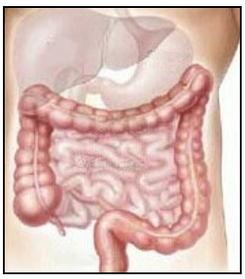
COLORECTAL CANCER RESEARCH

Month Ending December 17th, 2010



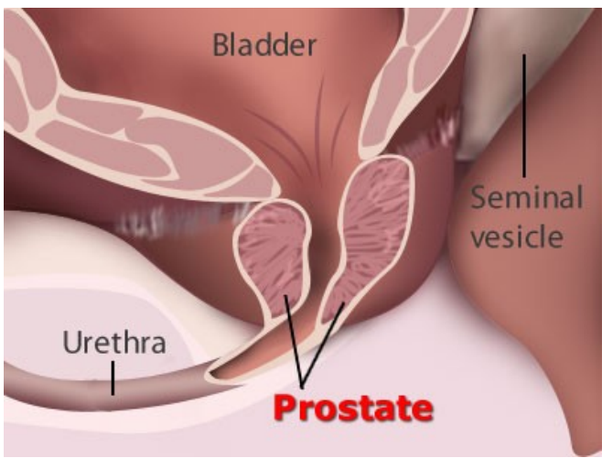
The following colorectal cancer research update extends from November 20 – December 17, 2010 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Prostate Cancer Hormone Treatments May Increase Risk of Colorectal Cancer (Nov. 22/10)

A large, retrospective population study suggests that prostate cancer treatments that lower male sex hormones may increase the risk of colorectal cancer. Men treated with gonadotropin-releasing hormone (GnRH) agonists or surgical removal of their testicles (orchiectomy) to lower their testosterone and PSA levels experienced an increased risk of colorectal cancer of about 20 to 40%. More than half of nearly 108,000 prostate cancer patients identified in the study received androgen deprivation therapy between 1993 and 2002. Approximately 90% of those men had been treated with GnRH agonists, and the rest had had orchiectomy. They were followed for about 5 years after their prostate cancer diagnosis. The researchers found a dose-response effect for GnRH agonists in which colorectal cancer risk increased with longer duration of treatment.



Location of the Prostate Gland in the human male.

Source: http://www.topnews.in/health/diseases/prostate-cancer

Most GnRH/LHRH are administered via injection

Source: http://www.ehow.com/about_5474293_prostate-cancer-hormone-therapy-drugs.html

Compared with prostate cancer patients who received no hormone treatments, those who had GnRH agonist therapy for 13 to 25 months had a 19% increase in colorectal cancer risk, those who had GnRH agonist therapy for longer than 25 months had a 31% increase in risk, and those who had orchiectomy had a 37% increase in risk. According to the lead author, an inverse association between androgen levels and colorectal cancer risk is biologically plausible. Androgen receptors are present in both normal and malignant human colonic tissues, and in various animal studies, administration of androgens protects against colon carcinogenesis, whereas androgen ablation promotes it. The authors went on to say that their evidence "may have broader implications beyond the field of prostate cancer" because nearly half a million men in the United States develop androgen deficiency each year".

Shahinian, VB, et al., risk of colorectal cancer in men on long term androgen deprivation therapy for prostate cancer. J Natl Cancer Inst. 2010 Dec.1; 102(23): 1760-70

2. DCA May Be Problematic for The Treatment of Colorectal Cancer (Nov. 22/10)

According to the results of this study from the University of Guelph, a do-it-yourself cancer treatment that many patients have ordered through the Internet can actually encourage growth in colorectal tumours. Dichloroacetate, or DCA, has been used for years to treat rare metabolic disorders, but became a potential wonder drug three years ago after researchers at the University of Alberta discovered it also

offered a new way to target tumour cells.

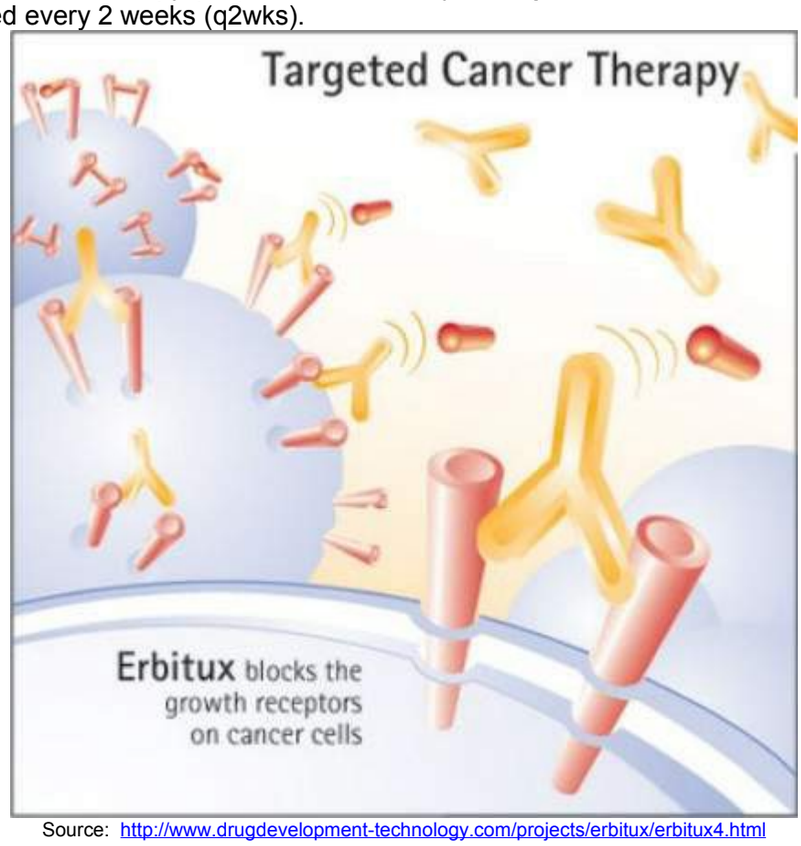
As the scientists scrambled to find money to test DCA in humans, hundreds of patients ordered the white powder over the Internet, ignoring warnings that it might harm them. A recent study showed it may be effective against brain cancer, but now there's evidence from Guelph that it doesn't work against colon cancer. Under normal conditions, DCA killed some cancer cells. But when levels of oxygen were reduced, as is often the case in tumours, it was not effective. And in some cases, tumours treated with DCA grew more than those that weren't. According to the lead author, DCA may well turn out to be an effective treatment in some cases, but it's not necessarily safe in all cases. There are people out there buying this drug off the Internet and self-medicating, (and) who knows what's going on in their tumour. They might actually be making it worse, according to the authors. Getting funding to study DCA is complicated by the fact that it can't be patented as a new drug because it's been around for three decades. After the University of Alberta's Evangelos Michelakis discovered that it shrank several types of tumours in rats without harming healthy tissue, he couldn't get any pharmaceutical companies to invest

the money needed to bring it to market as a cancer treatment. The university raised $200,000 to do the small trial with patients who had an aggressive form of brain cancer. At the time of the initial discovery, Michelakis said: "This is the Holy Grail of cancer therapeutics — how to kill cancer cells and spare normal ones." Conventional chemotherapy targets fast-growing cells and kills both cancerous and normal tissue, which is why patients often lose their hair and suffer other debilitating side effects. It also held the promise of treating many different types of cancer because it exploits a metabolic pathway common to most cancerous cells. The bottom line is that cancer is not a single disease, so it's unrealistic to expect a single drug to be a 'magic bullet' that's effective against every type of cancer, authors maintain. Michelakis and his colleagues have stressed that patients should not self-medicate with DCA. They have warned that DCA ordered over the Internet may contain dangerous impurities and is often sold in a highly acidic form that could cause "catastrophic" complications. It also could interact with other drugs patients are taking to treat cancer.

Coomber, Brenda, et al., Sodium dichloroacetate (DCA) reduces apoptosis in colorectal tumor hypoxia. Cancer Letters. Vol 297, Issue 1, pp. 75-83.

3. Erbitux Administered Every Two Weeks in Advanced Colorectal Cancer (Nov. 23/10)

Cetuximab, more commonly referred to as erbitux, has been approved using a weekly schedule, alone or in combination with chemotherapy (CT). However, many CT regimens in metastatic colorectal cancer (CRC) are delivered every 2 weeks (q2wks).



Source: http://www.drugdevelopment-technology.com/projects/erbitux/erbitux4.html

Preliminary data suggested that a simplified schedule using cetuximab every two weeks, 500 mg/m² , would be equivalent to the standard weekly administration. Medical data of all patients with advanced colorectal cancer who received cetuximab every two weeks were retrospectively collected and checked for consistency by an independent monitor in 4 European centers. Ninety-one patients were treated between 2005 and 2007 when the K-RAS mutational status of tumors was not determined routinely. They received a median of 4 (0–5) previous drugs, including previous weekly cetuximab in 38.5% of patients. Cetuximab every two weeks was associated with an irinotecan-based regimen in 85.7% of patients. The median number of cetuximab administrations was 6 (1–23). In the 84 patients beyond first-line therapy, response rate was 29.3%. The median progression-free survival was 3.0 months (range 2.2–3.8), and median overall survival was 9.0 months (range 6.2–11.8). According to researchers, cetuximab every two weeks appears safe and effective in heavily pretreated patients and convenient in combination with biweekly CT schedules.

Bouchahda, M., et al., Feasibility of cetuximab given with a simplified schedule every 2 weeks in advanced colorectal cancer: a multicenter, retrospective analysis. Medical Oncology. Doi: 10.1007/s12032-010-9716-8

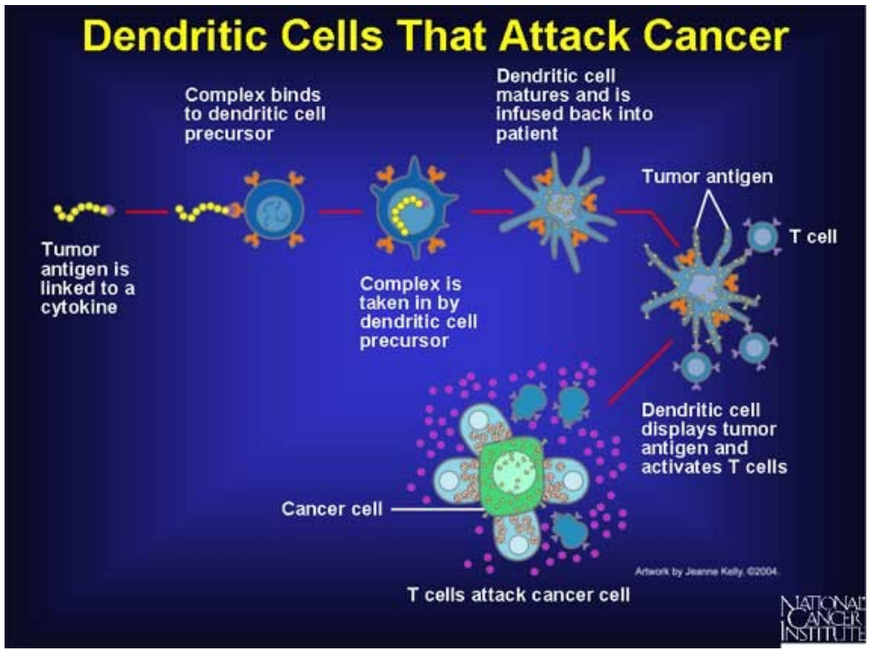
4. Using Patients' Own Tumour Cells to Create Effective Cancer Vaccine (Nov. 24/10)

Doctors at Dartmouth-Hitchcock Medical Center in New Hampshire have built personalized cancer vaccines that use the patient's own immune system to fight colorectal cancer. The key to success was first removing bulky liver tumors and then using the vaccine to kill any tiny cancers remaining in the body. Five years after getting the vaccine, two-thirds of patients whose systems produced an immune response to the vaccine were alive and cancer free. Following surgery to remove colorectal cancer that had spread to the liver, patients received a vaccine, made just for them, that combined dendritic cells (see explanation below) from their blood with protein from their tumor. Dendritic cells are part of the immune system. Their role is to recognize foreign bodies, such as viruses or bacteria, and trigger a response

from other immune cells that surround and destroy invaders. However, since cancers are not recognized as “foreign”, they aren’t easily attacked by the immune system. A goal of cancer research has been to trick the immune system into seeing cancers as targets to be destroyed. But previous dendritic cell research hasn’t been successful in reducing large tumors. The reason: The small number of T-cells that are generated by a vaccine can’t destroy a large tumor. However, what they may be able to do is search out and destroy tumor cells that exist as only microscopic tumor deposits. Once patients were brought into a measurable tumor-free condition with surgery, the anti-tumor T-cells induced by the DC vaccine may help keep them that way. Dr. Barth, lead investigator, operated on 24 colorectal cancer patients to remove tumors that had spread to their livers. About a month later they received the vaccine. Fifteen of those patients (63%) had an immune response to the vaccine. The patients who showed immune response were much more likely to be alive and cancer-free five years after treatment. Sixty-three percent (63%) of them had not had cancer return compared to only 18% of those who didn’t have a response. The vaccine is non-toxic, compared to chemotherapy, which may have serious side effects. Talking about the future of dendritic cell research, Dr. Barth said, “ It’s your own immune system doing the fighting. I’m optimistic that this really will have an impact.”

Dendritic Cell Therapy:

An approach to cancer therapy takes advantage of the normal role of the dendritic cell as an immune educator. Dendritic cells grab antigens from viruses, bacteria, or other organisms and wave them at T cells to recruit their help in an initial T cell immune response. This works well against foreign cells that enter the body, but cancer cells often evade the self/non-self detection system. By modifying dendritic cells, researchers are able to trigger a special kind of autoimmune response that includes a T cell attack of the cancer cells. Because a cancer antigen alone is not enough to rally the immune troops, scientists first fuse a cytokine to a tumor antigen with the hope that this will send a strong antigenic signal. Next, they grow a patient's dendritic cells in the incubator and let them take up this fused cytokine-tumor antigen. This enables the dendritic cells to mature and eventually display the same tumor antigens as appear on the patient's cancer cells. When these special mature dendritic cells are given back to the patient, they wave their newly acquired tumor antigens at the patient's immune system, and those T cells that can respond mount an attack on the patient's cancer cells.



Source: ***http://www.cancer.gov/cancertopics/understandingcancer/immunesystem/Slide34***

Barth, Richard, et al., A randomized trial of ex vivo CD40L activation of a dendritic cell vaccine in colorectal cancer patients: tumor specific immune responses are associated with improved survival. Clinical Cancer Research, vol. 16, Number 22: 5369

5. Guiding Treatment in Stage II Colon Cancer (Nov. 29/10)

For people with stage II colon cancer, it's difficult for doctors to sort out who can benefit most from adjuvant chemotherapy (chemotherapy administered after surgical removal of the primary tumour). With stage I disease, the tumor is smaller and has not spread beyond the inside of the colon. Many people with stage I disease can be treated with surgery alone. With stage II disease, however, the tumor has begun to spread into the wall of the colon. The surgeon can remove the entire tumor that they can see. But, once the tumor spreads into the muscle wall of the colon, there's always a possibility that a few cancer cells have already escaped. In these cases, chemotherapy would be necessary to ensure the best chances of not having the cancer come back. Unfortunately, doctors don't always know if a person has the type of stage II colon cancer that has likely spread beyond the colon. Chemotherapy is lifesaving for many people, but it comes with a number of side effects. If a person can be cured without those side effects that is the option doctors would like to offer their patient. This conundrum - determining which patients with stage II colon cancer need chemotherapy and which don't - has led researchers to seek better ways to identify who can benefit most from the more aggressive treatment. Hence, the development of the coloprint gene expression signature. Researchers gathered colon cancer tissue samples from 188 people and scanned for genetic changes that appeared in each person's tumor. By plugging these results into a sophisticated computer program, the researchers identified a set of 18 genes that can be used to predict which patients with stage II colon cancer are more likely to relapse (have cancer come back). This

information will tell us who can benefit more from chemotherapy treatment and who is likely to have effective treatment with surgery alone. In patients with stage II colon cancer, those who had a specific "signature" of genetic changes in the 18 genes in their colon cancer cells were 3.34 times more likely to relapse (have cancer return) than patients whose colon cancer cells did not show this signature of gene changes. This is extremely valuable information. If a patient doesn't have the gene signature indicating cancer that is more likely to come back, chemotherapy would not be prescribed to them following surgery. Nobody wants to take these very powerful and potentially toxic medications if they don't need to. But if doctors knew it could save your life, it would make the decision to get chemotherapy a lot easier to make. This test will help people weigh the pros and cons of certain treatment options. One of the most difficult things for oncologists to determine is which people can benefit most from chemotherapy and who would be better off without it. The coloprint test is an objective way to help doctors know who to treat more aggressively with chemotherapy, and for whom surgery alone is enough.

Salazar, Ramon, et al., Gene expression signature to improve prognosis prediction of stage II and III colorectal cancer. J Clinical Onc, Published online before print November 22, 2010, doi: 10.1200/JCO.2010.30.1077 JCO November 22, 2010 JCO.2010.30.1077

6. 2010 Advances for the Treatment of Colon Cancer (Nov. 26/10)

2010 has brought several promising results in the fight against cancer. Among these advances is a better understanding of the genetic underpinnings of colon cancer and how best to treat it. Targeted therapies (see below) are the future of cancer treatment and this applies to colon cancer as well. Targeted therapies focus on blocking the part of cellular processes that are abnormal in cancer cells, but that are not altered in healthy cells. This increases the chances that you can treat the cancer without as much damage to normal tissues in the body. Less damage, hopefully, leads to fewer treatment side effects. Within the last couple of years, doctors have begun to consider the genetics of each person's colon cancer cells to decide how to treat each person most effectively. This is the first step in effective use of targeted therapies. KRAS (see below) refers to a gene that can be altered (mutated) in colon cancer cells. Studies show that if this alteration (mutation) is present, the targeted therapy medications cetuximab (Erbitux®) and panitumumab (Vectibix®) are not as effective and should not be used. These targeted therapies can be lifesavers, but only for people who do not have the KRAS genetic mutation in their colon cancer. One notable colon cancer advance of 2010 is research showing that another gene mutation, called BRAF (see below), also plays a role in determining who can benefit from targeted therapies. The study found that people who do not have the BRAF mutation (or the KRAS mutation) in their colon cancer cells benefit the most from cetuximab treatment. A second notable advance in colon cancer treatment focused on what BRAF tells us about prognosis, or a person's expected course of disease. For people who have relapsed (had cancer come back) after treatment for stage II and III colon cancer, BRAF can help determine who is likely to have more aggressive disease, which will affect their overall survival. This might seem somewhat insignificant, but it's very important. Understanding who is more likely to have aggressive disease can help researchers determine how best to treat them to improve survival. If everyone is lumped together, regardless of the different characteristics of their colon cancer cells, it's more difficult to determine how best to treat each individual person. And individualized treatment tailored to each unique person's cancer is the ultimate goal. Treatment that is highly individual to each situation is more likely to be effective and may be less likely to cause toxic side effects.

Targeted Therapies:

Targeted therapies interfere with carcinogenesis. Carcinogenesis means cancer development, or the pathway that takes a cell from normal to cancerous. Examples of targeted therapies include growth factor receptor blockers, angiogenesis inhibitors, apoptosis-inducing medications, monoclonal antibodies, and cancer vaccines. For an example of how a targeted therapy might work, you can think about apoptosis, which is the "programmed cell death" that prevents most damaged cells from becoming cancerous in the first place. Cancer cells have figured out how to avoid apoptosis; a targeted therapy would block the chemical changes that allow cancer cells to avoid apoptosis. The cancer cells then die. Other examples include targeted therapies that block growth factors in cancer cells and therapies that block the cancer cells' ability to form vessels for its own blood supply, a necessary step for any tumor to keep growing. There are many different ways that targeted therapies "target" just the changes that make a cancer cell cancerous.

KRAS:

KRAS refers to a gene that can be altered (mutated) in colon cancer cells. Studies show that if this alteration (mutation) is present, the anti-EGFR medications cetuximab (Erbitux®) and panitumumab (Vectibix®) are not as effective and should not be used. This is good news, because it points the way toward the future in which we will see more personalized cancer care. If genetic testing of a person's cancer cells can provide useful information, treatment plans can be tailored to better meet each person's needs.

BRAF:

A gene that makes a protein called B-RAF which is involved in sending signals in cells and in cell growth. This gene may be mutated (changed) in many types of cancer, including colorectal cancer, which causes a change in the B-RAF protein. This can increase the growth and spread of cancer cells.

http://coloncancer.about.com/b/2010/11/26/notable-colon-cancer-advances-2010.htm

7. COX-2 Inhibitors for Hand and Foot Syndrome Resulting from Xeloda (Nov. 29/10)

Hand-foot syndrome (HFS) is a common adverse event that can be induced by capecitabine better known as xeloda. Authors hypothesized that capecitabine- based chemotherapy can cause over

expression of COX-2 in tumor and healthy tissue, which finally induces HFS in hands and feet. Based on this, they believed that a selected COX-2 inhibitor (celecoxib) could ease HFS. Researchers designed a prospective clinical study to test this hypothesis. From August 2008 to January 2010, 110 patients with stage II/III colorectal cancer who were eligible for adjuvant chemotherapy (chemo administered after surgical removal of the primary tumour) were enrolled in the study and divided into 4 groups by random. There were sixteen patients in the capecitabine group, and fifteen patients in the capecitabine and celecoxib group. Thirty-four patients were in XELOX (capecitabine plus oxaliplatin) group, and thirty-six patients in XELOX+ celecoxib group. All 101 patients finished chemotherapy and follow-up interviews. The group that had received capecitabine and celecoxib had ***a significantly reduced frequency of >grade 1 hand-foot syndrome (29 vs. 72%), and >grade 2 (11.76% vs. 30%***). Five patients experienced grade 3 HFS in capecitabine group and only 1 patient had grade 3 HFS in capecitabine and celecoxib group. There were 5 patients in capecitabine group who refused to go on chemotherapy because of HFS, but there was none in capecitabine and celecoxib group. From the results of this study, researchers learned that celecoxib could reduce HFS that was induced by capecitabine. They, therefore, recommend that celecoxib can be used in capecitabine-based chemotherapy.

Table 1. Patient Management of Hand-Foot Syndrome: Capecitabine Related

Grade	Clinical Feature	Functional Status	Suggested Interventions
1	Numbness, **paresthesia**, **dysesthesia**, tingling, painless swelling or erythema of the hands and/or feet	Activities of daily living generally unaffected	Call nurse or doctor when symptoms first appear. Do not "wait and see." **Skin care:** § Reduce friction and pressure: kneeling for long periods of time; leaning on elbows; power walking, jogging, or regular walking for long periods of time; using hand tools; gardening § Wear sunscreen; avoid exposure to heat § Use mild soap to bathe; pat (don't rub) skin dry § Keep shower and bath water lukewarm to cool; avoid hot tubs and long exposure to hot water § Keep skin moist; gently apply moisturizing creams or topical emollients. Apply at night and wear loose-fitting cotton gloves; avoid rubber ones (dishwashing gloves), since they retain heat § Put hands and feet in cool water to relieve symptoms **Clothing:** § Wear comfortable, loose-fitting clothes, shoes, and gloves § Do not go barefoot; wear shoes or slippers when possible
2	Painful erythema and swelling of the hands and/or feet, skin remains intact	Activities of daily living more difficult	
3	Moist desquamation, ulceration, blistering, or severe pain of the hands and/or feet, tissue breakdown	Activities of daily living interrupted: unable to work; difficulty walking and using hands	

Source: http://www.managecrc.com/articles/ArticleReader.aspx?article=215&page=1

Zhang, Rong-Xin, et al., The effect of cox-2 inhibitor on capecitabine-induced hand-foot syndrome in patients with stage II/III colorectal cancer: a phase Ii randomized prospective study. J of Cancer Research and Clinical Oncology. Doi: 10.1007/s00432-010-0958-9

8. Intermittent vs. Continuous Chemo in Advanced Colorectal Cancer (Dec. 6/10)

In advanced colorectal cancer, chemotherapy is usually administered without pauses and until progression but patients can experience cumulative toxicity and cannot tolerate a heavy therapeutic charge. The aim of the present trial was to evaluate whether an intermittent chemotherapy with levo-leucovorin + 5-fluorouracil (5-FU) + irinotecan (CPT-11) [commonly referral to as folfiri] was at least as effective as the same regimen given continuously, both administered until progression, in patients affected with advanced colorectal cancer and not previously exposed to chemotherapy for metastatic disease. A total of 337 patients from 27 institutions were randomized between intermittent and continuous administration of folfiri, until progression in both groups. The main end point that was being measured was overall survival (OS), the secondary was progression-free survival (PFS) and finally toxicity. At a median follow-up of 41 months, OS was 18 months in arm A and 17 months in arm B. Also PFS (time before the disease got worse) was comparable in the two groups (6 months in both), and even grades 3-4 toxicity (mainly myelosuppression, fever and diarrhea) was similar. Second-line oxaliplatin-based treatment was administered in a similar percentage (66%) in the two arms. The median chemotherapy-free period (drug holiday) in arm A was 3.5 months. Researchers concluded that reducing the charge of therapy in this population did not diminish the efficacy of treatment. Further studies with this strategy, including biologics, are warranted.

Labianca, R, et al., Intermittent versus continuous chemotherapy in advanced colorectal cancer: a randomized "GISCAD" trial. Ann Oncol. 2010 Nov. 15 (Epub ahead of print).

9. Discontinuation of Avastin Does Not Worsen Disease Course (Dec. 15/10)

Bevacizumab (better known as avastin) is an antiangiogenic agent that inhibits vascular endothelial growth factor (VEGF) activity – controlling the growth of the tumour's blood vessels. Although bevacizumab is effective against several types of solid tumors, there is concern, based on preclinical studies, that cessation of bevacizumab treatment may result in more aggressive tumor growth, invasion, and metastasis due to a rebound effect. To investigate the likelihood of rebound after cessation of bevacizumab, this study used data from randomized placebo-controlled phase III clinical trials to evaluate clinical outcomes following discontinuation of treatment due to adverse events (AEs). There were no significant differences in mortality rates or progression outcomes among patients who discontinued bevacizumab vs those who discontinued placebo. This was a retrospective analysis of data from five multicenter, randomized, double-blind, placebo-controlled, phase III clinical trials of bevacizumab in patients with metastatic renal cell carcinoma, metastatic pancreatic cancer, metastatic breast cancer, and **metastatic colorectal cancer**. Patients who discontinued bevacizumab or placebo treatment due to AEs other than disease progression were compared. A total of 4205 patients were included. No significant difference between the two groups was observed from the time of discontinuation to progression or death, either in the individual studies or the pooled data Contrary to expectation, this study did not find any significant difference in mortality or disease progression when comparing patients who discontinued bevacizumab and those who discontinued placebo.

Miles, D, et al., Disease course patterns after discontinuation of bevacizumab: pooled analysis of randomized phase III trials. J Clin Oncol. 2010 Nov. 22; Epub ahead of print.

10. Low Magnesium Levels as a Predictor of Erbitux Efficacy (Dec. 17/10)

KRAS wild-type mutational status is necessary but not sufficient to get benefit from epidermal growth factor receptor inhibitors, such as erbitux and vectibix. Predictive markers are currently being evaluated. In this study, researchers investigated early hypomagnesemia (lowered level of magnesium in the blood) as a predictor of efficacy and outcome in terms of time to progression (TtP) and overall survival (OS) in a cohort of patients affected by advanced colorectal cancer KRAS wild-type erbitux-treated. One hundred and forty-three patients affected by stage IV colorectal cancer KRAS wild type receiving erbitux + irinotecan (CTX+IRI) as third-line anticancer treatment and resistant to oxaliplatin- and irinotecan-based chemotherapy were retrospectively included. Magnesium blood levels were measured before the first day and 7, 14, 21 and 28 days after CTX+IRI infusion. The median magnesium basal value showed a statistically significant decrease after the start of CTX+IRI treatment. Patients with an **early decrease of magnesium levels >50% compared with the basal level had a higher tumor response rate (55.8% versus 16.7%)**, a longer TtP (6.3 versus 3.6) and a longer median OS (11.0 versus 8.1). Researchers have shown that early hypomagnesemia could be a predictor of efficacy and outcome in those patients. Magnesium circulating level is an easy and inexpensive biomarker to routinely be detected in patients treated with cetuximab.

Vincenzi, B., et al., Early magnesium modifications as a surrogate marker of efficacy of cetuximab-based anticancer treatment in kras wild type advanced colorectal cancer patients. Annals of Oncology. Advance Access: 10.1093/annonc.mdq550

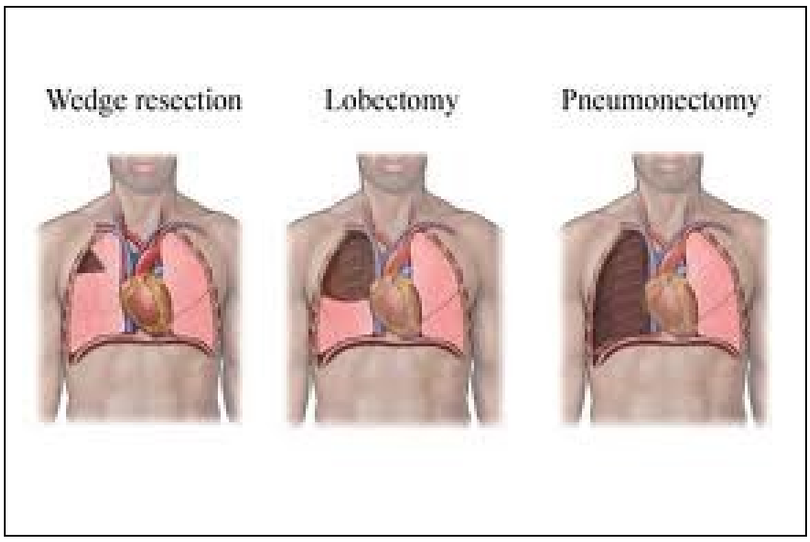
SURGICAL THERAPIES

11. Survival Improves After Resection of Colorectal Liver/Lung Resection (Dec. 6/10)

Resection of liver and lung colorectal metastases produced superior survival, compared with resection of liver metastases alone, in this retrospective analysis of 1,260 consecutive patients. After a median follow-up of 49 months, 5-year overall survival was 40% in patients with colorectal cancer who underwent resection of liver metastases alone, compared with **50%** in those who underwent **resection of both liver and lung metastases** , reported by M.D. Anderson's Dr. Eddie Abdalla. The presumed explanation for the improved survival is that patients with liver and lung metastases had less-extensive recurrence (27%) than did the rest of the cohort (69%. Recurrence also was seen in 33% of patients with lung-only metastases and in 22% with liver-only metastases. Although recurrence in the study was substantial, it can often be retreated. Among 78 patients who developed recurrence, 33 (42%) were retreated with resection, radiofrequency ablation, or chemotherapy, resulting in a 5-year disease-free survival of 25%. Extrahepatic disease, long associated with poor outcome, has been considered a contraindication to resection. More recent studies are challenging this belief, citing advances in systemic chemotherapy and surgical technique as well as improved multidisciplinary management and patient selection. The only significant predictors of worse survival in patients with resection of both liver and lung metastases were a rectal primary tumor and a carcinoembryonic antigen (CEA) level before resection of liver metastases of more than 5 ng/mL . Interestingly, liver metastasis greater than 5 cm, positive margins at resection of liver metastases, synchronous lung metastases, and even disease-free intervals were not significant. "Occurrence of lung metastases that are subsequently resected is not a poor prognostic factor or a contraindication to resection of colorectal liver metastases," Dr. Abdalla said. In all, 32 of the 112 patients with liver-plus-lung metastases had a rectal primary tumor, compared with 254 of the 1,148 patients with liver-only metastases. Their median preoperative CEA levels were 3.2 and 3.7, respectively.

Preoperative chemotherapy was used in 69% of patients before resection of liver metastases and in 50% of patients before resection of lung metastases.

Different types of lung resections



Source: http://www.treatment-for-lung-cancer.info/Treatment-for-Lung-Cancer-with-Surgery.html

Liver Resection

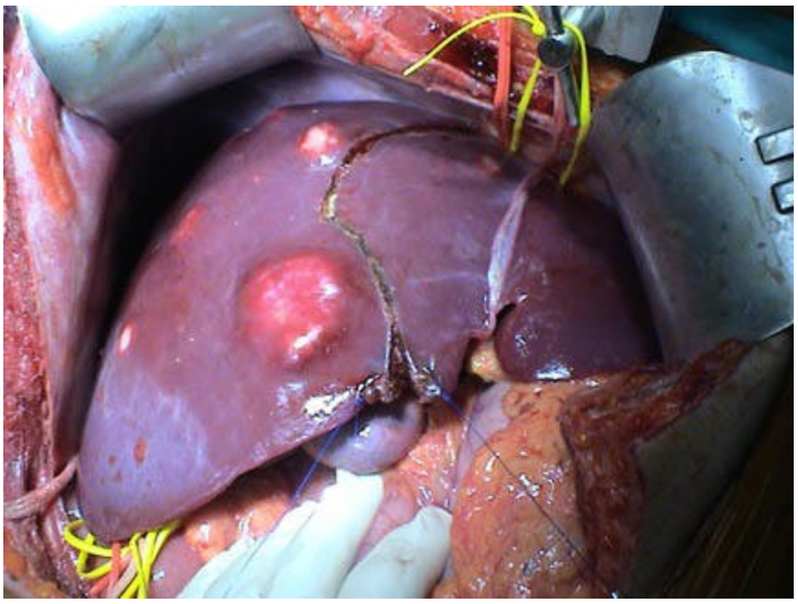


Figure 1: Showing Liver Metastases from Colorectal Cancer

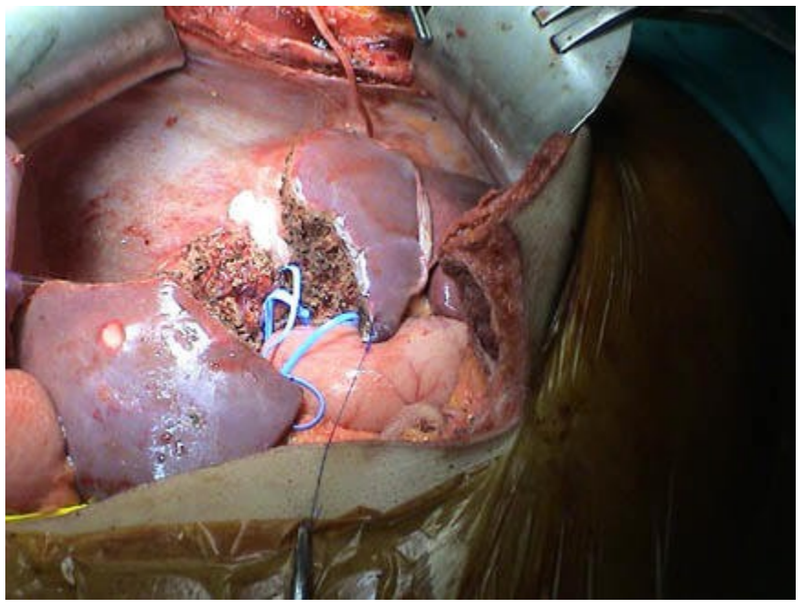


Figure 2: Showing Extent of Liver Resection

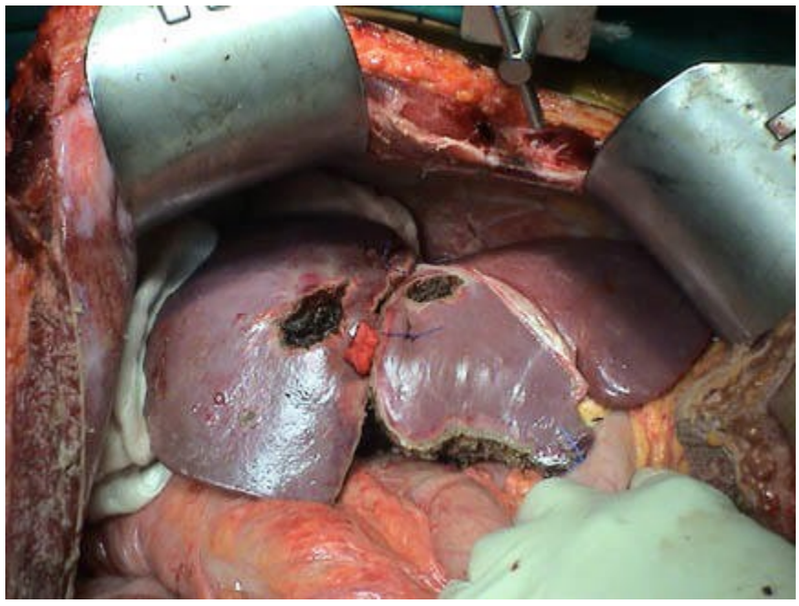


Figure 3: Showing Liver After Complete Resection

Source: ***http://www.akspublication.com/paper06_jan-jun2008.htm***

http://www.oncologystat.com/news/Survival_Improved_After_Colorectal_Liver_Lung_Mets_Resection.html;jsessionid=903C720BC80B98FB14DA81B36605CEB8

12. Surgery Complications Delay Chemo (Dec.8/10)

The results of this study indicate that patients who have complications after colorectal cancer surgery are less likely to get chemotherapy, even when it is clearly recommended for their diagnosis. In addition, patients with complications were more than twice as likely to have their chemotherapy delayed for more than 120 days after diagnosis or two months after surgery, which is considered the appropriate timeframe for receiving chemotherapy. Surgical complications are typically thought to be short-term problems, but the study suggests there is a clear link between downstream cancer care and complications that occur during surgery. This is critical because chemotherapy in this subset of colorectal cancer patients has clear lifesaving benefit. The study looked at data from 17,108 patients who had surgery for stage III colorectal cancer. Chemotherapy is recommended for all stage III colorectal cancer patients and has been shown to improve survival as much as 16% after five years. Because chemotherapy stresses the body and slows healing, medical oncologists are generally reluctant to give chemotherapy to patients who are frail or unwell because of complications from surgery. The researchers also maintain that some patients may opt out of chemotherapy after experiencing surgical complications. Complications include pneumonia, urinary tract infections, heart attack, wound infections, and need for additional surgery or abscess drainage. Researchers believe that some of these complications can be prevented but are the cause of chemo delay.

Hendren, Samantha, et al., Surgical Complications Are Associated With Omission of Chemotherapy for Stage III Colorectal Cancer. **Diseases of the Colon & Rectum*, 2010; 53 (12): 1587-1593 DOI: 10.1007/DCR.0b013e3181f2f202***

RADIATION/INTERVENTIONAL RADIOLOGY

13. CT Scans Not as Disconcerting As Originally Thought (Nov. 30/10)

Many types of imaging tests, such as x-rays and CT scans, expose people to radiation. Typically, the amount of radiation is small enough that it doesn't pose a measurable risk to health. When people have multiple scans, however, the radiation exposures can start to add up. This has raised concern among health experts that CT scans, which may use more radiation than conventional x-rays, can contribute to increased risk of cancer in people who get these scans. A new study provides reassurance that the risk is small. Last year, the National Council on Radiation Protection and Measurement issued a report which detailed that Americans receive seven times more radiation from diagnostic scans today than they did in 1980. A recent article in the Journal of the American Medical Association (JAMA) found that use of advanced imaging in emergency departments, which includes CT scans, tripled between 1998 and 2007. These numbers point to a clear trend of more CT scans and high-tech imaging methods in recent years. To study the potential connection between CT scans and cancer risk, researchers used Medicare data from two time periods - 1998-2001 and 2002-2005. A total of 10.8 million people were included in this study. 42% of people in the first time period had at least 1 CT scan and 49% of people in the second time period had 1 or more scans. Abdominal scans accounted for the most total radiation exposure in these groups. Using a well-accepted statistical method to assess radiation exposures and cancer risk, the researchers found that:

- 0.02% of cancers in the group studied during the first time period were due to radiation exposure from CT scans
- 0.04% of cancers in the group studied during the second time period were due to radiation exposure from CT scans

The lead researcher on the study, indicated that these numbers were lower than expected. He pointed out however, "...while the risk of secondary cancers appears to be lower than we thought, we still have to monitor our use of such imaging and keep track of the consequences." The bottom line is that the number isn't zero, which means more work needs to be done to make these scans safer. Fortunately, experts on medical imaging expect that within the next few years, new CT machines will become available. These machines are projected to reduce the amount of radiation delivered during the scan by 10 to 100 fold. Researchers urged that patients should be told not to be afraid of getting a CT scan if there is a medically appropriate reason. However, some scans may be ordered for financial reasons, such as a way for a health care center to generate more fees. People need to take care of themselves and make sure the CT scan really is necessary. Some scans are, others are not. If you need a CT scan, consider whether you've had them before. If not, a single scan is unlikely to expose you to additional cancer risk. If you've had many medical tests that expose you to radiation, discuss this with your doctor. There may be other options for getting the information needed to guide your medical care and cancer treatment decisions.

Radiological Society of North America (RSNA) 96th Scientific Assembly and Annual Meeting: Abstract SSK08-04 Presented December 1, 2010.

SCREENING

14. New Blood Test To Detect Colon Cancer Now Available in Canada (Nov. 20/10)

A new test from Epigenomics and Warnex Medical Laboratories is infiltrating the ranks of the colon cancer screening world. On Dec. 6 the companies announced the Canadian launch of their diagnostic blood testing service. The test is derived from a blood sample and detects cell-free methylated DNA of the Septin9 gene shed into the bloodstream by colorectal tumors. The Septin9 blood test is meant to identify colorectal cancer after it has developed and potentially already spread outside of the bowel wall. It is not meant to prevent colorectal cancer. And when compared to the Virtual Colonoscopy or CT Colonography, researchers claim that the purpose of CT colonography, unlike the Septin 9 Test, is to identify precursor polyps before cancer develops. The goals of the two tests are very different. In the PRESEPT study, Septin9 detected two-thirds of colorectal cancers with a specificity of only 88%. That means one in every three cancers would be missed. If this were applied to a screening population, where cancer is present in about one in every 500 adults, there would be more than 60 false-positive tests for every cancer detected. The sensitivity and specificity for cancer detection in CT Colonography is >95%. An attractive option might be following the Septin9 blood test with CT colonography because the risk of cancer is too low to justify colonoscopy in all cases. The Septin 9 Test is not funded by provincial health care plans but may be ordered and purchased by physicians for $445.00 from Warnex, a private laboratory based in Laval, Quebec.

deVos, Theo, et al., Circulating Methylated SEPT9 DNA in Plasma Is a Biomarker for Colorectal Cancer Clinical Chemistry 55:7/ 1337-1346

http://www.diagnosticimaging.com/practice-management/content/article/113619/1755266

15. Genetic Screening Recommended for Lynch Syndrome (Nov. 21/10)

A new study has researchers calling for widespread screening for genetic mutations that greatly increase the risk of colorectal cancer. The screening, with an initial cost of about $2,600, is cost-effective on par with mammography. About one in 370 Americans has Lynch syndrome, which predisposes people to endometrial cancer as well, and one in 35 colorectal-cancer patients is positive for the syndrome. Fewer than 2 percent of Americans who have the syndrome are aware of it. Doctors should assess risks based on family history and other factors and test those whose chance of having the syndrome exceeds 5 percent. Risk-assessment tools take a couple of minutes to fill out and can be found online. A computer model that looked at 100,000 simulated individuals found that the average cost-effectiveness ratio, a measure of expenses per life year gained, would be $26,000, well below a common benchmark of $50,000. Risk assessment and subsequent screening of young adults could reduce colon-cancer incidence in those with mutations by 12.4% and endometrial cancer by 8.8%, the researchers found. Ohio State has played a key role in investigating the syndrome and has pushed for routine testing of colon-cancer patients. Testing someone who already has cancer for the syndrome could help predict their risk of other cancers and would open the door to testing of family members, who then might avoid the disease. Once a specific mutation is found, relatives can undergo much cheaper testing, at a cost of about $300. Clues that should prompt screening are the strength of family history of those cancers; a person's age when the disease was diagnosed; and patterns within a family or multiple cancers in one person. Dr. Henry Lynch of Creighton University in Nebraska, who discovered the syndrome, said he was pleased with the study's results and hopes that widespread screening becomes the standard of care. Breast-cancer mutations are much more widely tested for but are about half as common as Lynch syndrome. Dr. Randall Burt, who worked on the study and practices at the Huntsman Cancer Institute in Utah, said he thinks wide distribution of the study's findings will help shift how doctors view screening for the syndrome. Hampel said people working in genetics should come up with tools that will more quickly and easily help busy primary-care doctors look for a variety of syndromes. *A calculator that estimates risk of Lynch syndrome can be found online at www. dana-farber.org/pat/cancer/gastrointestinal/crc-calculator/ or by searching for "Premm model."*

Dinh, Tuan A, et al., Health Benefits and cost-effectiveness of primary genetic screening for Lynch Syndrome in the general population. Cancer Prevention Research, published online November 18, 2010. **doi: 10.1158/1940-6207.CAPR-10-0262**

16. FIT Deemed Most Efficient for CRC Screening (Nov. 24/10)

Annual screening by fecal immunochemical testing -- a test that detects blood in the stool, has high sensitivity and specificity, and might improve participation rates through increased patient acceptability -- reduces the risk of colorectal cancer and colorectal cancer related deaths, and reduces healthcare costs in comparison to all other screening strategies and to no screening. These are the conclusions of a complete economic evaluation performed by Braden Manns and colleagues from the University of Calgary, Alberta, Canada. Clinical guidelines recommend screening for colorectal cancer in average risk individuals at 50 years of age and older, yet some countries, such as the UK, do not currently have population-based colorectal cancer screening programs. Also, many countries with colorectal cancer screening programs do not offer a choice of screening method. In order to inform health policy decision making, the authors used an incremental cost utility analysis, a sophisticated modeling technique, and two hypothetical patient cohorts (individuals with an "average risk," i.e. no family history of colorectal cancer, aged 50-64 and 65-75) to compare different colorectal cancer screening methods. In their analysis, the authors considered all costs, such as treatment costs, and non-medical costs (such as costs of travelling to the screening centre), associated with each colorectal cancer screening method. The modeling was based on assumptions consistent with a North American context. The authors found that annual fecal immunochemical testing was more effective and less costly compared to all strategies (including no screening). Using this screening modality, among the lifetimes of 100,000 average-risk patients, the number of deaths from colorectal cancer was reduced from 1393 to 457. Even after the authors accounted for many different scenarios, screening for colorectal cancer with fecal immunochemical testing remained the most cost effective screening option. The authors conclude: "Health policy decision makers should consider prioritizing funding for colorectal cancer screening using fecal immunochemical testing."

Heitman SJ, et al., Colorectal Cancer Screening for Average-Risk North Americans: An Economic Evaluation. **PLoS Med*, 7(11): e1000370 DOI: 10.1371/journal.pmed.1000370***

17. Tests Between Colonoscopies Deemed Necessary For High Risk Patients (Dec. 7/10)

Among patients with a family or past history of colorectal cancer (CRC), testing between colonoscopies helps detect colorectal cancer and advanced tumors that are either missed or develop rapidly, according to a new study in *Gastroenterology*. By using fecal immunochemical testing -- a new type of stool blood test -- in the interval between surveillance colonoscopies, researchers were able to detect cancer much sooner than if they had waited for the scheduled surveillance. In fact, in those patients who consistently returned a negative fecal immunochemical test, the chance of finding cancer or advanced adenoma was

significantly reduced. A joint guideline from the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer and the American College of Radiology recommends that average-risk adults, beginning at the age of 50, should receive a colonoscopy every ten years and that annual fecal immunochemical tests (FIT) are acceptable choices for colorectal cancer screening in between this ten-year span (any positive FIT should be followed up with a colonoscopy). Guidelines suggest more frequent colonoscopies for certain high-risk groups. In this study, 1,736 patients with a confirmed family or personal history of colorectal cancer were followed for 8,863 person years of surveillance; some for as long as 20 years. The study inclusion criteria required that patients had received at least an initial and one subsequent surveillance colonoscopy with adequate examination and retrieval of tissue, performed with a training-accredited colonoscopist present. In the 1,071 asymptomatic subjects who returned at least one FIT after the colonoscopies, the test detected 12 out of 14 cancers and 60 out of 96 advanced adenomas. In FIT-positive cases, the diagnosis was made sooner by 25 months for cancer and by 24 months for advanced adenomas before the regularly scheduled colonoscopy. The study results suggest that interval fecal immunochemical testing in a high-risk colonoscopy program can be used for detecting missed or rapidly developing lesions. Patients at increased risk for developing CRC due to a family history or past history of CRC are recommended to have colonoscopic surveillance at regular intervals, often more frequently than recommended for the average-risk population. Patients with only one or two small adenomas with low-grade dysplasia are recommended to have their second surveillance colonoscopy after an interval of 10 years. However, for these individuals, there is a greater risk of delay in detecting rapidly progressing or missed lesions. Using annual fecal occult blood tests in the interval between surveillance colonoscopies could be a strategy that helps manage this risk. FIT, which uses an antibody specific for human hemoglobin, is being increasingly used because it is more sensitive for cancer and adenomas.

Young, Graeme P., et al., Interval fecal immunochemical testing in a colonoscopic surveillance program speeds detection of colorectal neoplasia. Gastroenterology, Vol. 139, Issue 6,, pp. 1918-1926, December 2010

18. Low Dose Aspirin Helps Detect Colorectal Cancer in FOBT (Dec. 7/10)

Taking a low-dose aspirin prior to having a fecal occult blood test appears to increase the ability of the test to detect colorectal cancer, according to this new study. The fecal occult blood test, which looks for blood in the stool, is a common test used to detect colon cancer because advanced colorectal tumors often bleed. Moreover, use of low-dose aspirin is a common practice in people ages 55 and older because studies show the therapy can reduce the risk of cardiovascular disease and cancer. The study, from German researchers, examined 1,979 patients for the accuracy of fecal occult blood testing. Researchers found the **test's sensitivity** -- the correct identification of positive results -- was 70.8% for low-dose aspirin users compared with 35.9% for nonusers. **Test specificity** -- the correct identification of negative results -- was slightly lower among users of low-dose aspirin. It appears that low-dose aspirin use increases the likelihood of bleeding from a colorectal tumor, thus increasing the odds that the test will detect blood. The findings raise the hypothesis that test performance may be enhanced by temporary use of low-dose aspirin.

Brenner, Hermann, et al., Low dose aspirin use and performance of immunochemical fecal occult blood tests. JAMA ***2010;304(22):****2513-2520.* ***doi: 10.1001/jama.2010.1773***

19. Colorectal Cancer Screening Reminders Deemed Helpful (Dec. 17/10)

The use of colorectal cancer screening reminders may be effective in getting people to be screened, according to the results of these studies. In the first study, researchers analyzed data from 1,103 patients aged 50 to 75 who were overdue for colorectal cancer screening. Subjects were randomly assigned to receive or not receive an electronic reminder message. At one month, screening rates were higher for those who received the message (8.3 versus 0.2%), but at four months the difference wasn't significant. About half (54%) who received the message viewed it. In the second study data from 628 subjects aged 50 to 79 who had an expired order for screening colonoscopy was analyzed. They were randomized to usual care or to receive a reminder letter, a brochure, a DVD about colorectal cancer, and a phone call. Screening rates at three months were 9.9% in the intervention group versus 3.2% in the control group. At six months, rates were 18.2 and 12.1%, respectively. At present, health systems could reasonably choose to begin screening promotion with low-cost interventions like simple mailings followed by more expensive, but potentially more effective interventions such as one-on-one patient navigation or interventions aimed at eliminating structural barriers for patients who remain unscreened, researchers concluded.

Sequist, Thomas et al., Electronic patient messages to promote colorectal cancer screening. Archives of Internal Medicine, Publsihed online December 13, 2010. Doi: 10.1001/archinternmed. 2010.467

Cameron, Kenzie, et al., Patient outreach to promote colorectal cancer screening among patients with an expired order for colonoscopy. Archives of Internal Med. Published online December 13, 2010. Doi: 10.1001/archinternmed.2010.468

OTHER

20. ChipDX Predicts Recurrence of Early Stage Colon Cancer (Dec. 8/10)

A New York-based online molecular diagnostics and personalized medicine company called ChipDX discovered and validated a genetic signature for early-stage colon cancer and is developing an online screening application to enable clinicians to more accurately identify risk of recurrence. In the study ChipDX demonstrates how the 163-gene signature stratifies colon cancer patients into high- and low-risk groups for recurrence with greater accuracy than current methods. Researchers discovered a set of genes that were strongly associated with outcome, independent to current measurements of prognosis. By combining measurements of these genes, performed with Affymetrix® GeneChip® technology, and a robust predictive algorithm, researchers were able to predict which individuals were at the greatest risk of recurrence within a five-year follow-up period. This unique signature's ability to generate a highly personalized assessment of recurrence risk may one day assist physicians in deciding whether individuals with early-stage colon cancer should receive chemotherapy in addition to surgery. Currently, ChipDX is making the algorithm available for research use only through an online gene expression analysis platform at www.ChipDX.com and is reviewing regulatory requirements and partners to market it as a test for future diagnostic use. Physicians currently use a method called clinical staging to measure the extent of disease spread at the time of diagnosis. Patients who are diagnosed with early-stage tumors (1-2) generally do not receive chemotherapy; however, approximately 20% of stage-2 patients develop recurrence within five years. In the study, the ChipDX algorithm is shown to stratify early-stage colon cancer patients with greater accuracy than clinical staging. Ultimately, researchers hope their predictive gene signature will help doctors to identify these early-stage 'high-risk' patients and offer them more personalized treatment options based on a set of genes related to survival above and beyond traditional assessments of outcome. If treatment is tailored to the precise nature of a patient's tumor, the life-saving potential is greater. ChipDX developed its prognostic algorithm by analyzing data from a 2009 study of 232 US-based colon cancer patients (Smith, et al., 2009). An independent validation series of 60 stage 2 and 3 Australian colon cancer patients was used to validate the discovery (Jorissen, et al., 2009). Both studies utilized Affymetrix® GeneChip® Human Genome U133 Plus 2.0 Array profiles of colon cancer patients. The method of gene expression data analysis performed was designed to identify genes significantly associated with recurrence independent of the patient's age at diagnosis, tumor grade, or disease stage.

Van Laar, RK, et al., An online gene expression assay for determining adjuvant therapy eligibility in patients with stage 2 or 3 colon cancer. British J of Cancer (2010), 103, pp. 1852-1857

21. Rare Genetic Syndrome May Increase Risk of Colon Cancer (Dec. 10/10)

Patients diagnosed with a genetic condition known as Cowden syndrome (CS) face an increased risk for colon cancer, according to the results of this study. And because such patients typically have a larger-than-normal head circumference, head size should be used as a screening marker for such elevated cancer risk. CS is caused by mutations in the tumor suppressor gene *phosphatase and tensin homolog* (*PTEN*). Patients typically have mucocutaneous (involving both skin and mucous membrane) lesions, large-sized heads, and increased risk for breast, thyroid, and endometrial cancers. Although the gastrointestinal (GI) tract is also affected, there have not been large, systematic studies of GI cancers in people with CS. Researchers investigated GI cancers and other lesions in 127 patients with *PTEN* mutations associated with CS. The syndrome affects about one in every 200,000 people. People with big heads -- defined as greater than 58 centimeters in men and 57 centimeters in women -- should see a genetic counselor to determine whether they should be screened for colon, breast, thyroid and uterine cancers. While exploring the characteristics of Cowden syndrome, the research team found a larger-than-normal head size in about 75% of people with the genetic mutation that causes the syndrome. Previous estimates had been 25%. Their analysis, which involved 127 Cowden syndrome patients, also revealed that a similarly large percentage have gastrointestinal polyps, which increase the risk of early-onset colorectal cancer. The research team also found an association between a known cause of Cowden -- an abnormality in the so-called PTEN gene -- and a 200 times greater risk for developing colorectal cancer. Researchers concluded that screening for these patients for colon cancer should start in their early- to mid-30s at the latest, and it should be annual screenings.

Heald B, et al. Frequent gastrointestinal polyps and colorectal adenocarcinomas in a prospective series of* PTEN *mutation carriers. Gastroenterology 2010;139:1927–1933.

NUTRITION & HEALTHY LIFESTYLE

22. DASH Diet Helpful for Colon Cancer (Nov. 22/10)

The DASH diet, which stands for Dietary Approaches to Stop Hypertension (DASH), is a way of eating that was developed to help people with high blood pressure bring those numbers down to a healthier level. And according to the results of this study, the DASH diet can also help to prevent colon cancer. To study the connection between following a DASH diet and risk of colon cancer, researchers collected diet information from 132,746 men and women. They collected the information about typical dietary habits at several points in time, throughout nearly three decades of following this large group of men and women. Using the diet information, the study authors calculated a DASH diet score for each study

participant. The higher a person's score, the more closely he or she were following the DASH diet guidelines. This is what the researchers found:

- People who most closely followed the DASH diet had a 20% lower risk of being diagnosed with colon cancer compared with people not following the DASH diet guidelines.
- People who most closely followed the DASH diet had a 27% lower risk of being diagnosed with rectal cancer compared with people not following the DASH diet guidelines.

The study authors concluded that closely following "the DASH diet (which involves higher intakes of whole grains, fruit, and vegetables; moderate amounts of low-fat dairy; and lower amounts of red or processed meats, desserts, and sweetened beverages) was associated with a lower risk of colorectal cancer." Eating in a way that is consistent with the recommendations of the DASH diet can significantly lower a person's risk of colon and rectal cancer. Appearing below are some helpful hints for incorporating the DASH diet into your daily routine:

- **Calcium**: One key nutrient in the DASH diet is calcium. To get plenty of calcium, a big part of the DASH diet is eating at least 3 servings of low-fat dairy foods, such as skim milk and low-fat or no-fat yogurt. A serving is one cup.
- **Potassium**: Potassium works with sodium to regulate blood pressure in the body. Too little potassium, coupled with too much sodium, leads to high blood pressure. The best sources of potassium are vegetables, fruit, and beans. In particular, green leafy vegetables, low-sodium tomato products (soup and juice), and beans prepared without salt will give you lots of potassium. These same foods, vegetables, fruit, and beans provide colon cancer protection too.
- **Magnesium**: Like potassium, not getting enough magnesium can also lead to higher blood pressure. The best sources of magnesium are whole grains, such as oats, oat bran, whole wheat flour, bulgur wheat, brown rice, and buckwheat; vegetables, including spinach, tomatoes, beet greens, and okra; beans, especially soy beans, black beans, lima beans, navy beans, chickpeas, and lentils; fruit and fruit juice, especially citrus (orange juice and grapefruit juice); nuts and seeds, such as pumpkin seeds, Brazil nuts, and almonds; and dark chocolate in particular is one of the best sources of magnesium.
- **Sodium**: Sodium, especially when it comes from processed meats, is a problem for both high blood pressure and colon cancer risk. If you enjoy meat, make it fresh and keep it to 3 ounces or less per day for best health.
- **Vitamin D**: Getting enough vitamin D is turning out to be vitally important for staving off a whole host of chronic diseases, from cancer to heart disease. For people who already have cancer, having more vitamin D in the body is linked with better survival and lower risk of cancer coming back again.
- **Folate**: When it comes to colon cancer, folate is a double-edged sword. Not enough folate, especially during childhood and teen years, appears to increase colon cancer risk in adults. Too much folate, later in life and when it comes from dietary supplements and folate-fortified foods, seems to increase colon cancer risk. This sounds confusing, but the answer is simple: Get folate from vegetables (green leafy are best), fruit, beans, and whole grains. Skip folate supplements (unless you're pregnant or planning to become pregnant) and skip folate-fortified processed foods such as baked goods, chips, crackers, and other treats.
- **Fiber**: If followed properly, the DASH diet is loaded with fiber. Fiber from foods such as vegetables, beans, and whole grains appears to reduce colon cancer risk. Unfortunately, fiber supplements alone won't do the trick. A healthy diet with plenty of fiber-rich foods is your ticket to optimal colon health.
- **Fat**: The DASH diet is low in fat, especially the so-called "bad" fats -- saturated and trans fats. These same fats aren't good for the colon either. Hence, abstaining from ingesting these bad fats is helpful.

Fung, Teresa, et al., The Mediterranean and dietary approaches to stop hypertension (DASH) diets and colorectal cancer. The Amer J of Clin Nutr. doi: 10.3945/ajcn.2010.29242, November 2010 vol. 92 no. 6 1429-1435

23. Folic Acid and Vitamin B12 Supplements May be Harmful (Nov. 23/10)

Heart disease patients in Norway, a country where folic acid is not fortified into food, noticed higher cancer and death risks after receiving vitamin B12 and folic acid treatments. Many studies have found relationships between folate and colorectal cancer risk, but the association is non-existent in other cancers. Researchers explain a deficiency in folate may promote cancer initially, but high folic acid dosage may promote cancer cell growth. Folic acid fortification has been mandatory in many countries since 1998, including Canada. This helps reduce neural-tube birth defect risks. This study, among others, has recently raised questions about cancer risk in relation to folic acid. For the study, researchers performed placebo trials on 6,837 patients having ischemic heart disease. Patients were either treated with B vitamins or a placebo, and the study took place from 1998 to 2005. Follow ups were performed through 2007. Randomly selected, patients received one of four supplements:

(1) folic acid, vitamin B12, and vitamin B6;
(2) folic acid and vitamin B12;
(3) vitamin B6;

(4) placebo.

Researchers discovered 288 individuals who did not receive vitamin B12 and folic acid supplementation were diagnosed with cancer, when compared to 341 individuals who did not receive either. This denotes a 21% increased risk. Also, an increased death risk of 38% was noticed when comparing those who did not receive either folic acid or vitamin B12 to those who received neither. The largest cancer increase in patients receiving both folic acid and vitamin B12 was lung cancer. No significant changes were noticed in patients who took the vitamin B6 supplement. Researchers explain additional research is required and this may cause new safety regulations on food fortification and supplementation.

Mason, Joel, et al., Effects of folic acid plus vitamin b12 vs. placebo in myocardial infarction survivors. JAMA. 2010;304(16):1783. doi: 10.1001/jama.2010.1473

24. Apples Help with Colorectal Cancer (Nov. 25/10)

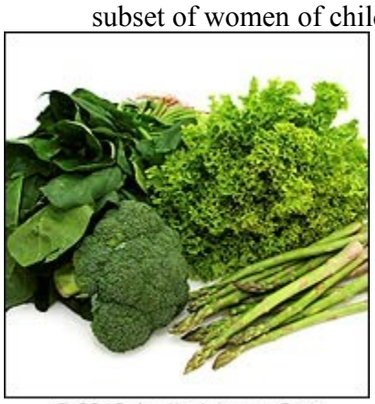
Recent research claims that eating an apple daily may reduce the risk of developing colorectal cancer. Research has also shown that the risk of all cancers can be reduced by between 30 to 40% by making simple lifestyle changes, such as eating more fruits and vegetables, taking regular exercise and watching your weight. Earlier studies have also claimed that an apple is a wealthy resource of flavonoid and polyphones, both dominant antioxidants, which help reduce cholesterol and fight free radicals. They also help combat premature aging and protect against skin diseases.

In this study, researchers compared 592 patients suffering from colorectal cancer with 765 patients without the disease at the same hospital. Those with cancer had eaten 9.5 servings of fruit a week, compared to those without the disease, who had 11 servings a week. After a certain period, the researchers found a reduced risk of developing the disease among those who ate one apple a day, while eating more than one apple a day reduced the risk by about half. Eating other fruit or vegetables did not have the same effects on the risk of colorectal cancer. According to the researchers, the protective properties of apples may be as a result of their high content of flavonoids, which act as antioxidants, and are concentrated in the skin of apples, preventing molecules or free radicals from inflicting damage on tissues and can inhibit cancer onset and cell proliferation. Antioxidants were five times more prevalent in the apple skin than the actual flesh - so wash, but do not peel before you eat them.

http://doctor.ndtv.com/storypage/ndtv/id/4828/type/news/Apples_keep_away_colorectal_cancer.html

25. High Folic Acid Intake Linked to Cancer (Dec. 14/10)

A new study has suggested that increased consumption of folic acid can reduce birth defects including neural tube defects, congenital heart disease and oral clefts but high intakes of folic acid may be linked to adverse events such as colorectal cancer. Researchers at Children's Hospital of Eastern Ontario Research Institute and The Hospital for Sick Children conducted the study. For the study, red blood cell folate concentrations were examined in 5248 Canadians aged 6 to 79 years. The study found that less than 1% of Canadians showed folate deficiencies and 40% showed high folate concentrations. However, in the subset of women of childbearing age, 22% were below the concentration considered safe to guard against neural tube defects.



Some medical practitioners argue that many women of childbearing age need high-dose folic acid supplements and that doubling the level of folic acid fortification in the food supply should be considered. This argument has sparked considerable debate because folic acid fortification targets women of childbearing age by exposing the entire population to high levels of folic acid. Given the absence of folate deficiency in the general population and the apparent shift toward Canadians having high serum folate concentrations, there appears to be little rationale for doubling folic acid levels in the Canadian food supply. Correction of folate deficiency and improved folate status, in part through fortification, has been associated with positive health outcomes such as the dramatic reduction in neural tube defects. However, given speculations about the possible adverse effects associated with high levels of folic acid, including increased risk of certain cancers in those with pre-existing neoplasms, further attempts to improve the folate status of Canadian women of childbearing age by increasing fortification levels should be approached cautiously, according to the researchers.

Colapinto, Cynthia, et al., Folate status of the population in the Canadian health measures survey. Canadian Med Assoc Journal, December 13, 2010. Doi: 10.1503/cmaj.100568