

COLORECTAL CANCER RESEARCH UPDATES

Month Ending November 18th, 2011



The following colorectal cancer research update extends from October 15th, 2011 – November 18th, 2011 inclusive and is intended for informational purposes only.

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DRUGS / SYSTEMIC THERAPIES

1. Phase III Trial Involving Regorafenib Has Been Unblinded After Showing Promising Results (Oct. 24/11)

A Phase III study evaluating Bayer HealthCare Pharmaceuticals' regorafenib (Bay 73-4506) in patients with metastatic colorectal cancer (mCRC) has been unblinded to allow patients in the placebo arm to start receiving the investigational oral multikinase inhibitor. The **CORRECT STUDY** is being conducted in 760 mCRC patients whose disease had progressed after approved standard therapy. Patients are randomized to receive either regorafenib plus best supportive care, or placebo plus best supportive care. A planned interim data analysis has now shown that in comparison with placebo, regorafenib therapy led to a statistically significant improvement in overall survival. In light of the findings, the study's data monitoring committee recommended unblinding the study so that the patients receiving the placebo could be identified and switched over to receive regorafenib. Regorafenib is an oral, multi-targeted kinase inhibitor drug. A kinase inhibitor targets certain key proteins that are essential for the survival of a cancer cell. By specifically blocking those proteins, regorafenib may stop cancer cell growth. The protein receptors that the drug is designed to inhibit are: angiogenic, stromal, and oncogenic receptor tyrosine kinases. There are clinical trials that are underway involving regorafenib in combination with folfox and folfox in the U.S. The Phase II trial that is currently recruiting is regorafenib in combination with folfox in second line therapy in patients who are kras and braf mutant and it is being led by Dr. Richard Goldberg in the U.S. For a list of U.S. Centres and trial information, please click on the following link: <http://clinicaltrials.gov/ct2/show/NCT01298570> .

<http://www.genengnews.com/gen-news-highlights/bayer-s-phase-iii-colorectal-cancer-trial-unblinded-after-promising-interim-data/81245874/>

2. Oxaliplatin-Based Chemo in Resected Colorectal Cancer with Liver Metastases (Nov. 4/11)

Surgical resection alone has been validated as a standard treatment for patients with liver metastases from colorectal cancer. There is, however, a high rate of recurrence that is still an issue to be overcome. This study aimed to assess the efficacy of adjuvant chemotherapy (chemo administered post surgery) using an oxaliplatin-based regimen in patients who underwent hepatic **and** primary colorectal cancer resection. Sixty patients who received oxaliplatin-based postoperative chemotherapy combined with curative resection of primary colorectal cancer and synchronous (same time) liver metastases between January 2000 and February 2008 were retrospectively reviewed. The investigators examined survival, and prognostic factors. The median overall survival (OS) was 62.8 months and median relapse-free survival (RFS – time before the disease came back) was 32.8 months. The 1-, 3- and 5-year survival rates were 95.0, 68.8 and 55.5%, respectively. The relapse-free interval and modality of liver resection were independently associated with OS. The investigators concluded that oxaliplatin-based adjuvant chemotherapy after radical resection resulted in increased OS and RFS with acceptable tolerability compared to surgery alone. However, it is not yet clear whether postoperative oxaliplatin-based chemotherapy improves outcome compared to patients treated with 5-fluorouracil plus leucovorin.

Kim, Hye Ryun, et al., Efficacy of oxaliplatin based chemotherapy in curatively resected colorectal cancer with liver metastasis. Oncology. Vol. 81, No. 3-4, 2011.

SURGICAL THERAPIES

3. Surgical Resection of Recurrent Pulmonary Metastases Yields Good Outcomes (Oct. 20/11)

This study reviewed data on 156 patients who underwent curative surgery of pulmonary metastasis from colorectal cancer (CRC). Repeat pulmonary surgery was performed in 25 patients; the present study examined the outcomes and factors associated with prognosis after repeat pulmonary surgery. The 5-year survival rate after the first pulmonary surgery was 56.2%. The 5-year survival rate after repeat pulmonary resection was 42.1%. Hilar or mediastinal lymph node metastasis at the time of the repeat surgery was significantly associated with poor survival. The investigators concluded that repeat pulmonary surgery for metastatic CRC provides satisfactory outcomes but hilar or mediastinal lymph node involvement is consistently associated with a poor prognosis after the first and repeat pulmonary resections.

Hilar Lymph Nodes: Any of the lymph nodes in the hilum or the triangular depression or indented region at the junction of each lung and its bronchi.

Mediastinal Lymph Nodes: Mediastinal lymph nodes are lymph nodes located in the mediastinum. The mediastinum is an area in the central part of the chest in between the two lungs.

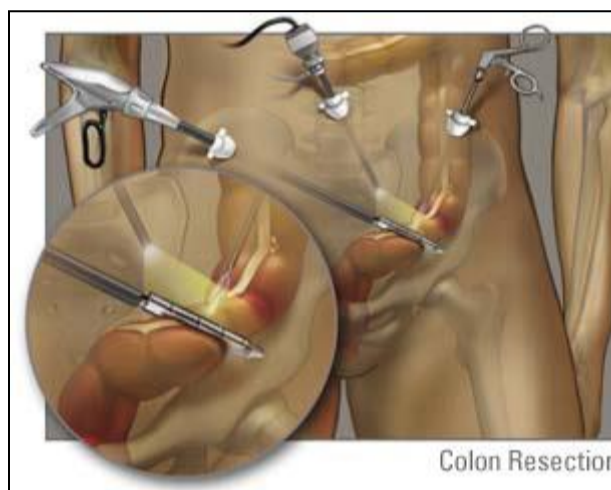
Kanzaki, R, et al., Outcome of surgical resection for recurrent pulmonary metastasis from colorectal carcinoma. Am J Surg. 2011 Oct;202(4):419-26. Epub 2011 Aug 6

4. Minimally Invasive Surgery Leads to Improved Short Term Outcomes (Nov. 6/11)

The investigators of this study maintain that minimally invasive surgery (MIS) techniques are beneficial compared with open techniques. According to them, there is a paucity of data of the potential advantages of MIS in colon cancer surgery for veterans. Therefore, they hypothesize that use of MIS in colon cancer resections in a Veterans Affairs Medical Center will lead to improved short-term outcomes without compromising oncologic outcomes. A retrospective analysis of a prospectively maintained database was performed. They compared surgical, short-term, and oncologic outcomes in MIS versus open surgery. When analyzing the results, MIS patients had significantly less blood loss, surgical time, days to return of bowel function, and hospital and intensive care unit stays. Also, they had a greater and more adequate lymphadenectomy (surgical removal of lymph nodes), and were less likely to experience a postoperative complication. Their survival analyses showed no difference in overall and disease-free survival. The investigators, therefore, concluded that the use of MIS in colon cancer leads to improved short-term outcomes and similar oncologic outcomes when compared with open surgery.

About Minimally Invasive Surgery:

Minimally invasive surgery (MIS), also called **laparoscopic surgery**, **bandaid surgery**, or **keyhole surgery**, is a modern surgical technique in which operations in the abdomen are performed through small incisions (usually 0.5–1.5 cm) as opposed to the larger incisions needed in laparotomy. Keyhole surgery makes use of images displayed on TV monitors to magnify the surgical elements. See image below.



Source: <http://www.ideasforsurgery.com/wp-content/uploads/2008/07/colorectal.jpg>

Orcutt, Sonia, et al., Minimally invasive surgery in colon cancer patients leads to improved short term outcomes and excellent oncologic results. Amer J of Surg. Vol. 202, Issue 5: pp. 528-531.

RADIOTHERAPY / INTERVENTIONAL RADIOLOGY

5. Using PET/CT for RFA in Patients with Liver Mets (Oct. 20/11)

According to the investigators of this study, there is little data in the literature about the use of PET in the management of patients undergoing Radiofrequency Ablation (RFA) of colorectal liver metastases (CLM). The aim of this study was to look at the use of PET versus contrast-enhanced CT (ce CT) scans on the initial assessment and follow-up of patients with CLM undergoing laparoscopic RFA. The patients who had PET scans pre-RFA and post-RFA were identified from a prospective database within a 14-year period. The findings of PET scans were compared to those of ce CT. A total of 134 patients had PET scans prior to laparoscopic RFA and 104 (28%) had PET/CT scans in follow-up, with comparison ce CT done within a month in 82 patients. In follow-up, PET/CT findings were:

- equivalent to ce CT in 55 patients (67%),
- **superior** in 22 (27%), and
- inferior in 5 (6%).

Pre-RFA or post-RFA PET imaging did not affect overall survival. The patients in whom the benefit of PET/CT was most noted were those with multiple bilobar tumors (tumors appearing on both lobes of the liver). The investigators concluded: “Although there was no survival benefit, PET/CT was superior to ce CT in demonstrating recurrence after RFA in approximately a quarter of the patients with CLM. The patients who would benefit most from a PET/CT seem to be those with multiple and bilobar tumors, who develop liver recurrence in follow-up after RFA.”

Sahin, Dursun Ali, et al., The utility of pet/ct in the management of patients with colorectal liver metastases undergoing laparoscopic radiofrequency thermal ablation. Annals of Surg Onc. Doi: 10.1245/s10434-011-2059-7

6. Percutaneous Cryoblation of Pulmonary Mets (Nov. 10/11)

This study sought to evaluate the safety and efficacy of cryoablation for metastatic lung tumors from colorectal cancer. The procedures were performed on 24 patients (36–82 years of age, with a median age of 62; 17 male patients, 7 female patients) for 55 metastatic tumors in the lung, during 30 sessions.

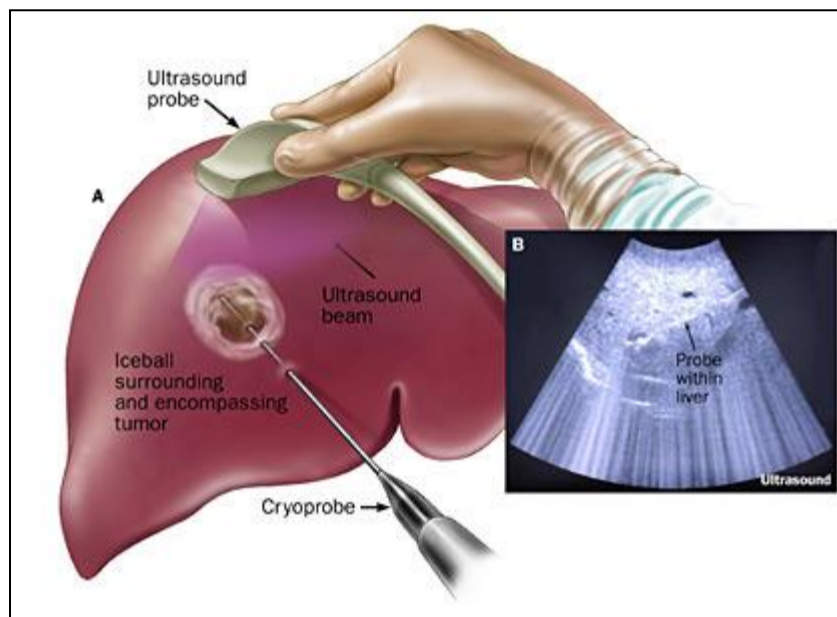
The procedural safety, local progression free interval, and overall survival were assessed by follow-up computed tomographic (CT) scanning performed every 3–4 months. The major complications were:

- pneumothorax, 19 sessions (63%),
- pleural effusion, 21 sessions (70%),
- transient and self-limiting hemoptysis, 13 sessions (43%) and
- tract seeding, 1 session (3%).

The 1- and 3-year local progression free intervals were 90.8% and 59%, respectively. The 3-years local progression free intervals of tumors ≤ 15 mm in diameter was 79.8% and that of tumors >15 mm was 28.6%. The 1- and 3-year overall survival rates were 91% and 59.6%, respectively. The investigators concluded that the results indicated that percutaneous cryoablation is a feasible treatment option. The local progression free interval was satisfactory at least for tumors that were ≤ 15 mm in diameter.

About Cryoablation (or Cryotherapy):

Cryoablation is a technique used for removing cancerous tissue by killing it with extreme cold. During cryotherapy, liquid nitrogen or argon gas flows into a needle-like applicator (a cryoprobe) creating intense cold that is placed in contact to diseased tissue. Physicians use image-guidance techniques such as ultrasound, computed tomography (CT) or magnetic resonance (MR) to help guide the cryoprobes to treatment sites located inside the body, whether it be the lungs, liver, kidney, prostate, etc.



Cryoablation being performed on a liver tumour through the assistance of ultrasound guidance.

Source: http://www.hopkins-gi.org/GDL_Disease.aspx?CurrentUDV=31&GDL_Cat_ID=AF793A59-B736-42CB-9E1F-E79D2B9FC358&GDL_Disease_ID=A349F0EC-5C87-4A52-9F2E-69AFDB80C3D1

Yamauchi, Yoshikane, et al., Percutaneous cryoablation of pulmonary metastases from colorectal cancer. PLoS ONE 6(11): e27086: doi: 10.1371/journal.pone.0027086

SCREENING

7. Music May Help Increase Polyp Detection Rate (Nov. 1/11)

This new study has revealed that listening to Mozart's music while performing colonoscopy may help physicians increase their detection rates of precancerous polyps. The study found adenoma detection rate increased when done with the music compared to without it. Adenomas are a type of colon polyp that is considered a precursor for invasive colorectal cancer (CRC). When detected early, polyps can be removed during a colonoscopy exam, preventing the development of colorectal cancer. In this randomized, controlled trial, two endoscopists each with experience completing at least 1000 colonoscopies, performed screening colonoscopies and were randomly assigned to music - where Mozart was played - or no music. Adenoma detection rates from this study were then calculated and compared to the baseline rates. "Both endoscopists had higher adenoma detection rates listening to music when compared with their baseline rates," said lead researcher Dr. O'Shea. "Adenoma detection rate is linked to a reduction in colorectal cancer incidence so it is an important quality indicator for colonoscopy." "Anything we can do to get those rates up has the potential to save lives." "While this is a small study, the results highlight how thinking outside the box - in this case using Mozart - to improve adenoma detection rates can potentially prove valuable to physicians and patients," he added.

Oshea and Wolf, Amer Coll of Gastro 2011 Annual Scientific Meeting. Poster #646. The Mozart Effect and Adenoma Detection.

8. Clear Liquids Before Colonoscopy?

(Nov. 5/11)

Normal preparation instructions for a colonoscopy call for clear liquids the day before the test. But this study questions whether or not they are really necessary for doctors to get clear view of the colon? A small randomized study reported in a poster at the American College of Gastroenterology 2011 Annual Scientific Meeting found that a full liquid diet including milk, yogurt, pudding, fruit and veggie juices — even ice cream — was just as good as a more restricted clear liquid diet in finding polyps. Doctors doing the exams didn't know which patients had clear liquids only and who got to eat a full liquid diet, but rated them equally effective in satisfactorily cleansing the colon. In addition, the number of patients where polyps were found wasn't different in the two diets. One patient on a clear diet wasn't able to finish the prep — which also included 2 liters of Moviprep. Researchers randomized 34 patients preparing for a colonoscopy the next day to either a traditional clear liquid diet or a full liquid diet that included milk, milkshakes, creamed soup, pudding, cream, fruit and vegetable juices, yogurt, and ice cream. Strangely, even with more food choices, there was no difference in patient satisfaction. The team of researchers concluded: "Our study demonstrates that a full liquid diet does not worsen bowel preparation, decrease the ability to detect polyps, or increase total colonoscopy time, when compared with a clear liquid diet. Patient's overall satisfaction scores were similar for full and clear liquid diets."

Gutkin, Ellen, et al., Full Liquid Diet vs Clear Liquid Diet for Colonoscopy Preparation: Preliminary Results. Poster #P412, ACG 2011, Scientific Meeting.

9. Colonoscopy Linked to Lower Risk for Proximal Colon Cancer

(Nov. 5/11)

The risk for both distal (left-sided) and proximal (right-sided) colorectal cancer (CRC) dropped after older patients had colonoscopy, according to results of a US study presented at the American College of Gastroenterology (ACG) 2011 Annual Scientific Meeting and Postgraduate Course. In contrast, flexible sigmoidoscopy was associated with a lower risk for distal, or left-sided, CRC only, researchers from the Mayo Clinic in Jacksonville, Florida, announced. This finding is the latest salvo in the ongoing battle to determine the best way to **screen** for colon cancer. The study's goal was to determine whether risk for colorectal cancer fell more after colonoscopy compared with flexible sigmoidoscopy or no lower endoscopy among older patients. The most surprising part is that the study showed that for colonoscopy, there is a risk reduction for the proximal colon. According to the investigators, previous studies did not show that. The analysis draws on Medicare patient data from 1998 to 2005. The results showed that upon follow-up, colorectal cancers were found in:

- 0.5% of the 12,266 patients who initially underwent colonoscopy;
- 1.0% of the 6402 patients who initially underwent flexible sigmoidoscopy; and
- 1.5% of the 41,410 patients in the control group, who did not undergo screening lower endoscopy.

"We do believe colonoscopy is still the preferred method to **screen** and prevent colon cancer," said Dr. Wang, who was the study's lead author. For the study, Dr. Wang and colleagues reviewed a sample of the national Surveillance, Epidemiology, and End Results (SEER) database for patients aged 67 to 80 years at first outpatient colonoscopy or flexible sigmoidoscopy between 1998 and 2002. They excluded patients with inflammatory bowel disease, history of polyps, or a family history of colorectal cancer. Hence, the study included the average risk patient. The study period was limited to allow a minimum of 3 years of follow-up after colonoscopy. The study sample was composed of patients who had a first colonoscopy, flexible sigmoidoscopy, or no lower endoscopy screening. About one third of the flexible sigmoidoscopies and two thirds of the colonoscopies were performed by gastroenterologists. All patients were followed until colorectal cancer was diagnosed, death, or December 31, 2005. Earlier studies on the relationship of colonoscopy to colon cancer reduction had mixed results, according to Dr. Wang. He notes that studies from Canada have indicated that colonoscopy reduces colon cancer by 40% — or the same rate as sigmoidoscopy — and suggested that colonoscopy did not reduce deaths from right-sided colon cancers. Dr. Wang noted that the Canadian data were based on **diagnostic**, not screening, colonoscopies. "So these patients who had diagnostic colonoscopies may be at a higher risk of cancer in the first place". For diagnostic colonoscopies, there was protection against distal colon cancer but not proximal colon cancer.

American College of Gastroenterology (ACG) 2011 Annual Scientific Meeting and Postgraduate Course. Abstract #12. Presented October 31, 2011.

PSYCHOSOCIAL

10. Fatigue Worsens During Chemo & Therefore Difficult To Deal With

(Nov. 10/11)

Swiss patients with lung cancer, breast cancer, colorectal cancer, or lymphoma were observed while they received chemotherapy over a 3 month period. Of the symptoms monitored, a lack of energy and feeling drowsy were the most frequent. For many, fatigue was present at the onset of treatment, but this increased significantly as they progressed through their treatments. The study results are important because coping with fatigue is difficult. Hearing of a study like this helps patients give themselves permission to feel the way they do. And it is equally important as well for loved ones of those with cancer

to understand that cancer fatigue isn't like ordinary fatigue. Accepting that chemotherapy-induced fatigue is unlike normal fatigue is the first step to helping the body recover from the treatment that has wreaked havoc on it. And, when loved ones can better understand cancer-induced and chemotherapy-induced fatigue, they can better assist in the cancer journey.

<http://lungcancer.about.com/b/2011/11/10/fatigue-worsens-during-chemotherapy.htm>

OTHER

11. **Researchers Find Link Between Bacterium and Colon Cancer** (Oct. 14/11)

Scientists at Dana-Farber Cancer Institute and the Broad Institute have found strikingly high levels of a bacterium in colorectal cancers, a sign that it might contribute to the disease and potentially be a key to diagnosing, preventing, and treating it. They report the discovery of an abnormally large number of *Fusobacterium* (a bacterium that causes gum disease and appendicitis) cells in nine colorectal tumor samples. While the spike does not necessarily mean the bacterium helps cause colorectal cancer, it offers an enticing lead for further research, the study authors say. The journal is also publishing a paper by researchers from the BC Cancer Agency and Simon Fraser University in Canada that reports similar findings from research conducted independently of the Dana-Farber/Broad Institute collaboration. A confirmed connection between *Fusobacterium* and the onset of colorectal cancer would mark the first time any microorganism has been found to play a role in this type of cancer. The discovery was made by sequencing the DNA within nine samples of normal colon tissue and nine of colorectal cancer tissue, and validated by sequencing 95 paired DNA samples from normal colon tissue and colon cancer tissue. Analysis of the data turned up unusually large amounts of *Fusobacterium*'s signature DNA in the tumor tissue. "Tumors and their surroundings contain complex mixtures of cancer cells, normal cells, and a variety of microorganisms such as bacteria and viruses," says the study's senior author, Matthew Meyerson, MD, PhD, of Dana-Farber and the Broad Institute. "Over the past decade, there has been an increasing focus on the relationship between cancer cells and their 'microenvironment,' specifically on the cell-to-cell interactions that may promote cancer formation and growth." While the relationship -- if any -- between colorectal cancer and *Fusobacterium* is unclear, there are intriguing hints that the bacterium may play a role in the cancer, says Meyerson. Previous studies have suggested that *Fusobacterium* is associated with inflammatory bowel diseases such as ulcerative colitis, which can raise people's risk of developing colon cancer. "At this point, we don't know what the connection between *Fusobacterium* and colon cancer might be," Meyerson observes. "It may be that the bacterium is essential for cancer growth, or that cancer simply provides a hospitable environment for the bacterium. Further research is needed to see what the link is." Researchers are embarking on comparison studies of *Fusobacterium* levels in larger numbers of patients with colorectal cancer and in those without the disease. Also planned are studies to determine whether the bacterium can be used to induce colon cancer in animal models.

Castellarin M, et al., Fusobacterium nucleatum infection is prevalent in human colorectal carcinoma. Genome Research, 2011; DOI: 10.1101/gr.126516.111

Kostic AD, et al., Genomic analysis identifies association of Fusobacterium with colorectal carcinoma. Genome Research, 2011; DOI: 10.1101/gr.126573.111

12. **Metformin May Reduce Colon Cancer risk in Type II Diabetes** (Oct. 17/11)

The investigators of this study maintain that treatment with metformin has been associated with a significantly lower risk for cancer cell growth, thereby reducing the risk for cancer overall. According to data from a recent meta-analysis, this effect continues in colorectal cancer among patients with type 2 diabetes treated with the drug. "The results indicate that metformin therapy was associated with an estimated reduction of 37% in the risk of colorectal cancer among patients with type 2 diabetes," the researchers write. Zhi-Jiang Zhang, MD, PhD, of the department of epidemiology and biostatistics in the School of Public Health at Shanghai Jiao Tong University in China, and colleagues pooled available studies on the effect of metformin on colorectal cancer among patients with type 2 diabetes. Five studies published from January 1966 to March 2011 that included 108,161 patients were identified. Metformin was associated with a significantly lower risk for colorectal neoplasm compared with non-metformin treatment. Zhang and colleagues excluded one study on colorectal adenoma, which left four studies containing 107,961 patients with diabetes and 589 incident colorectal cancer cases during follow-up. Again, they found that metformin was associated with a significantly lower risk for colorectal cancer. "If metformin therapy ultimately proves effective on reducing the risk of colorectal cancer, it would likely be recommended for the overwhelming majority of diabetes patients for both blood glucose control and cancer prevention," the researchers write. Further investigation into this correlation is warranted, they said.

Zhang, ZJ, et al., Reduced Risk of Colorectal Cancer With Metformin Therapy in Patients With Type 2 Diabetes A meta-analysis. Diabetes Care, 2011; 34: pp. 2323-2328.

13. **Erectile Dysfunction Common with Colorectal Cancer Treatment** (Oct. 18/11)

Erectile dysfunction is common after treatment for colorectal cancer, but "clinicians are inadvertently neglecting, misleading, and offending such patients," according to a small study from the United Kingdom. The results come from a detailed survey of 28 patients; it offers a "snapshot" of the impact of erectile dysfunction after treatment for colorectal cancer and shows that the problem is "poorly managed," according to the study author. Coordination of care of patients after treatment for cancer is universally challenging, the study author maintains. "More efficient methods are needed to rapidly triage patients with functional problems such as erectile dysfunction." "Managing the sequelae of treatment is an important aspect of care". In-depth interviews showed that erectile dysfunction caused profound distress for most of the men," they report. "The majority did not receive adequate information, diagnosis, or treatment." Some clinicians were dismissive of the problem, and there was evidence of ageism, the researchers report. For example, one man experiencing erectile dysfunction after treatment reported that his doctor told him: "At your age, I don't think it will matter." Clinicians should be aware that there is "considerable potential for offending older men by making assumptions about their sexual behavior or motivation," the researchers note. Other men complained that they had not been warned that it might be a problem, or that the information they had been given was inadequate. Another point for clinicians to bear in mind, the researchers add, is that phosphodiesterase type 5 inhibitors, such as *Viagra*, "are not a panacea." The third and last point they make is that "most men are not going to ask for help with erectile dysfunction." Hence, they suggest that a more tailored and coordinated approach to caring for these patients should be provided. "Colorectal cancer nurse specialists are well placed to give information, coordinate treatment, and monitor progress, but such an intervention needs to be developed and fully evaluated," they add. There is a paucity of data on the problem of erectile dysfunction after cancer treatment, notes the lead author. In colorectal cancer, the problem can be caused by damage to nerves during surgery or radiation. But chemotherapy, particularly newer agents associated with neurotoxicity, might also cause nerve damage, she notes. In addition, psychological factors can come into play; many respondents to the survey reported that their sexual desire was dampened by bowel dysfunction or having a stoma. The patient's partner is likely to play an important role in the sexual rehabilitation of these men with colorectal cancer, just as it has been shown to be important in prostate cancer, she adds. Better understanding of what causes the problem is crucial to developing effective interventions.

Temple, Larissa, et al., Men's experience of erectile dysfunction after treatment for colorectal cancer: qualitative interview study. BMJ. Published online October 18, 2011. 343doi: 10.1136/bmj.d5824

14. **Detecting Precancerous Colon Cells** (Oct. 20/11)

After demonstrating that light accurately detected pre-cancerous cells in the lining of the esophagus, Duke University bioengineers turned their technology to the colon and have achieved similar results in a series of preliminary experiments. This technology could be a non-invasive way for physicians to detect abnormal cells, or dysplasia, which have the potential of turning cancerous. These cells are in the epithelium, or lining, of various tissues, including the esophagus and **colon**. Current biopsy techniques require physicians to take many random tissue samples, and for some disorders of the colon, these procedures can be disfiguring and life-changing. Instead of taking tissue samples, the new system would aim short bursts of light from the tip of an endoscope at locations suspected of having disease. When light is directed at these tissues, it scatters. Researchers can collect and analyze that scattered light looking for the tell-tale signs of dysplasia. Significantly, the technique is noninvasive so no tissue is taken and no dyes or contrast agents are needed. In particular, they are trying to spot characteristic changes within the cells of the epithelium. In the case of pre-cancerous cells, the nuclei are misshapen and larger than normal cells, and they scatter light in their own unique way. The important thing for clinicians is being able to detect these changes in the nuclei in cells just below the surface, which might not be detected by just looking at the lining of the colon through an endoscope alone. The technology that developed for cancer detection is known as angle-resolved low coherence interferometry (a/LCI). In this process, light is shined into a cell and sensors capture and analyze the light as it is reflected back. The technique separates the unique patterns of the nucleus from the other parts of the cell and provides representations of its changes in shape. This approach could be the future of diagnosing dysplasia of the colon. The old-fashioned techniques used haven't changed in years. This could be a real game-changer in how they detect, characterize and even treat precancerous or cancerous lesions. For some gastrointestinal biopsies, the procedure itself has inherent risks such as bleeding or perforation, so a non-invasive technique could greatly improve a patient's quality of life. In their experiments, the Duke team used the device on samples of colon removed from 27 patients suspected to have colon cancer. The researchers then compared the results obtained from their device to the actual findings made by pathologists, and found that the overall accuracy of the device was 85%. Interestingly, the accuracy of the same technology was 86% when used during a recent clinical trial involving patients suspected of having Barrett's esophagus, a precursor to esophageal cancer. The study author said he believes the new approach could be especially useful for people with inflammatory bowel disease, since they tend to have a higher incidence of dysplasia in the colon. Since approximately 85% of all cancers begin within the layers of the epithelium in various parts of the body, the researchers believe that the new system could also work in such cancers as those of the trachea, cervix or bladder.

Migaly, John, et al., Detection of intestinal dysplasia using angle-resolved low coherence interferometry. Journal of Biomedical Optics, 2011; 16 (10): 106002 DOI: [10.1117/1.3631799](https://doi.org/10.1117/1.3631799)

15. Passed Gas May Yield Colorectal Cancer Clue (Oct. 20/11)

Studies by Japanese researchers on intestinal gas and its sulfur-containing compounds may help develop new measures to detect colorectal cancer by examining flatulence. The studies will likely save patients a lot of hardship — and medical bills. Screening for the cancer today is conducted through measures such as injecting a barium enema or inserting a colonoscope into the anus. A team led by Shinya Yagi, an associate professor of quantum engineering at Nagoya University, found through studying flatulence omissions of colorectal cancer patients that they are likely to have 10 times more of a gas element called **methyl mercaptan** than that of a healthy person. The research took 22 samples of intestinal gas from patients and 16 samples from those without cancer. Yagi and his team collected samples in special bags containing metal particles that were designed to absorb the consisting elements of gas. The collection bags were then taken to the Synchrotron Radiation Center at Hiroshima University for tests. The research revealed that cancer tumors secrete gaseous sulfur-containing compounds, and the amount of methyl mercaptan tended to grow for patients in later stages of colorectal cancer. The screening method is not yet ready for practical use since at this point it must undergo further testing to refine the methods. "The key thing to do is gather the gas first thing in the morning, when it is the most condensed. That will result in finer results. The amount of methyl mercaptan will not translate directly to the level of bad smell, because flatulence contains other elements that the human nose detects as the smell. Yagi said the idea for his study came through his research of exhaust gas, such as sulfur oxide. The specialist on nanoparticles was contacted by Nagoya-based dentist Kazue Yamagishi, who was studying the correlation between periodontal disease and foul breath. The answer was blowing in the wind for both of their projects. Yagi teamed up with Yamagishi and they began their study in 2005. Their effort was published in GUT, a specialist English medical journal about the digestive system in August this year titled "Generation of gaseous sulfur-containing compounds in tumor tissue, and suppression of gas diffusion as an antitumor treatment." Nature Review magazine followed it up with an article on Yagi and Yamagishi in October. According to the U.S. National Cancer Institute, the cause of colorectal cancer, in which cells in the colon or rectum form a tumor, is still unknown. But studies have shown that factors such as age, family history, diet and smoking come into play for one's chances of developing the disease. Yagi told The Japan Times that proving the correlation between flatulence and cancer scientifically had to go through a variety of procedures, including using laboratory rats. Naturally, it was also challenging to convince cancer patients to release intestinal gas into a bag. "We got mixed reactions from the patients and their families as well. Many thought we were joking to be asking them to do such a thing," Yagi said. Pundits say the technology could eventually be applied to other cancer screenings, including detection of lung cancer from a patient's breath.

<http://www.japantimes.co.jp/text/nn20111022a2.html>

16. Neurogenesis May Be Indicative of Poor Outcomes (Oct. 24/11)

Neurogenesis is the formation and development of nerve cells and according to this study, it is associated with colorectal cancer progression and, therefore, may be predictive of poor outcomes for patients. The investigators identified 50% reductions in five-year overall survival and disease-free survival for patients whose tumors exhibited high degrees of neurogenesis compared with those whose tumors contained no detectable neurogenesis. Significantly greater reductions in five-year overall and disease-free survival were seen in patients with stage II disease and high degrees of neurogenesis, than in lymph node-negative patients with no neurogenesis. Significantly lower five year overall and disease-free survival was found in patients with stage II disease and high degrees of neurogenesis, than those with stage III disease with no neurogenesis. Neurogenesis was stimulated in colorectal cancer cells and there was evidence of neuroepithelial interactions between nerves and tumor cells in vitro. The researchers concluded: "Neurogenesis is indicative of poor survival and recurrence and is an independent prognostic factor for poor outcomes in colorectal cancer".

Albo, Daniel, et al., Neurogenesis in colorectal cancer is a marker of aggressive tumor behavior and poor outcomes. Cancer. November 2011. Vol. 117, Issue 21: pp. 4834-4845.

NUTRITION & HEALTHY LIFESTYLE

17. Dietary Patterns May be Linked to Colorectal Cancer in Women (Oct. 24/11)

According to the results of this study, researchers may have found a specific dietary pattern linked to levels of C-peptide concentrations that increase a woman's risk for colorectal cancer. High red meat intake, fish intake, sugar-sweetened beverage intake, but low coffee, whole grains and high-fat dairy intake, when taken as a whole, appeared to be associated with higher levels of C-peptide in the blood. C-peptide is a marker of insulin secretion that can be measured in a person's blood. High levels of insulin may promote cell growth and multiplication. One of the major characteristics of cancer is aberrant cell growth. Higher levels of C-peptide, and, therefore, insulin, may promote cancer cell growth. Colon cancer seems to be one of the cancers that are sensitive to insulin. This research has helped to put together a fuller picture of what may be going on in terms of mechanisms and the relationship between

food and colorectal cancer risk. Researchers surveyed a sample of women every two years about general health information including whether or not they had been diagnosed with colorectal cancer. The researchers also assessed women's diets in a separate questionnaire mailed to them every four years. The dietary questionnaire listed more than 130 types of foods and asked the women how often they were consuming each type. After 22 years of follow-up, 985 cases of colorectal cancer and 758 cases of colon cancer were diagnosed among the women. The researchers found that those women who most often consumed high amounts of **red meat, fish and sugar-sweetened beverages** and low amounts of **high-fat dairy, coffee and whole grains** had a 35% increased risk for colorectal cancer. The researchers also compared the dietary information of women who were lean and active with that of women who were overweight and sedentary. They found that people who were overweight or inactive seemed more sensitive to this dietary pattern. Their risk for colorectal cancer was much higher than those people who were lean and active. Overweight people are already at risk for insulin resistance. The researchers think that if you then add this unique dietary pattern on top of that, which was associated with higher C-peptide levels, they are much more prone to develop colorectal cancer. People should pay attention to the foods they consume for a multitude of health reasons. Although avoiding the dietary patterns that the researchers found is not necessarily the most comprehensive way to prevent colorectal cancer, it definitely targets one pathway of the disease.

American Association for Cancer Research (2011, October 24). Dietary patterns may be linked to increased colorectal cancer risk in women. <http://www.aacr.org/home/public--media/aacr-in-the-news.aspx?d=2511>

18. **Hot Dogs May Not Be Linked to Colon Cancer** (Oct. 26/11)

A U.S. government requirement that vitamin C or one of its close relatives be added to hot dogs, to reduce the amount of nitrites found in this popular food, may not have lowered the rate of colon cancer cases after all, a new study suggests. Back in 1978, the U.S. Food and Drug Administration mandated that the meat industry include vitamin C (ascorbate) or its close cousin, erythorbate, in hot dogs to offset the amount of nitrites. Nitrites are added to cured, processed meats such as hot dogs to enhance their flavor and color, and to extend their shelf life. The problem is that during the cooking process, nitrites combine with amines in meat to form cancer-causing nitrosamines. Since vitamin C was added to hot dogs, the researchers found that there has been a sharp drop in the number of people who die from colon cancer, but the **incidence of colon cancer has not changed that much**. The amount of nitrites in hot dogs was reduced as a result of these changes. But, if it were true that these changes reduced risk for colon cancer, it possibly should have been evident by now, researchers maintain. It's not. The decrease in death rate from colon cancer was likely due to earlier detection and improved treatment, not changes in the nitrite content of hot dogs. The hot dog issue is a tough one to study, the researchers claim. "Not everyone eats a ton of hot dogs, so it is a difficult risk factor to control for. Nitrites are probably bad and cause all sorts of problems, but colon cancer may not be one of them."

American Association for Cancer Research (2011, October 24). Could Additives in Hot Dogs Affect Incidence of Colon Cancer? <http://www.aacr.org/home/public--media/aacr-in-the-news.aspx?d=2512>

19. **More Evidence That Obesity is Tied to Colon Cancer?** (Nov. 3/11)

According to the results of this study, older adults who are heavy, especially around the middle, appear to have a higher risk of developing colon cancer than their thinner peers. The findings add to evidence that obesity is a risk factor for colon cancer. They also suggest that exercise could be an important part of the picture, particularly for women. The study included more than 120,000 Dutch adults ages 55 to 69 who were followed for 16 years. During that time, approximately 2% developed colorectal cancer (tumors of the colon and/or rectum); most were diagnosed with colon cancer. The risk, researchers found, was 25% higher for men who were significantly overweight or obese at the outset, versus normal-weight men. And waist size appeared to matter most: Men with the biggest bellies -- gauged by their self-reported "trouser size" -- had a 63% greater risk of colorectal cancer than men who were trimmest around the middle. The findings were more complex among women, though. A large waistline was only linked to a higher cancer risk in women who also got little exercise (less than 30 minutes per day). Women who topped a "44" in pants size and got little exercise were 83% more likely to develop colon cancer than women who had smaller waistlines and exercised more than 90 minutes per day. (A "44" in Europe translates to about a size 16 in the U.S.) The study "provides further evidence that excess body fat may contribute to a higher risk of colorectal cancer," lead researcher states. "It is important to maintain a healthy body weight throughout life, as this may lower your risk of colorectal cancer". "It also makes sense that excessive abdominal fat would be particularly linked to the disease. Studies have tied abdominal obesity to other health conditions, like diabetes and heart disease. And belly fat seems to be particularly linked to chronic, low-level inflammation in the body, the researchers explain. That inflammation is thought to be involved in a number of disease processes. One of the most intriguing observations was that abdominal fat was associated with colorectal cancer in women only when combined with low exercise levels. It's not clear why that might be, or why the pattern was seen only in women, but the finding hints that calorie balance -- how much you take in through food, and how much you burn through exercise -- may be important. Hence, women should focus on maintaining a healthy lifestyle rather than simply paying attention to what the scale says.

20. American Ginseng Combats Colon Cancer (Nov. 17/11)

According to the results of this study, researchers have discovered that American ginseng may be a potential therapeutic agent in preventing colon cancer. The study authors fed mice a Western diet of 20% fat, either in combination with 250-ppm American ginseng or without. What they found was that American ginseng significantly inhibited inflammation of the colon and tumor growth promoted by the Western diet. Researchers observed that mice fed the high fat diet and American ginseng experienced a reduction in the spread of tumors and increased apoptosis – programmed cell death – as opposed to the mice that received no ginseng. Apoptosis is essential in health because of its role in eliminating old, unhealthy and unnecessary cells. When apoptosis does not work correctly, disease can occur, including cancer. This study is the first to report that an extract of ginseng can inhibit development of tumors in the colon even when a Western diet is consumed. The study authors concluded that, “Further study of this promising natural agent for chemoprevention of colon cancer is warranted.”

About Ginseng:

Ginseng is a slow growing herb, which consists of a light colored root, a single stalk and long oval green leaves. Ginseng contains complex carbohydrates called saponins or ginsengsines. It possesses anti-inflammatory, antioxidant, and some believe may have anti-cancer elements.



Source: <http://www.disabled-world.com/artman/publish/ginseng.shtml>

Dougherty U, et al., American ginseng suppresses Western diet-promoted tumorigenesis in model of inflammation-associated colon cancer: role of EGFR. BMC Complement Altern Med 2011 Nov 9; 11(1):111.

21. Fiber From Whole Grains Can Cut Colorectal Cancer Risk (Nov. 17/11)

Researchers from Britain and the Netherlands found that the more total dietary fiber and cereal fiber people consumed, the lower their colorectal cancer risk. For example, people who consumed an extra 90 grams of fiber from whole grains a day, also had a 20% lower risk of colorectal cancer. However, these researchers didn't find that getting extra fiber from vegetables or fruits was linked with the decreased colorectal cancer risk, which means that there might be something else in the whole grains at work, too. Researchers reviewed the results of 25 studies that included nearly 2 million people. They found that for each additional 10 grams of total dietary fiber and cereal fiber consumed a day, the person's colorectal cancer risk decreased by 10%.



Study researcher Dagfinn Aune claimed that even if a person starts off with a low level of fiber consumption -- say, 5 grams a day -- and increase it by 10 grams -- to 15 grams a day -- that could still be beneficial at lowering colorectal cancer risk. This study highlights the importance of a diet rich in fiber. Soluble fiber is most helpful in improving colon transit times. As the contents of the colon move at a better rate, there is thought to be less toxic exposure to the interior of the colon thereby reducing risk of developing colon cancer.

Aune, Dagfinn, et al., Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. BMJ 2011;343doi: 10.1136/bmj.d6617(Published 10 November 2011)

22. Study Shows Aspirin Prevents Colon Cancer (Nov. 18/11)

High-risk colon cancer can be added to the list of diseases for which aspirin may have a protective effect, based on the results of a recent study. The study was conducted in Britain and it followed 861 people with a known genetic predisposition to colorectal cancer, a condition known as Lynch Syndrome. This

condition accounts for 3-5% of colon cancer cases and affects 1 in 1,000 people in the general population. The randomized control trial consisted of two groups:

- one group that took 600 milligrams of Aspirin – which is equivalent to two regular strength Aspirin-
- the other group received placebo pills full of starch.

The protective effect became apparent in five years in the group that took Aspirin. One of the study authors commented: “If you give two Aspirin a day for two years to people with hereditary bowel cancer, then after five years their cancer risk would be reduced by more than half.” This will change the current course of treatment for those with a genetic predisposition. It must be noted that this study is only proven in those with Lynch syndrome. Dr Des. Leddin, a gastroenterologist, advised that before going on the Aspirin regimen, patients should talk to their physicians since the risk of daily use includes stomach bleeding and stroke. Asad Umar, a cancer prevention expert at the U.S. National Cancer Institute said, “We’re not ready to say Aspirin is useful for the general public...There are still a lot of toxicity concerns.” Further investigation may research if Aspirin has any protective effect on those without any type of family history of colon cancer.

Burn, John, et al., Long-term effect of aspirin on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomized controlled trial. The Lancet. Early Online Publication. 28 October 2011. doi:10.1016/S0140-6736(11)61049-0