off stomach, esophageal or colorectal cancer. In a study of more than 100,000 healthy individuals who were placed on a daily low-dose aspirin regiment, researchers in Atlanta discovered that the painkilling drug can reduce the risk of developing cancer and slow the spread of the disease. Specifically, they found that there was a 40% reduced chance of deaths from gastrointestinal cancers, including esophageal, stomach and **colorectal** cancers, as well as a 12% lower risk of death from other forms of cancer over the course of a decade. Combined, low-dose aspirin was found to reduce the risk of cancer-related death by 16%. Although earlier research had found similar results, the new paper adds to the evidence in favor of taking the drug as a protective measure. Doctors have previously called for low doses of aspirin to be taken from middle age, especially for people with a family history of cancer or heart disease, which it is also thought to protect against. Most of the study participants were over the age of 60, and none of them had any previous history of cancer. A total of 100,139 men and women took part in the research. While the study "bolsters the case that daily aspirin may help protect against cancer, it also shows that "the effect seems weaker than previously thought. The final chapter on the popular but controversial drug has yet to be written, experts say, because like earlier research the new work has considerable limitations.

Jacobs, Eric, et al., Daily Aspirin use and Cancer Mortality in a Large US Cohort. J of the National Cancer Institute. First published online: August 10, 2012