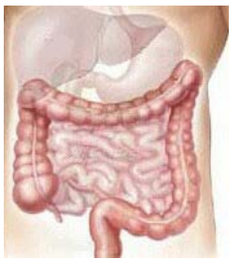
COLORECTAL CANCER RESEARCH

Month Ending August 14, 2009



The following colorectal cancer research update extends from July 18 – August 14, 2009 inclusive and is intended for informational purposes only.

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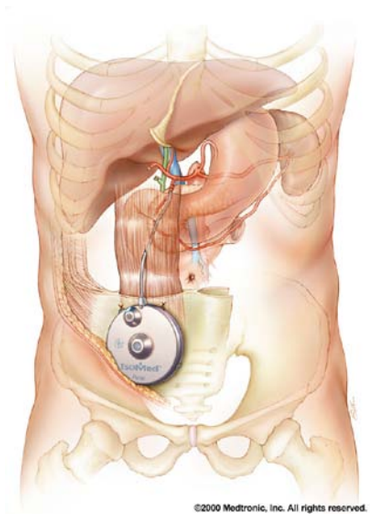
DRUGS / SYSTEMIC THERAPY

1. Hepatic Arterial Infusion Plus Folfox After Liver Resection (Jul. 17/09)

The results of an early phase I study emanating from Sloan Kettering found that infusing the chemotherapy floxuridine (FUDR) with dexamethasone (decadron), a steroid, directly into the liver (also known as **Hepatic Arterial Infusion – See image below**) along with systemic folfox chemotherapy after liver resection, was effective. The purpose of the study was to determine the maximum tolerated dose of folfox therapy that could be administered with hepatic arterial infusion (HAI) of floxuridine and dexamethasone after hepatic resection. 35 patients with resected liver metastases entered the trial. Within a followup of approximately 43 months, the 4 year survival and progression free survival (time before cancer got worse) were **88%** and **50%** respectively. The principal investigator concluded that adjuvant therapy after liver resection with HAI of FUDR/Dexamethasone plus systemic therapy of folfox appeared feasible and effective. Further studies were recommended.



Hepatic Artery Infusion Pump Placement
The placement of a hepatic artery infusion pump into the blood supply of the liver allows chemotherapy medication to be delivered directly into the liver. The placement of a pump into the hepatic artery after liver resection has allowed for additional chemotherapy to be delivered after surgery for up to six months. Results of two randomized trials have shown significant improvement in disease-free survival. To view the report on these trials, please visit : http://www.medtronic.com/neuro/hai/physician/overview.html.

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Kemeny, Nancy, et al., Phase I trial of adjuvant hepatic arterial infusion (HAI) with floxuridine (FUDR) and dexamethasone plus systemic oxaliplatin, 5-Fluorouracil and leucovorin in patients with resected liver metastases from colorectal cancer. J Annals of Oncology. Vol. 20, Number 7, pp. 1236-1241

2. Avastin Plus Folfiri in First Line Therapy of Metastatic Colorectal Cancer (Jul. 24/09)

Avastin, or bevacizumab, has been reported to significantly improve overall survival and progression free survival (time before disease gets worse) when combined with first-line therapy of Folfiri (irinotecan + 5FU + Leucovorin) in patients with metastatic colorectal cancer. This phase IV study evaluated the efficacy and safety of first-line avastin in combination with Folfiri. 209 metastatic colorectal cancer patients who had never been treated (treatment naïve) were enrolled and received avastin and Folfiri every 2 weeks. The treatment continued until there was evidence of disease progression. The results indicate that the average progression free survival was 11.1 months, which is comparable to those results observed in published phase III studies wherein avastin was used with folfiri. The average overall survival was 22.2 months and overall response rate was 53.1%. The disease control rate was 85.6%. Investigators concluded that avastin combined with first-line folfiri is an effective and well-tolerated therapy option for patients with metastatic colorectal cancer.

Sobrero, Alberto, et al., Phase IV Study of bevacizumab in combination with infusional fluorouracil, leucovorin and irinotecan (Folfiri) in first line metastatic colorectal cancer. Oncology; vol. 77, No. 2, 2009. pp. 113-119.

3. Xelox Shown to Be More Effective Than Standard 5FU Chemo in Adjuvant Colon Cancer (Jul. 24/09)

This Phase III study (NO16968) demonstrated that oral Xeloda (capecitabine) plus oxaliplatin (known as Xelox) is superior to a commonly used intravenous chemotherapy 5FU with Leucovorin in increasing the

time that patients with adjuvant (post surgical) colon cancer lived without their cancer returning when given immediately after their primary surgery. The results show that those stage III patients who participated in the study by taking Xelox immediately after surgery of their primary lived longer without their cancer being detectable than those who took intravenous 5FU with leucovorin. The study included 1886 patients who were randomly assigned to one of two trial arms (Xelox vs. 5FU/Leucovorin) for a total of 24 weeks after their surgery and was conducted at 240 study sites across 29 countries. Significantly more patients receiving Xelox were alive without cancer three years after treatment began.

www.roche.com/media/media_releases/med-cor-2009-07-20.htm

4. Men & Patients Under 70 More Likely to Experience Skin Rash from Erbitux Therapy (Jul. 25/09)

This study demonstrated that men and patients under 70 years of age are more likely to have a severe skin rash from Erbitux therapy than women or older people. Epidermal growth factor receptor (EGFR) inhibitors such as erbitux can result in a severe rash in 5-10% of patients and can detract from quality of life. The objective of this study was to identify clinical predictors of severe erbitux-induced rash in the hope of using these factors in the design of future trials. 933 erbitux–treated patients enrolled in the trial where erbitux was combined with folfox for the treatment of stage III colon cancer and were evaluated for clinical risk factors of severe rash. Within this group, 50 patients (5%) developed a severe rash. More men compared to women developed such a rash (7% vs. 3%). And a greater number of younger patients, who were younger than 70 years of age, also developed a rash (6% vs. 1%). Investigators concluded that men and younger patients are at greater risk for a severe erbitux-induced rash although overall the risk is low.

Jatoi, Aminah, et al., Clinical Predictors of Severe Cetuximab-Induced Rash: Observations from 933 Patients enrolled in North Central Cancer Treatment Group Study NO147. Oncology; Vol. 77, No. 2, 2009. pp. 120-123.

5. New Colon Cancer Vaccine Proving to be Effective (Jul. 27/09)

A groundbreaking new colon cancer vaccine is showing great promise in clinical trials. The treatment is the first-ever preventative cancer vaccine that attacks emerging pre-cancerous tumors or adenomas, wiping them out before they become deadly. The promising clinical trial is currently underway at the University Of Pittsburgh School Of Medicine. Researchers have been recruiting patients for the Phase II clinical trials since 2008 and expect to continue through 2011, to work out any issues with the new vaccine. The vaccine works by using the body's own antibodies to fight against the abnormal version of a mucous protein called MUC1, which is found in many types of cancer, including colon cancer, pancreatic cancer and including most breast tumors. Other cancer vaccines have been developed to fight a cancer-causing virus or to attack existing tumors, but this is the first vaccine that targets cancerous tissue before it develops into an actual tumor. The study is trying to determine if a patient's immune system can be used as a surveillance mechanism to prevent the development of cancer. This type of vaccine would be particularly useful to treat patients at high-risk for developing colon cancer, as many precancerous polyps, called advanced adenomas, give off abnormal levels of the protein MUC1. About half of all advanced adenomas and the majority of colorectal cancers contain high-levels of MUC1 and there are moderate amounts of the protein found in the lining of normal intestines. The vaccine could reduce the need for frequent colonoscopies in many patients. Although, not all advanced adenomas produce abnormal levels of MUC1, therefore, some patients may still require colonoscopies. So far, the vaccine has been well tolerated by the patients in the trial, with just a few instances of some redness and soreness at the injection site and the occasional short-term fever, but no major side effects reported. The vaccine has already proven safe in patients with advanced pancreatic cancer. People wishing to access the trial may do so by visiting the Clinical Trials.gov website at www.clinicaltrials.gov/ct2/show/NCT00773097 .

Rice, Jocelyn, et al., A Vaccine for Colon Cancer, MIT Technology Review, July 27, 2009

6. Genetic Testing Can Help Determine Irinotecan Dosage (Jul. 28/09)

For those patients with metastatic colorectal cancer, chemotherapy with irinotecan is a standard treatment that has been shown to improve survival. But for more than 1 in 10 of these patients, a variation in their DNA means that this treatment could result in a severe reduction in their white blood cell count (neutropenia), leading to a high risk of bacterial infection and possible subsequent death. A new genetic test can identify those with the variation in order to lower the treatment dose — however, it has been unclear whether the testing is worthwhile. A new cost-effectiveness study led by scientists at Weill Cornell Medical College has determined that so-called pretreatment pharmacogenetic testing (genetic testing of a drug) is only beneficial if the dose-reduced treatment is shown to be nearly as effective as the full dose. If the lower dose is as effective, the test could prevent many cases of severe neutropenia, an abnormally low count of an important type of white blood cell known as neutrophil. It would also mean better life expectancy and lower cost of care. The study used a computer simulation model that follows hypothetical patients treated with the FOLFIRI (5-fluorouracil/leucovorin with irinotecan) chemotherapy regimen for metastatic colorectal cancer. The model assumed that under usual care, patients received a full dose of irinotecan. With genetic testing, irinotecan dosage was reduced 25% in individuals identified using the genetic test as having the UGT1A1*28 gene. The results indicated that testing would avoid 84 cases of severe neutropenia, including 4.4 deaths; and that the genetic testing for the UGT1A1*28 gene may actually be cost effective, but only if irinotecan dose reduction does not reduce efficacy. .

7. Reolysin May Address Kras Mutated Colorectal Tumors (Jul. 28/09)

For colorectal cancer patients with mutations in the Kras gene, there may be an alternative therapy that is currently being developed for them. An oncolytic virus (referring to viruses that kill cancer cells more often than they kill normal cells) called Reolysin, is being developed that can kill cancer cells with this particular mutation and with EGFR (epidermal growth factor receptor) mutations as well; and is currently well-advanced into clinical trials in the US, Canada and the UK. Reolysin preferentially replicates in cancer cells that have an activated RAS pathway. Approximately two thirds of all cancers have an activated RAS pathway, including most metastatic disease. A large number of mutations, including mutations in EGFR, Kras along the RAS pathway lead to RAS pathway activation. Reolysin works by exploiting any mutation that leads to an activated RAS pathway. These mutations allow the virus to replicate inside tumor cells, producing thousands of copies of itself. To date, more than 280 patients with various forms of cancer have been treated with Reolysin in Canada, the US and the UK. Side effects are mild. Some patients have reported a combination of mild, flue-like symptoms which resolve quickly.

www.oncolyticsbiotech.com/Reolysin

8. Pfizer Invests $6 Million in Canadian Research to Develop PGx Drugs for Colorectal Cancer (Jul.29/09)

Pfizer Global Research and Development will collaborate with two Ontario institutes to discover and validate targets that could be used to diagnose, predict, or treat colorectal cancer. Under the collaboration, Pfizer will invest C$6 million ($5.4 million) in a partnership with the Ontario Institute for Cancer Research (OICR) and the Ontario Cancer Institute (OCI) at the Princess Margaret Hospital (PMH) in Toronto. The Ontario Ministry of Research and Innovation also is investing C$900,000 in the Project. The goal of the project is to develop new therapeutic targets and new diagnostics, as well as discover new diagnostic markers in colon cancer patients, on the basis of their individual cancer genotypes. OICR and OCI will conduct genomics and molecular pathology studies and develop a large clinical biobank to identify molecular signatures that will be used to develop biomarkers for early detection, monitoring, and treatment of cancer. The institutes will also use existing Ontario Government support to build related research infrastructure, such as equipment and tissue banks, which in turn will be used to identify molecular signatures in colorectal cancer patients.

www.genomeweb.com/pfizer-gives-54m-ontario-cancer-research-project

9. New Drug That Blocks Cell Changes in Clinical Trials (Jul. 31/09)

An oral drug that blocks activity of enzymes that change proteins in cells that leads to cancer is being tested at the National Institute of Health. R935788 or Fostamatinib, a protein kinase inhibitor, is in a phase II clinical trial for patients with several types of advanced cancer, including colorectal cancer. Patients whose cancer has gotten worse on previous treatment are eligible to participate. The trial is being conducted at the NIH Clinical Center in Bethesda, Maryland. Patients will take fostamatinib twice a day during 4 week cycles. Patients are also required to see a doctor at the NIH Clinical Center at the beginning of each cycle. Weekly blood tests and blood pressure checks can be done in an outpatient clinic or by the patient's own doctor. There is no charge for medical care received at the National Institute of Health (NIH) Clinical Center in Bethesda. Patients need to pay their own travel costs for the first screening visit, but once enrolled the National Cancer Institute pays for transportation to the Washington area. During outpatient visits, NCI pays a small daily amount for hotel and meals. To inquire about eligibility or the trial itself, please visit: http://bethesdatrials.cancer.gov/clinical-research/search_detail.aspx?ProtocolID=NCI-09-C-0138&date=07-29-09

www.C3:ColorectalCancerCoalition.org/ResearchUpdate

10. Adding Vectibix to Chemotherapy Folfox Improves Outcomes (Aug. 7/09)

This study demonstrated that the addition of the targeted therapy Vectibix (panitumumab) to chemotherapy delayed cancer progression in metastatic colorectal cancer patients. This benefit was only observed in patients whose tumors did not contain a mutation in the KRAS gene. Targeted therapies are anticancer drugs that interfere with specific pathways involved in cancer cell growth or survival. Some targeted therapies block growth signals from reaching cancer cells; others reduce the blood supply to cancer cells; and still others stimulate the immune system to recognize and attack the cancer cell. Depending on the specific "target", targeted therapies may slow cancer cell growth or increase cancer cell death. Vectibix inhibits cancer cell growth and survival by targeting a protein known as the epidermal growth factor receptor (EGFR). Vectibix appears to benefit only those patients whose cancers do not contain a mutation in a gene known as KRAS. KRAS mutations occur in an estimated 40-50% of metastatic colorectal cancers and can be identified by testing a sample of tumor tissue. To evaluate the effectiveness of Vectibix in the initial (first-line) treatment of metastatic colorectal cancer, researchers

conducted a Phase III clinical trial known as PRIME (Panitumumab Randomized trial In combination with chemotherapy for Metastatic colorectal cancer to determine Efficacy). The study enrolled 1,183 patients who were assigned to receive treatment with FOLFOX chemotherapy alone or FOLFOX plus Vectibix. Among patients without KRAS mutations, the addition of Vectibix significantly improved progression-free survival (time before disease got worse). In contrast, among patients with KRAS mutations, the addition of Vectibix worsened progression-free survival. Side effects of Vectibix included skin rash, low magnesium levels, and diarrhea. The results of this study suggest that the addition of the targeted therapy Vectibix to first-line chemotherapy improves progression-free survival among patients with metastatic colorectal cancer. The benefit only applies to patients whose tumors do not contain KRAS mutations.

Amgen News Release. Vectibix® In Combination With Chemotherapy Significantly Improved Progression-Free Survival In First-Line Metastatic Colorectal Cancer. Available at: http://www.amgen.com/media/media_pr_detail.jsp?year=2009&releaseID=1318284 Accessed August 10, 2009.

11. The Use of Aspirin in Colorectal Cancer Treatment (Aug. 12/09)

Aspirin use is associated with a reduced risk of colorectal cancer; however, the relationship between aspirin use and survival after colorectal cancer is not known. In an observational study that included 1279 men and women who were diagnosed with nonmetastatic colorectal cancer and followed up for a median 11.8 years, Chan and colleagues found that initiation of regular aspirin use after diagnosis was associated with a significantly lower risk of colorectal cancer–specific and overall mortality, particularly among patients whose tumors over express the enzyme called cyclooxygenase 2 (COX-2). Aspirin blocks the enzyme COX2, which is thought to play a role in cancer's spread. It is important to note that the study was observational, meaning researchers merely observed what patients were already doing, such as taking aspirin regularly for headaches. It is possible that factors other than aspirin accounted for the difference in cancer deaths. All the patients in the study had surgery for colon cancer and many also had chemotherapy. Among the 549 participants who used aspirin regularly after their diagnosis, 81 died from colorectal cancer (about 15%). In contrast, among the 730 people who did not use aspirin, 141 died of the disease (about 19%). In an editorial, Neugut from the Columbia University Medical Centre, discusses aspirin as an adjuvant therapy for colorectal cancer. Both articles have been posted on the Colorectal Cancer Association of Canada's website under the heading Research.

Chan, Andrew T., et al., Aspirin use and Survival after diagnosis of colorectal cancer. JAMA; Vol. 302, No. 6, August 12, 2009. pp. 649-659

SURGICAL THERAPY

12. Evaluating More Lymph Nodes May Not Be Helpful in Identifying Late-Stage Colorectal Cancer (Jul. 21/09)

Surgically removing and evaluating an increasing number of lymph nodes does not appear to identify a greater number of patients with stage III colorectal cancer, according to this study. More than 80% of newly diagnosed colorectal cancer patients will have locoregional disease (limited to a small region) and will be offered surgery that may cure their illness. The status of lymph nodes near the cancer has been recognized as the most powerful prognostic factor for recurrence and survival in these patients. Accurate lymph node staging also is important for determining prognosis and the need for adjuvant chemotherapy. In addition, lymphadenectomy (lymph node removal) may be therapeutic; several studies have shown a positive association between the number of lymph nodes removed and survival for patients with negative and positive lymph nodes. In 1990, the World Congress of Gastroenterology first proposed a minimum threshold of 12 lymph nodes to be removed during surgery for colorectal cancer. This benchmark has since been adopted as a quality measure for surgical practice by many. Then in 2004, researchers from 3 medical centers in the US embarked on an initiative to increase the number of lymph nodes removed druing surgery. In this study, researchers evaluated 701 consecutive colorectal cancer cases treated with surgery from 1996 through 2007. The medical records they analyzed included surgeries done before and after the initiative began. The initiative appeared successful in increasing the number of lymph nodes removed - when patients operated on in January 2005 or after were compared with those who had surgery before the initiative began; both the average number of lymph nodes removed (17.3 vs. 12.8) and the percentage of patients who had at least 12 lymph nodes removed (71.6% vs. 53%) increased. However, the proportion of patients diagnosed with stage III colorectal cancer did not change, with 204 of 553 (36.9%) of the earlier disease cases and 48 of 148 (32.4%) of the late disease cases having positive lymph nodes. Researchers note that "overall, the improvement in lymph node yield demonstrates the value and impact of communication through a multidisciplinary initiative engaged in adherence to recommended standards and improving quality of care. However, the data suggest that mandatory harvest of a minimum of 12 lymph nodes as a quality indicator or performance measure appears unfounded".

Kukreja, Sachin, et al., Increased Lymph Node Evaluation with Colorectal Cancer Resection. Archives of Surgery; Vol. 144, No.7, July 2009. pp.612-617

13. Laparoscopy vs. Conventional Open Hepatectomy in The Surgical Treatment of Liver Mets (Jul. 24/09)

The safety of laparoscopic major liver resections is still uncertain. The aim of this study was to compare the results for laparoscopic right hepatectomy with those for open right hepatectomy. Patients undergoing laparoscopy were compared with retrospectively selected patients who underwent open right hepatectomy. The surgical and post surgical outcomes were compared. 72 patients were analyzed: 22 in the laparoscopic group and 50 in the open hepatectomy group. The operating time was similar but the blood loss was significantly less in the laparoscopic resections. Hospital stays were short for the laparoscopic group as was general morbidity. Laparoscopy improved surgical and post surgical outcomes for the open hepatectomies in selected patients. This is the first comparative study to demonstrate an advantage of laparoscopy for a major liver resection. The researchers recommend that more randomized studies with a greater number of cases be performed to confirm the role of laparoscopy in major liver resections.

Dagher, Ibrahim, et al., Laparoscopic versus open right hepatectomy: a comparative study. The American J of Surgery. Vol. 198, Issue 2, pp. 173-177. (August 2009)

14. New Laparoscopic Colon Surgery Technique (Jul 24/09)

Dr. David Blumberg, a colorectal surgeon in Pittsburgh has pioneered a novel laparoscopic colon surgery technique. This novel colorectal operation is successful 95-98% in allowing patients with colorectal cancer, diverticulitis, colon polyps, Crohn's disease & ulcerative colitis to be cured through tiny band-aid size incisions. Dr. Blumberg's pioneering work was reported in the journals Surgical Innovations in September 2008 and Surgical Laparoscopic, Endoscopic and Percutaneous Techniques in February and June of this year. This novel laparoscopic colon surgery technique enables patients suffering from colorectal cancer, diverticulitis, polyps, Crohn's disease & ulcerative colitis to have a 95-98% success rate. This innovative technique, Band-Aid colon surgery, is particularly beneficial for patients with obesity and patients who had prior abdominal surgery. In these complicated patients, traditional laparoscopic colon surgery has a failure rate of 20-40%. In contrast Band-Aid colon surgery has a 95-98% success rate in these patients with obesity and prior abdominal surgery. Laparoscopic surgery is a technique that uses a long, thin telescope-like instrument (the laparoscope) attached to a video camera that projects images onto a video monitor. Through 3-4 additional "band-aid" cuts (1-2 inch) in the skin, the surgeon inserts instruments to hold the intestine, remove the diseased segment and reconnect the bowel. The abdomen is additionally expanded with carbon dioxide to distend the abdomen to give the surgeon "working space" to perform the operation. While traditional laparoscopic colon surgery is performed only partially laparoscopically, band aid colon surgery is performed completely laparoscopically. This allows a higher success rate and leaves only band aid size incisions. Band-aid colon surgery is a revolutionary colorectal surgical technique perfected by Dr. David Blumberg. This laparoscopic colon surgery results in less discomfort, quicker recovery, and improved cosmetic look. It also reduces the recovery time by half and assures successful treatment of patients' illnesses while minimizing the trauma of traditional surgery. Should you wish to access more information on the procedure or Dr. Bloomberg, please visit the website at www.bandaidcolonsurgery.com or http://www.wpxi.com/health/2964942/detail.html

www.bandaidcolonsurgery.com

15. Laparoscopic Rectal Surgery Compared to Open Rectal Surgery For Rectal Cancer (Aug. 13/09)

According to two studies, laparoscopic surgery for rectal cancer has a similar complication rate to open surgery, with less blood loss, rapid intestinal recovery, shorter hospital stay, and no compromise on the oncological outcomes. A surgical team in France compared two similar groups of patients with rectal cancer that had not spread beyond the rectum. 238 had laparoscopic surgery, 233 a more traditional open surgery. They found that there was no difference in deaths immediately after surgery, surgical complications, or quality of surgery. After five years:

- 3.9% of patients in laparoscopic group had cancer return locally versus 5.5 % of open operations, but this was not a significant difference.
- Cancer-free survival was also not different, with 82% of laparoscopic and 79% of open patients alive without recurrences.
- Overall survival (death from any cause) was lower among patients who had open surgery (72% were alive) compared to 83% in the laparoscopic group. This difference was almost entirely found in stage III patients.

During 36 laparoscopic operations (15%), surgeons had to change tactics and perform an open surgery, but this had no negative impact on death after surgery, local recurrence, or survival. Study results were limited because patients were not randomized. All surgeries were performed by a team of colorectal surgeons in a single hospital center using standardized approaches to surgery. Surgeons removed all signs of cancer in more than 90% of both laparoscopic and open operations. The Spanish team had similar conclusions based on their results wherein 204 patients with mid and low rectal tumours were treated with either open or laparoscopic surgery.

Lujan, J, et al., Randomized clinical trial comparing laparoscopic and open surgery in patients with rectal cancer. British J of Surgery. Vol 98, Issue 9, pp. 982-989.

Laurent, Christophe, et al., Laparoscopic vs. open surgery for rectal cancer: long term oncologic results. Annals of Surgery: July 2009; Vol. 250, Issue 1. pp.54-61.

RADIATION / INTERVENTIONAL RADIOLOGY

16. Acupressure Bands Treating Radiotherapy-Induced Nausea (Jul. 22/09)

The little elastic wrist bands with the plastic dots or semi-circles sewn into or glued to them are called acupressure bands and are advertised as a natural way to alleviate nausea due to motion sickness. New research shows they just may be an effective tool for people receiving radiation therapy to treat cancer as well. Previous research on this topic indicates that acupressure bands may be helpful for lessening chemotherapy-related nausea, so not surprisingly, a study to determine whether this non-toxic, inexpensive, non-invasive approach can help those receiving radiation therapy was designed. Researchers conducted a controlled trial and found that indeed, acupressure bands can help lessen radiation therapy nausea. Also encouraging is that the researchers designed a way to control, as much as possible, for the effect of "expectation" that the bands would help. They showed that even when people do not *expect* the acupressure bands to reduce their nausea, they work anyway. This research may not seem like much to most people, but for anyone who's undergone cancer treatment and struggled with nausea, these findings are nothing short of encouraging. Acupressure bands are cheap and easy-to-use, they can be purchased over-the-counter, and they have very little likelihood of causing any harm.

Putting Acupressure Bands to Work for You As Recommended by the Researchers:

- □ Acupressure bands should be used ***in addition*** to your regular anti-nausea (antiemetic) medications. They are not meant to replace medication, only to help your medication work more effectively.
- □ If you plan to use acupressure bands, let your doctor know so he or she can make a note of it in your medical chart.
- □ Acupressure bands are very unlikely to cause any harm, but if you have a condition or have had any treatments that affect circulation in your arms, ask your doctor if it is OK to use these bands. For example, some cancer surgeries can result in lymphedema in the arms (swelling of the arms) - Having something constrict the wrist may worsen this condition.

Roscoe, Joseph, et al., Acupressure Bands are effective in reducing radiation therapy-related nausea. J of Pain and Symptom Management. Online edition: doi10.1016/jpainsymman2008.09.006

17. Ontario Making Cancer PET Scans Available (Jul. 23/09)

Ontario is making positron emission tomography (PET) scanning a publicly insured health service available to cancer and cardiac patients under conditions where PET scans have been proven to be clinically effective. PET scanning is a nuclear medicine diagnostic imaging exam. PET scanning can provide information on both the location and the extent of the metabolic activity of abnormal tissues such as cancer and it has the potential to identify the areas of abnormal metabolic activity that is not always found through the use of MRIs or CT scans. For the services that will be insured, PET is useful in determining the stage or extent of some cancers to aid in treatment decisions. PET has also been determined to be useful in making treatment decisions in certain advanced heart conditions. Ontario's decision has been informed by advice received from Ombudsman Andre Marin. The Ministry of Health and Long-Term Care will ensure that resources are in place to continue clinical evaluations for additional health indications where PET scanning may prove beneficial. In addition, the ministry is committed to assessing and evaluating future technologies in an expeditious and transparent manner. For individuals with indications for which PET scans are not currently funded, physicians will continue to be able to make a request through the PET Access Program, where each application for funding is considered on a case-by-case basis. The ministry will work towards making this process and the decision-making behind it more transparent, and ensure that resources are available to process applications in a timely manner. The government is making PET scanning available as an insured service this fall, for certain evidence-based health indications, based on results from the Ontario studies of its effectiveness on patient outcomes. By October 2009, insured PET scans will be performed in Ottawa, London, Toronto, Hamilton and Thunder Bay. Ontario has established one of the largest PET infrastructures in Canada with 10 PET scanners at nine centres.

www.news.ontario.ca/mohltc/en/2009/07/ontario-making-cancer-and-cardiac-pet-scans-available.html

18. Accuracy of High Resolution MRI in Preoperative Staging of Rectal Cancer (Jul. 27/09)

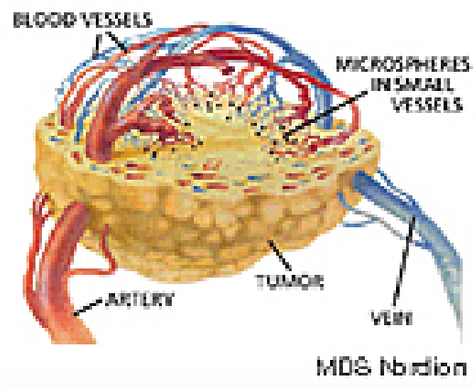
To achieve better prognosis and quality of life for patients with rectal cancer, extent of surgery and neoadjuvant (presurgical) chemoradiotherapy should accurately reflect disease extent. The aim of this study was to evaluate accuracy of high-resolution magnetic resonance imaging (HRMRI) for preoperative staging of rectal cancer. Between 2001 and 2003, 104 patients with primary rectal cancer were examined with HRMRI and underwent radical surgery. Transmural invasion (penetrating the rectal wall) depth and lymph node metastasis were assessed according to the tumor–node–metastasis (TNM) system by both HRMRI and histopathology (refers to the examination of a biopsy or surgical specimen by a pathologist, after the specimen has been processed and histological sections have been placed onto glass slides), and results were compared. There were 15 T1, 25 T2, 50 T3, and 14 T4 tumors. High Resolution MRI was moderately accurate for prediction of mesorectal lymph node metastasis **(74%)** and highly accurate regarding transmural invasion depth **(84%)**, and mesorectal fascia could be visualized quite accurately **(96%)** and lateral pelvic node involvement accuracy was **(87%)**. Therefore, researchers concluded that HRMRI appears useful for preoperative decision-making in rectal cancer treatment.

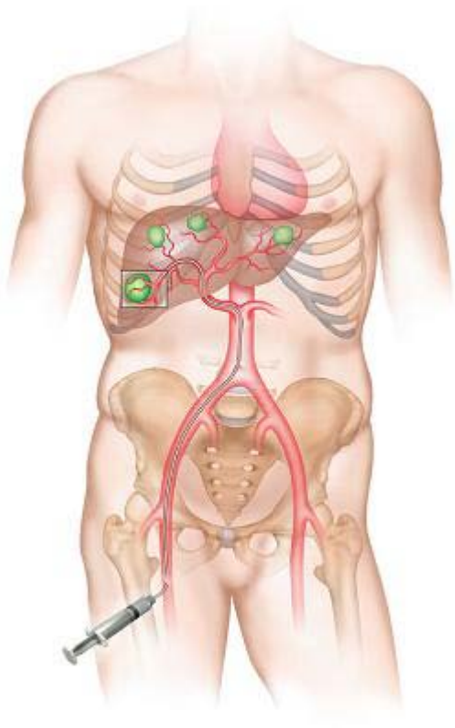
Akasu, Takayuki, et al., Accuracy of High Resolution Magnetic Resonance Imaging in Preoperative Staging of Rectal Cancer. Annals of Surgical Oncology. Published online ahead of print: doi: 10.1245/s10434-009-0613-3

19. Treatment of 5FU Resistant Patients With Liver Mets Using Yttrium-90 Resin Microspheres Plus Systemic Irinotecan (Aug. 7/09)

Liver metastases are the principal cause of death in patients with advanced colorectal cancer (CRC). Irinotecan is a chemotherapeutic agent used in the treatment of CRC and has demonstrated synergistic potential when used with radiation therapy. Radioembolization (the injection of micron-sized embolic particles loaded with a radioisotope) with yttrium-90 microspheres has demonstrated increased response and survival rates when given with fluorouracil (5FU) chemotherapy. This study's goal was to evaluate the maximum-tolerated dose of simultaneous irinotecan and radioembolization in fluorouracil-refractory patients (patients who became resistant to 5FU) with CRC hepatic metastases. 25 irinotecan-naïve patients who had experienced relapse after previous chemotherapy were enrolled into three dose-escalating groups and radioembolization was administered during the first chemotherapy cycle. Most patients experienced acute, self-limiting abdominal pain and nausea. Mild lethargy and anorexia were common. 11 (48%) of 23 patients had a partial response, and 9 patients (39%) had stable disease. The median progression-free survival (time before disease got worse) was 6.0 months; the median survival was 12.2 months. Researchers concluded that concomitant use of radioembolization plus irinotecan did not reach a maximum-tolerated dose. The recommended dose of irinotecan in this setting is 100 mg/m^2 on days 1 and 8 of a 3-week cycle.

Microspheres





Microspheres

A small incision is made in the patient's groin and a flexible catheter will be guided into the liver under x-ray vision. The catheter is moved through the hepatic artery, which is one of 2 blood vessels that feed 90% of the liver mets, and positioned by the interventional radiologist to allow for targeted infusion of the Y90 microspheres to the liver tumours. Microspheres take about 15 minutes to be infused and the whole procedure takes about one hour from beginning to end. To access a video on microspheres or Theraspheres, please click on the following link: http://www.mdsnordion.com/therasphere/product-therasphere.asp

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http://images.google.com/imgres?imgurl=http://sirtex.com/images_custom/torso.jpg&imgrefurl=http://sirtex.com/content.cfm%3Fsec%3Dworld%26MenuID%3DA040E9B4&usg=__86hK1pSYCTsAWSLgTwk_CMAIlPk=&h=236&w=169&sz=15&hl=en&start=52&sig2=pAAuVNhVx226lr7qv_PxSg&tbnid=ks-qRkljFqZm7M:&tbnh=109&tbnw=78&prev=/images%3Fq%3DY90%2Bsir%2Bspheres%26gbv%3D2%26ndsp%3D20%26hl%3Den%26sa%3DN%26start%3D40&ei=AL-ESsqfNJTGlAe9hOnABQ And:

http://www.mdsnordion.com/therasphere/product-therasphere.asp

Van Hazel, Guy, et al., Treatment of fluorouracil-refractory patients with liver metastases from colorectal cancer by sing yttrium-90 resin microspheres plus concomitant systemic irinotecan chemotherapy. J of Clinical Oncology. Published online ahead of print Aug. 3, 2009. Doi: 10.1200/JCO.2008.20.8116

SCREENING

20. Screening Yielding False-Positive Results Are Common (Jul.20/09)

Researchers affiliated with the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial have reported that the risk of obtaining a false-positive result from screening for prostate, lung, colorectal, and ovarian cancer is high and becomes cumulatively higher with ongoing screening—after 14 screening tests, the cumulative risk of a false-positive is 60.4% for men and 48.8% for women. Cancer screening has become an important component of preventive care because cancer is most treatable when caught in the early stages of development. In many instances screening has been shown to reduce mortality from cancer. More specifically, there is also evidence that **colorectal screening** reduces mortality. However, it is unclear whether or not screening for some types of cancer reduces the mortality rates, as evidence indicates that some slow-growing cancers are being over diagnosed; in such cases patients would often die of other causes before the cancer started causing symptoms. As a result, there is some controversy over the frequency and interval of cancer screening. The PLCO Cancer Screening Trial is a randomized, controlled trial that was designed to evaluate the effects of prostate, lung, colorectal, and ovarian cancer screening on disease-specific mortality. The study included 68,436 patients aged 55 to 74 who were randomized to receive screening or usual care. Participants received up to 14 screening tests over the course of three years. For women, the tests included vaginal ultrasounds, chest X-rays, sigmoidoscopies to examine the colon, and measurement of an ovarian cancer marker called CA-125. Men underwent chest X-rays, digital rectal examination, sigmoidoscopy, and measurement of prostate specific antigen (PSA). After four screening tests, the cumulative risk of a false-positive result was 36.7% for men and 26.2% for women. After 14 tests, the cumulative risk for a false-positive result jumped to 60.4% for men and 48.8% for women. Furthermore, the cumulative risk of undergoing an unnecessary invasive biopsy procedure based on the results of a false-positive screening test was 28.5% for men and 22.1% for women. The high rate of false-positives does not mean that all screening is “bad”; however, it indicates one of the risks of consistent, long-term screening. It is important to understand both the risks and benefits of screening and to make informed choices about preventive care.

Crosswell, JM., et al., Cumulative incidence of false-positive results in repeated multimodal cancer screening. Annals of Family Medicine, 2009; Volume 7, pp.212-222

21. Isolated Lung Mets In Colorectal Cancer Should Be Screened (Jul. 26/09)

The absence of liver mets in patients with colorectal cancer should not preclude a search for lung metastases, according to this study. Although pulmonary metastases from colorectal cancer usually result from hepatic metastases, the findings suggest that the true incidence of isolated lung metastases in colorectal cancer may be as high as **3%-12%** in patients with **rectal cancer** and **1%-6%** in patients with **colon cancer**. Thus, staging and surveillance of all patients with colorectal cancer should include an evaluation for possible lung involvement. In all, 754 patients who were diagnosed with colorectal cancer between December 2003 and August 2007 were included in the review. The patients, whose mean age was 68 years, had rectal cancer (196 patients) or colon cancer (558, including 369 with left-side lesions and 189 with right-side lesions). Isolated lung metastases were determined by confirmed biopsy of the lung lesion or through imaging suggestive of lung metastases in the absence of live lesions on CT scan up to 6 months after diagnosis of the primary cancer. Based on these criteria, isolated lung metastases were reported in 23 (12%) of the rectal patients and in 33 (6%) of the colon cancer patients, including 25 in patients with left-side lesions and 8 in patients with right-side lesions. Of the 23 rectal cancer patients with isolated lung metastases, 19 underwent surgical resection, and of these, 16 were at stage T3 or

higher and 15 were at nodal stage N1 or higher. Isolated lung metastases were synchronous (defined as occurring within 6 months of the primary cancer) in 20 of the 33 colon cancer patients and in 9 of the 23 rectal cancer patients, noting that the lung involvement was diagnosed from the start in 13 of the colon cancer patients and in 5 of the rectal cancer patients. Researchers concluded that an analysis of the patients with and without isolated lung metastases showed that the site of the primary cancer was significant for isolated lung metastases, with the **rectal cancer** patients being twice as likely as the colon cancer patients to develop lung involvement.

Tan, Ker Kan, et al., How uncommon are isolated lung metastases in colorectal cancer? A review from Database of 754 patients over 4 years. J of Gastrointestinal Surgery. Vol. 13, Number 4, pp.642-648

22. Colorectal Cancer Screening Is Over- and Underused (Jul. 28/09)

This study wished to determine if colorectal cancer screening was reaching older eligible patients, and is screening targeted to patients who are expected to live long enough to benefit from it? Researchers studied Veterans Affairs and Medicare claims data for a group of patients (age, ≥70) who had at least one outpatient visit at one of four VA medical centers and were eligible for screening (i.e. did not have colon cancer or had not had screening). Of 27,000 patients, 46% received colorectal cancer screening (fecal occult blood testing, colonoscopy, sigmoidoscopy, or barium enema) during a 2-year observation period. Of patients aged 70 to 74 who had no medical comorbidities (other existing illnesses), only **51%** received screening. Yet, of patients aged 80 or older who had multiple comorbidities and life expectancies of less than 5 years (5-year mortality rate, 66%), 34% were screened. A greater number of outpatient visits was associated with receiving screening. Because patients with comorbidities had more visits, 50% of those with severe medical comorbidities and four or more visits were screened -- a screening incidence similar to that of healthier younger patients (who had fewer visits). The conclusion is strikingly clear -- we need to better target colorectal cancer screening to those most likely to benefit; however, how to do that is less clear. Practice guidelines and decision aids that compare the benefits of preventive services and life expectancy might help clinicians and patients make better decisions about screening.

Walter, LC., et al., Impact of age and comorbidity on colorectal cancer screening among older veterans. Annals of Internal Medicine: 2009;150: p.465

23. The Use of Colonoscopy To Predict Recurrent Adenomas (Jul.29/09)

This study found that results from two colonoscopies three years apart gave better information about whether a high-risk polyp would be found on a third exam than results from the second test alone. Even if a second colonoscopy, done three years after the first, showed no adenomas at all, 8 in 100 study participants with high-risk polyps on their first exam had developed a high-risk polyp by six years when they had a third colonoscopy. In this study, 564 participants had three colonoscopies: one at the beginning of the study, one three years later, and a third three years after that. All of the people in the study had at least one polyp at the beginning of the study, but not all had polyps considered to be high-risk. High risk patients had an adenoma 1 centimeter or larger, three or more adenomas, or a polyp with advanced pre-cancerous changes.

- Patients, whose first colonoscopy had high risk polyps but had no adenomas at all on a second study, had a 7.7% chance that their third exam would reveal a high-risk polyp.
- Those with initial high-risk adenomas and a low-risk second exam had a 1 in 10 chance of a high-risk third exam.
- Those who were low-risk on both a first and second colonoscopy had a less than 5% chance of having a high-risk polyp found during the third exam.
- Patients who were considered high risk at their second exam had a 1 in 5 (20%) chance that an advanced polyp would be found during their third test. For these patients, it made no difference whether they were high or low risk with their first colonoscopy.

Researchers concluded that information from 2 previous examinations may help identify low-risk patients that benefit little from intense surveillance. Surveillance guidelines might be tailored in selected patients to use information from 2 previous examinations, not just the most recent one.

Robertson, Douglas, et al., Using the results of a baseline and a surveillance colonoscopy to predict recurrent adenomas with high risk characteristics. Annals of Internal Medicine. Vol.151, Issue 2; pp.103-109

OTHER

24. Mutated Gene Increases Risk of Developing Colorectal Cancer (Jul.20/09)

A commonly found gene mutation, once thought to be a trivial abnormality, adds significantly to the risk of developing bowel cancer, according to this new study. People with the defect — present in one in every 36 Caucasians — and who had a cancer pre-disposing abnormality were three times more likely to develop bowel cancer. What researchers discovered is that people who carry two copies of the gene mutation known as H63D, and who also have the gene mutations linked to bowel cancer, are three times more likely to develop bowel cancer but fortunately, this particular gene mutation can be readily detected. The study looked at more than 350 people from Australia and Poland who carried a specific gene mutation associated with a type of bowel cancer known as hereditary nonpolyposis colorectal cancer or Lynch Syndrome. What this research highlights is that people with a family history of bowel cancer would do well to have regular colonoscopies in the hope of picking up the early warning signs and help prevent the cancer from developing. Being vigilant is critical, especially given that hereditary nonpolyposis colorectal cancer often strikes younger people who are less likely to get regular checks for bowel cancer.

Olynyk, John, et al., Haemochromatosis HFE gene polymorphisms as potential modifiers of hereditary nonpolyposis colorectal cancer risk and onset age. International J of Cancer. Vol. 125, Issue 1, pp.78-83.

25. Understanding Colorectal Cancer Metastases Formation (Jul.22/09)

Previously, only a few genes had been associated with the formation of metastases in colorectal cancer. Now, researchers in this study have identified 115 genes that are disregulated both in the primary tumor and in its metastases. In the future, their findings may help identify patients with aggressive tumors at an earlier stage. Beginning in glands in the bowel lining, colorectal cancer often remains undiscovered initially. However, the main problem is not the primary tumor, but the dangerous metastases. Metastases arise when single cells break off from the primary tumor and spread to other body regions via the blood vessels or the lymphatic system. In colorectal cancer, these cells usually settle in the liver, lungs, or lymph nodes. Since the affected patient seldom feels pain or shows other symptoms, the tumor is frequently not discovered until it has already formed metastases. To investigate which genetic mutations favor the formation of metastases, the researchers analyzed 150 tissue samples of colorectal cancer patients with and without metastases. The researchers identified 115 genes that are falsely regulated in both the primary tumors and their metastases. In this way, the researchers succeeded in identifying a genetic signature which distinguishes tumors with metastatic potential from those that do not metastasize. Of the 115 genes the researchers identified, they focused on one gene in particular called the BAMBI gene. They discovered that this gene is more active in metastatic tumors and metastases than in non-metastatic tumors. The research showed that the particular gene BAMBI is associated with two import signaling pathways and thus promotes metastasis formation. These signaling pathways (Wnt and TGF-beta) are, among other things, important in the developing embryo. In the future, the researchers hope to investigate the role of the other 114 genes more closely, in order to better understand the individual steps of metastasis formation.

Fritzmann, Johannes, et al., A colorectal cancer expression profile that includes transforming growth factor B inhibitor BAMBI predicts metastatic potential. Gastroenterology; Vol. 137, Issue 1, pp. 165-175. (July 1009)

26. Inflammation Associated with Stage II Colorectal Tumors Can Predict Prognosis (Jul.25/09)

A tumor inflammatory infiltrate is the level of white blood cells (neutrophils and leucocytes) associated with inflammation of the tumor. Apparently, measuring the levels of these white blood cells can help with the determination of a prognosis. A pronounced tumour inflammatory infiltrate (high levels of the white blood cells) has been known to confer a good outcome in colorectal cancer. The aim of this study was to examine the prognostic value of tumour inflammatory infiltrate in node negative or Stage II colorectal cancer. 200 patients underwent surgery for their stage II colorectal cancer and the inflammatory infiltrate was assessed. In patients with low grade inflammatory infiltrate, researchers found that these tumours were 3 times as likely to be deadly. On the other hand, the presence of high-grade infiltrate was associated with an immune response in the tumour and thereby improving survival. The researchers concluded that assessment of inflammatory infiltrate can provide independent prognostic information in stage II colorectal cancer. A high grade local inflammatory response may represent effective host immune responses impeding tumour growth.

Campbell, S.D., et al., Tumour inflammatory infiltrate predicts survival following curative resection for node-negative colorectal cancer. European J of Cancer. Vol. 45, Issue 12, August 2009, pp. 2138-2145.

27. Patients With Lynch Syndrome Often Underestimate their Cancer Risk (Jul. 30/09)

Lynch Syndrome, or Hereditary Nonpolyposis Colorectal Cancer (HNPCC), greatly increases risk of colon cancer in people who have this condition. Lynch syndrome results due to abnormalities in certain genes in the cells of the body. The condition has been known to increase the risk of cancers of the rectum, stomach, small intestine, liver, gallbladder ducts, upper urinary tract, brain, skin, prostate, uterus (endometrium), and ovaries. For most families with Lynch syndrome, a strong family history of various types of cancer is obvious. New Research from this study now suggests that even for people who have received genetic testing for Lynch syndrome, many may underestimate their true risk of developing

cancer. It turns out that when genetic test results for Lynch syndrome are "indeterminate", which means that no obvious gene mutation is found or that a mutation of unknown significance is found, most patients don't understand this, and most underestimate what it means for their personal risk for colorectal cancer. This research finding is discouraging for several reasons:

- Genetic counselors and/or doctors are not effective enough at explaining complex test results in a way that most people can understand, and act upon.
- When people don't really understand what a genetic test means, they may assume that they are fine, their risk is low, and they have nothing to worry about. This study suggests this is the case much of the time.
- If patients underestimate their risk of developing colon cancer, they may forgo necessary screening procedures, such as early and regular colonoscopy screening. This is a big mistake, because if colon cancer eventually is diagnosed, it is much more likely to be advanced, and less curable, than if caught with early screening.
- If patients underestimate their risk of developing colon cancer, they may not feel that it's important to take other preventive health measures, such as taking medications prescribed by their doctor to reduce risk, making regular physical activity a priority, eating a fiber-rich, healthy, plant-based diet, avoiding smoking, and talking to children and other relatives about their risk.
- If patients underestimate their risk of developing colon cancer, they may dismiss more aggressive management options such as a colostomy. While no one wishes to have their colon removed, if your risk of developing colon cancer is nearly 100%, it's far better to consider this surgery than to wait until you have advanced colon cancer, which is quite difficult to treat and cure.

Grover, Shilpa, et al., Colorectal Cancer risk perception on the basis of genetic test results in individuals at risk for Lynch syndrome. J of Clinical Oncology. Early Release, published online ahead of print Jul.20, 2009. doi:10.1200/JCO.2008.18.6940.

28. Women and Lynch Syndrome-Related Ovarian Cancer (Aug. 1/09)

According to the results of this study, women with Lynch syndrome-related ovarian cancer have survival rates twice that of their peers. More than 80% of women with a mutation in one of the mismatch repair genes (Inherited mutations that affect DNA repair: either MLH1, MSH2 or MSH6) were diagnosed at stage 1 or 2, and ten year cancer-specific survival was 80%, compared to 40% in women without mutations. Lifetime risk of getting ovarian cancer for Lynch patients was 10%, and combined with the excellent survival rate gave all Lynch women a 2% risk of dying from ovarian cancer.

Grindedal, Eli Marie, et al., Survival in women with MMR mutations and ovarian cancer; a multicentre study in Lynch syndrome kindreds. J of Medical Genetics. Published online first: 26, July 2009. doi: 10.1136/jmg.2009.068130

29. Targeting the Protein CCKR2 For Potential Drug (Aug. 2/09)

Colorectal cancer is associated with an **abnormally high** rate of increase in the number of cells lining the colon (called **colonic hyperproliferation**). In mice, overexpression of the human protein progastrin has been shown to cause colonic hyperproliferation and promote colorectal cancer, but the molecular mechanisms underlying this have been unkown. In this study, researchers have revealed a key link between the protein CCKR2 and progastrin-related colonic hyperproliferation. Initial analysis indicated that the CCK2R gene was upregulated (an increase in the number of receptors on the surface of target cells, making the cells more sensitive to a hormone or another agent) in mice that overexpressed human progastrin. Deletion of this gene in mice that overexpressed human progastrin abolished the colonic hyperproliferation induced by the high levels of human progastrin and drastically reduced the extent of experimentally induced colorectal cancer. As previously published data indicate that levels of progastrin might be elevated in individuals with colorectal cancer, the authors conclude that their study suggests that CCKR2 may be a viable target for the development of drugs to treat or prevent colorectal cancer.

Wang, Timothy, et al., Inactivating cholecystokinin-2 receptor inhibits progastrin dependent colonic crypt fission, proliferations, and colorectal cancer in mice. J Clinical Investigation. Published ahead of print online. Vol. 119, Issue 8; Doi:10.1172/JCI38918

30. Colon Cancer and Bone Metastases (Aug. 6/09)

It is well recognized that colorectal cancer does not frequently metastasize to bone. The aim of this retrospective study was to establish whether colorectal cancer ever bypasses other organs (such as the liver and lungs) and metastasizes directly to bone and whether the presence of lung lesions is superior to liver as a better predictor of the likelihood and timing of bone metastasis. Researchers performed a retrospective analysis on patients with a clinical diagnosis of colon cancer referred for staging using whole-body 18F-FDG PET and CT or PET/CT. They combined PET and CT reports from 252 individuals with information concerning patient history, other imaging modalities, and treatments to analyze disease progression. No patient had isolated bone metastasis at the time of diagnosis, and none developed isolated bone metastasis without other organ involvement during their survey period. It took significantly longer for colorectal cancer patients to develop metastasis to the lungs (23.3 months) or to bone (21.2 months) than to the liver (9.8 months). Researchers therefore concluded that metastasis only to bone

without other organ involvement in colorectal cancer patients is extremely rare, perhaps more rare than previously thought. The findings suggest that resistant metastasis to the lungs predicts potential disease progression to bone in the colorectal cancer population better than liver metastasis does.

Roth, Eira, et al., Does colon cancer ever metastasize to bone first? A temporal analysis of colorectal cancer progression. BMC Cancer 2009, Volume 9:274. doi: 10.1186/1471-2407-9-274

NUTRITION & HEALTY LIFESTYLE

31. Mistletoe and Cancer Patients (Jul. 20/09)

Mistletoe is often used as a complementary approach in oncology. Despite experimental anti-tumour effects and several reviews, there remains controversy about its clinical role. Potentially relevant trials were identified to perform a systematic review. To be included, randomized or comparative clinical trials at least had to examine mistletoe preparations standardized according to manufacturing process and to describe interventions explicitly. Additionally, cohort studies were included for reasons of external validity. 18 clinical trials (>6,800 participants) were included in the review. Due to the differences between trials, a meta-analysis (combining the results of several studies) was not generated by the researchers. Regarding efficacy, findings were inconsistent regarding life expectancy, relation to tumour entity, dosing and treatment duration. Yet, studies indicate that quality of life is improved for cancer patients. As these findings do not seem to be limited to one of the different mistletoe preparations reviewed, the treatment may be summarized under the umbrella term 'mistletoe therapy'. Regarding safety, 1 serious adverse event related to mistletoe was described; non-serious adverse events were local reactions at injection site. Allergic reactions were rare. Researchers concluded by saying that supportive 'mistletoe therapy' appears safe and beneficial for quality of life in adult patients with solid tumours. However, an urgent need to confirm its efficacy in patient-centred care in a more complex oncological setting is required. This has to be evaluated systematically in prospective observational trials with validated, multidimensional patient-rated Quality of Life questionnaires and comparisons of different preparations and dosages.

Melzer, Jorg, et al., Efficacy and Safety of mistletoe preparations (viscum album) for patients with cancer diseases. Forschende Komplementarmedizin – Research in Complimentary Medicine. Vol. 16, No. 4, 2009. Published ahead of print online. Doi:10.1159/000226249

32. Physical Activity & Diet Can Influence Quality of Life in CRC Patients Receiving Chemo (Jul. 27/09)

The relationship between colorectal cancer (CRC) risk and physical activity and dietary habits has been well-established, but less is known about this relationship in terms of quality of life (QOL) after receiving a diagnosis. Moreover, it is unknown whether this relationship is consistent across cancer stage or treatment setting. Thus, the purpose of this study was to assess current diet and physical activity behaviour in CRC survivors receiving systemic chemotherapy, and to examine potential associations between these behaviors, quality of life, and social support. **67 CRC** survivors currently receiving chemotherapy in Calgary, Alberta completed the survey package. Measures included demographic and medical data, physical activity levels, diet behaviour, Quality Of Life (QOL), and social support. In a largely metastatic sample (63%), over half were meeting national diet guidelines **(58%),** few were meeting national physical activity guidelines **(26%),** and a small number were meeting both **(17%).** However, further analysis revealed that **an impressive 88% were physically active at some level.** Neither behaviour was significantly associated with QOL or perceived social support. Furthermore, researchers report that there were no significant QOL differences between those treated with palliative intent or adjuvant therapy (post surgical therapy with curative intent). Important group differences emerged between those meeting and not meeting the guidelines, and associations between QOL, age, BMI, and provisions of social support. These findings provide insight into lifestyle behaviors of CRC survivors currently receiving systemic chemotherapy, and the differences in perceived QOL as affected by severity of disease and treatment setting. More studies in a larger sample of CRC survivors on chemotherapy are needed to confirm lifestyle behaviour patterns and identify factors related to quality of life that are unique to this population, especially those receiving metastatic treatment. Furthermore, the researchers maintain that the appropriateness of national diet and exercise guidelines for survivors being treated with palliative intent needs to be addressed.

Stephenson, Lynette, et al., Physical activity and diet behaviour in colorectal cancer patients receiving chemotherapy: associations with quality of life. BMC Gastroenterology 2009. Vol.9:60. doi: 10.1186/1471-230X-9-60

33. Most Older Long-term Cancer Survivors Have Poor Health Habits (Jul.28/09)

A new study finds that most older long-term cancer survivors who are interested in diet and exercise actually have poor health habits. This study also reveals that those survivors who do exercise and watch their diet have improved physical health and quality of life. The research indicates that greater efforts are needed to encourage elderly cancer survivors to live healthier lives. There are relatively few studies looking at older cancer survivors' health behaviors, but evidence suggests that many older long-term cancer survivors have suboptimal health habits. Researchers reviewed data from a total of 753 older (aged 65 years or over), long-term (five or more years post-diagnosis) breast, prostate, and **colorectal** cancer survivors to estimate the prevalence of poor health habits in this population. The study included

telephone interviews to determine individuals' eligibility for a diet and exercise intervention trial. Interviews assessed exercise, diet, weight, and quality of life, including physical functioning and mental health. The researchers found that older cancer survivors, all of whom were interested in a diet and exercise intervention study, generally had poor health habits. For example, they reported an average of only 10 minutes of moderate-to-vigorous exercise per week. This is far short of the national recommendation of more than 150 minutes of exercise per week. Also, only 7% met healthy eating recommendations set by national guidelines. Despite their suboptimal health behaviors, cancer survivors reported a level of mental and physical quality of life that actually exceeded levels typically found among older individuals. This may be explained in part by the study's design: investigators excluded survivors with significant health problems and functional limitations. The study also found that interviewees who exercised more and had better dietary habits experienced **better vitality and physical functioning**. On the other hand, individuals who were obese had **worse physical quality of life**. The findings point to the potential negative impact of obesity and the positive effect of regular exercise and a healthy diet on physical quality of life outcomes among older, long-term cancer survivors. Researchers add that only randomized clinical trials, however, can reveal whether lifestyle modification improves older, long-term cancer survivors' physical outcomes.

Mosher, Catherine, et al., Associations between lifestyle factors and quality of life among older, long-term breast, prostate, and colorectal cancer survivors. Cancer; Published Online: July 27, 2009 (DOI: 10.1002/cncr.24436); Print Issue Date: September 1, 2009.

34. Alcohol Intake and Colorectal Cancer Risk (Aug. 5/09)

This study supports much of what has already been shown about alcohol consumption and colorectal cancer risk in previous research: Moderate drinking won't significantly increase risk of colon cancer, but drinking larger amounts and drinking daily, will indeed take a toll on the colon. When comparing the risk of colon cancer in people who drink heavily (daily or multiple times per day), with people who drink moderately (less than daily) or not at all, researchers found heavy drinking increased risk of colon cancer by **80%.** Risk of other cancers, most notably esophageal and lung, was markedly increased in heavy drinkers as well. In all, the researchers found statistically significant relationships between heavy consumption of beer and spirits and 6 different cancers, including colorectal. As already noted, moderate drinking (less than daily) and wine consumption did not show the same effects.

Benedetti, Andrea, et al., Lifetime consumption of alcoholic beverages and risk of 13 types of cancer in men: results from a case-control study in Montreal. International J of Epidemiology, Detection and Prevention. Vol. 32, Issue 5; pp.352-362 (2009)

35. Exercise and Cancer Mortality in Men (Aug. 4/09)

There is a lack of evidence to show the role of exercise intensity in the prevention of cancer mortality since no previous studies have shown this relation. The researchers in this study, however, decided to assess the relationship of leisure-time physical activity with cancer mortality. The Finnish study was a long-term assessment involving a group of 2560 men, aged 42-60 years. They reported their leisure-time physical activity (that's exercise during free-time, not related to what you might get at work) and were followed by researchers for about 17 years. The study showed that the men who exercised at moderate-to-high intensity for at least 30 minutes per day had a ***37% lower risk of dying of cancer*** compared with the men who did not exercise regularly. Among the biggest benefits of regular exercise was a reduction in the risk of gastrointestinal cancers, including **colon cancer**. The researchers noted that this finding may be due to the effects of exercise on energy balance, including effects on managing body weight. This connection with metabolism and a healthy body weight are particularly important for preventing colon cancer. The study found that to get the highest level of cancer risk reduction, the men engaged in 30 minutes of "moderate-to-high intensity" exercise. The difficulty level of any exercise is subjective, meaning what feels tough to one person may be a walk in the park for another. But to get an idea of what this study looked at, consider the MET: *metabolic equivalents of oxygen consumption*. The MET is a standardized way of measuring how hard any particular physical activity is. If you've ever used a piece of cardio equipment, such as a treadmill or elliptical trainer, you can see the intensity of the exercise you're performing, in MET, on the machine's display panel. For those who don't have access to this type of equipment, consider that the average intensity of jogging in this study was listed as 10.1 MET. Swimming was considered 5.4 MET, rowing was 5.4 MET, and cycling was 5.1 MET. Lighter activities such as gardening and yard work were 4.3 MET, and walking was 4.2 MET. For this study, any activity above an average of 4 MET was considered moderate-intensity exercise. What this means is that anything from fast walking on up, in terms of intensity, should help you measurably decrease colon cancer risk. And while this study only considered men, the researchers noted that they would expect the same effects for women. To get your 30 minutes in each day, do whatever it is you enjoy and that fits into your lifestyle. Anything is better than nothing: In the study, even though the biggest benefit came from higher intensity exercise, even small amounts of activity did reduce cancer risk. The ultimate message is: What you do doesn't matter quite so much as just doing something.

Laukkamen, Jari, et al., Intensity of leisure-time physical activity and Cancer mortality in men. Br. J Sports Medicine. Published online first: 28 July 2009. doi:10.1136/bjsm.2008.056713.

36. How Fish Intake Can Affect Colon Cancer (Jul. 31/09)

An increase in the consumption of either oil-rich or lean fish to two portions weekly over six months does not markedly change apoptotic and mitotic rates in the colonic mucosa. In a multicenter, randomized,

controlled intervention trial, 242 patients with colorectal polyps, inactive ulcerative colitis or no macroscopic signs of disease were recruited and randomly allocated to receive dietary advice plus either 300 g/week of oil-rich fish (salmon), 300 g/week of lean fish (cod) or only dietary advice (DA) for 6 months. The total number of **apoptotic cells (dying cells)** per crypt (cluster of abnormal tube-like glands in the lining of the colon and rectum which form before colorectal polyps and are one of the earliest changes that can be seen in the colon that may lead to cancer) did not increase in the salmon or cod group compared with the DA group. The total number of mitotic cells (cells multiplying) per crypt decreased un- significantly in the salmon group and in the cod group compared with the DA group. Researchers therefore concluded that according to these results, an increase in the consumption of either oil-rich or lean fish to 2 portions weekly over 6 months does not markedly change apoptotic (dying) and mitotic (multiplying) rates in the colonic mucosa.

Pot, Gerda K, et al., Fish consumption and markers of colorectal cancer risk: a multicenter randomized controlled trial. American J of Clinical Nutrition. Vol. 90, No. 2, pp. 354-361.

37. How Colon Cancer Is Affected by Sugar Starvation (Aug. 6/09)

Scientists at the Johns Hopkins Kimmel Cancer Center have discovered how two cancer-promoting genes enhance a tumor's capacity to grow and survive under conditions where normal cells die. The knowledge, they say, may offer new treatments that starve cancer cells of a key nutrient - **sugar**. However, the scientists caution that the research does not suggest that altering dietary sugar will make any difference in the growth and development of cancer. Cancer cells adapt to living within the inner layers of a tumor, a place where circulating nutrients are relatively scarce. Researchers wanted to know what makes these cancer cells survive under such conditions. Their hunt quickly narrowed to one gene, GLUT1, which was consistently turned on at high levels in cells laden with KRAS and BRAF mutations (two of the most common colorectal cancer genes). Proteins made by GLUT1 are located on the cell surface and transport glucose into cells' interiors. With increased expression of the GLUT1 gene, cells make more GLUT1 transporters and ingest more glucose. Researchers believe that increased GLUT1 is a survival adaptation that makes cancer cells very efficient at gathering what little sugar exists in these areas. When cells with wild type Kras were subjected to a low glucose environment, very few cells survived. Most surviving cells expressed high levels of GLUT1 and 4% of these survivors had acquired new Kras mutations. Researchers concluded that these data suggest that glucose deprivation can drive the acquisition of Kras pathway mutations in human tumours.

Papadopoulos, Nickolas, et al., Glucose deprivation contributes to the development of Kras Pathway Mutations in tumour cells. Science. Published online ahead of print August 6, 2009. doi:10.1126/science.1174229

38. Preventing Colon Polyps Through Diet (Aug. 6/09)

As part of the long-running Polyp Prevention Trial, researchers randomly assigned study participants to eat their usual diet, or to switch to a low-fat, high-fiber, high-fruit and vegetable diet. This low-fat diet was designed to provide:

- □ No more than 20% of total calories from fat
- □ 18 or more grams of fiber each day
- □ 5-8 servings of vegetables and fruit each day

The latest findings from the Polyp Prevention Trial demonstrate again why this type of diet is promoted to reduce colon cancer risk: Study participants who regularly met all three of these dietary goals had a **35%** reduced risk of developing adenomatous polyps, compared to people eating their regular diet. In other words, in a group of over 2,000 people, all of whom had been screened for colon polyps, been found to have polyps, and had those polyps removed at the start of the study, eating a low-fat, high-fiber, high-fruit and vegetable diet reduced risk of getting polyps ***again***, by **35%**. This is rather meaningful because adenomatous polyps are the type of growth in the colon that if not removed, can develop into cancer. If the polyps are prevented, then the risk of developing colon cancer is reduced.

Sansbury, Leah, et al., The effect of strict adherence to a high-fibre, high fruit and vegetable and low fat eating pattern on adenoma recurrence. Amer J of Epidemiology. Advance Access July 30, 2009. doi: 10.1093/aje/kwp169

39. More Omega-3 For Colorectal Cancer Protection (Aug. 12/09)

This study suggests that increasing the intake of omega-3 fatty acids, and decreasing intakes of omega-6, could reduce the risk of colorectal cancer. The highest dietary ratio of omega-6 to omega-3 was associated with a 95% increase in the risk of women developing colorectal cancer, according to results of this study. The study adds to a small but growing body of evidence supporting the importance of balance between omega-3 and omega-6 fatty acids. Previously, the ratio of omega-3 to -6 has been linked to prostate cancer risk (*Clinical Cancer Research*, Vol. 12, Issue 15, *Journal of Clinical Investigation*, July 2007). According to researchers, data on how polyunsaturated fatty acids (PUFA) may impact on the risk of colorectal cancer have been *"inconsistent"*. Using data derived from two food frequency questionnaires, researchers investigated if PUFA intake could impact on colorectal cancer risk in Chinese

women. Their findings suggested that *"the dietary total omega-6 to omega-3 PUFA ratio was strongly associated with colorectal cancer risk"*. In fact, increasing ratios of omega-6 to omega-3 were associated with increased risks of colorectal cancer. Compared to women with the lowest ratio, women with the highest ratio of omega-6 to -3 had a relative risk of 95% higher. The omega-6 fatty acid arachidonic acid (AA) was also linked to an increased risk of colorectal cancer. Specifically, women with the highest average intakes had an associated risk 40% higher than women with the lowest average intakes. Previously, researchers from other groups have proposed the role of metabolites of omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and the omega-6 acid, arachidonic acid as playing an important role in the development of cancer. These three fatty acids compete to be converted by cyclooxgenase enzymes (COX-1 and COX-2) into prostaglandins, which can become either pro-inflammatory and increase tumour growth, or anti-inflammatory and reduce growth. In a subset of 150 cancer cases and 150 healthy controls, the researchers noted that an increasing omega-6 to omega-3 ratio is linked to increased levels of the pro-inflammatory prostaglandin E2 (PGE2). Researchers concluded that t*hese results suggest that dietary PUFA and the ratio of omega-6 to omega-3 PUFA intake may be positively associated with colorectal cancer risk, and this association may be mediated in part through PGE2 production.* .

Murff, H.J., et al., A prospective study of dietary polyunsaturated fatty acids and colorectal cancer risk in Chinese women. J Cancer Epidemiology Biomarkers and Prevention. 2009.18: pp.2283-2291