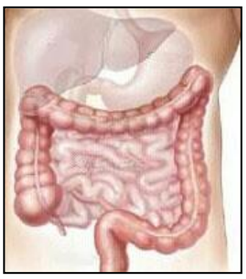
COLORECTAL CANCER RESEARCH

Month Ending September 16th, 2011



The following colorectal cancer research update extends from August 20th, 2011 – September 16th, 2011 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Cancer Fighting Virus Being Studied in Ottawa (Aug. 24/11)

A cancer-fighting virus can be delivered intravenously and appears to target solid tumours without harming the healthy tissue that is nearby. A preliminary trial involving 23 patients with advanced cancers who were given infusions of the **JX-594 virus** was designed in part to establish safe dosages and see if the viral therapy would indeed reach the tumours. This is the first time researchers have been able to show they can give the virus intravenously, it definitely gets to the tumour sites, spreads throughout them quite nicely and begins to destroy the tumour. The scientists increased the dosage -- for a total of five levels -- with successive patients. Seven of the eight patients in the two highest dose groups had evidence of viral replication in their tumour but not in the normal tissue, the study found, and six of the eight patients had a shrinking or stabilization of their tumours. The most common side-effect was mild to moderate flu-like symptoms that lasted less than a day. In this case, patients had run out of treatment options and bravely volunteered to take part in the clinical trial and receive a single infusion, which took about an hour and involved an overnight stay. Biopsies were obtained 8 - 10 days after the infusion and tissue was examined under a microscope. The JX-594 virus was designed by the company Jennerex Inc., from a strain used as a vaccine against smallpox. This virus is not smallpox but it looks enough like it to the immune system that when you get treated with it you are prevented from getting a smallpox infection. So this virus has been used for 200 years to treat people, or vaccinate people against smallpox. It's very safe, maintain researchers. And then it's just been taken and re-engineered to be more selective so it only grows in cancers and not normal tissues. Michael Wosnick, vice-president of research at the Canadian Cancer Society, said cancer-fighting viruses have been injected directly into tumours in humans before, but this trial indicates an intravenous viral therapy can find tumours and infect them. He described it as an exciting development but said it is a first step and larger clinical trials are required to determine the overall impact on patients. This allows you potentially to think about a systemic application through the whole body where the virus is now going to all those distant cancer sites, and all those distant cells and actually seeking out, and hopefully in the end destroying them. So this is a much more powerful approach than being able to inject in a tumour by tumour basis. Researchers are now starting a larger trial that will involve 120 patients and will give them multiple treatments, and hope to show the virus is better than the current therapies that are out there. The initial study also showed that it's possible to add non-viral genes that might have value. The research was supported by the Terry Fox Foundation, the Canadian Institutes of Health Research, the Ontario Institute for Cancer Research, the Ottawa Hospital Foundation, the Canada Foundation for Innovation, the Natural Sciences and Engineering Research Council of Canada and the Republic of Korea.

http://www.winnipegfreepress.com/canada/promising-new-way-of-fighting-cancer-128867493.html

2. Certain Antidepressants Could Cut the Risk of Colorectal Cancer (Aug. 25/11)

A type of drug that treats depression and migraines could also reduce the risk of colorectal cancer, according to researchers from Lincoln University. Tricyclic drugs, which account for almost a third of all prescriptions for antidepressants, cut the risk of bowel cancer by up to 21%, according to this study. Amitriptyline is a type of tricyclic antidepressant. It's used to treat depression and prevent migraines. Now scientists say it could reduce the risk of bowel cancer. The study, from experts at the universities of Nottingham, Warwick and Lincoln, found people had a lower cancer risk the longer they had been on the drugs and if they took them at a higher dose. Using GP records, the team identified 31,953 cancer cases for the study, published in the British Journal of Cancer. Analysis showed that people taking tricyclic antidepressants had a much lower risk of glioma and a lower risk of bowel cancer. The team said the research suggests 'tricyclics may have potential for prevention of both colorectal cancer and glioma'. The most notable side-effects of this type of drug is dry mouth, constipation and memory loss. But more seriously they can also induce anxiety, vomiting and irregular heart activity. Tricyclics are being replaced with newer drugs such as selective serotonin reuptake inhibitors that tend to be easier to go on and come off. But patients at higher risk of specific cancers could be picked up through DNA screening and possibly given the drugs.

Bates, Timothy, et al., Tricyclic antidepressants and the incidence of certain cancers: a study using the GPRD. British J of Cancer (2011) 104, 193-197.

3. Gemcitabine as Salvage Therapy in Refractory Advanced Colorectal Cancer Patients (Aug. 28/11)

This study sought to assess the efficacy of the chemotherapeutic agent gemcitabine in heavily pre-treated patients with advanced colorectal cancer. Patients who had been treated with gemcitabine biweekly in combination with capecitabine every two weeks were retrospectively reviewed. All the patients had previously received at least three chemotherapy regimens and 12 (55%) had also received a 4th line regimen. All the patients had been treated with a monoclonal antibody either against vascular endothelial growth factor receptor (VEGFR - Avastin) or epidermal growth factor receptor (EGFR – Erbitux or Vectibix - only if wild-type KRAS). The patients had had blood tests weekly, carcinoembryonic antigen (CEA) level measurement every 4 weeks and radiological assessment of their disease with CT

scans every 8/9 weeks. Twenty two patients were included; male-female, 14:8; age ranged from 43-73 years. The majority of the patients (17/22) had performance status (PS) ECOG 0-1 and the remaining patients (5/22) had PS 2 at the time of initiation of the gemcitabine-based regimen. Thirteen patients demonstrated a clinical benefit (2 patients had partial response, 2 had minor response, and 9 had stable disease), 6 patients progressed and 2 were not evaluable. Based on the results, the investigators concluded that gemcitabine had a **modest activity** in heavily pre-treated colorectal cancer patients and may be an option in good performance status patients.

Saif, Muhammad Wasif, et al., The efficacy of gemcitabine as salvage treatment in patients with refractory advanced colorectal cancer (crc): a single institution experience. AntiCancer Res. 2011 Sep;31(9):2971-4.

4. Study Aims to Reduce Recurrence and Neuropathy for Stage III Patients (Sept. 2/11)

If diagnosed with stage III colon cancer, patients will likely receive approximately six months of treatment with FOLFOX after surgery. Research shows that this treatment regimen helps prevent recurrence for some – but not all – patients with stage III colon cancer. A clinical trial has been launched to answer two questions about this current standard of care:

1. ***Will recurrence rates go down if both FOLFOX and celecoxib (a non-steroidal anti-inflammatory drug similar to aspirin) are used for treatment?***

2. ***Will recurrence rates stay the same and long term side effects decrease if FOLFOX is used for three months instead of six?***

FOLFOX can cause short- and long-term neuropathy, numbness and tingling in hands and feet that makes activities like buttoning shirts difficult. Long-term neuropathy seems to be related to the total amount of FOLFOX received. Celecoxib has been shown to prevent the formation of polyps, and the development of colon cancer in patients who have had polyps.

Patients in the trial will be randomized to one of four treatment arms:

- Six months of FOLFOX (standard of care)
- Six months of FOLFOX plus celecoxib for three years
- Three months of FOLFOX
- Three months of FOLFOX plus celecoxib for three years

Patients will be monitored for the course of the clinical trial by the treating physicians. Overall patient safety and treatment efficacy will be monitored by a Data Safety Monitoring Committee. As always, patients who participate in clinical trials may or may not directly benefit from the trial. They contribute to the treatment of future patients, whose treatment will be influenced by the results of this trial. This trial is called the **CLEAR Colon Trial**. It is being conducted by a national, publicly-funded clinical trial network called the Cancer and Leukemia Group B (CALGB) and is supported by the National Cancer Institute. For more information, read or download this informational document. **Trial Description and Summary:** http://www.cancer.gov/clinicaltrials/search/view?cdrid=675693&protocolsearchid=8263881&version=patient

http://fightcolorectalcancer.org/research_news/2011/09/new_trial_looks_to_reduce_recurrence_and_neuropathy_for_stage_iii_patients

5. Sequential v.s. Combination Chemotherapy for the Treatment of Advanced Colorectal Cancer (Sept. 3/11)

According to this study, the optimum use of chemotherapeutic drugs for advanced colorectal cancer has not been defined. The aim of this study was to investigate whether combination treatment is better than the sequential administration of the same drugs in patients with advanced colorectal cancer. In other words, is administering 5FU in combination with oxaliplatin better upfront than administering those same agents sequentially on their own. In this open-label, randomized, phase III trial, investigators randomly assigned patients (1:1 ratio) with advanced, measurable, non-resectable colorectal cancer having a performance status 0 - 2 to receive **either:**

Sequential Group

First Line treatment:	5FU + Leucovorin
Second Line treatment:	5FU + Leucovorin + Oxaliplatin (FOLFOX)
Third Line Treatment:	5FU + Leucovorin + Irinotecan (FOLFIRI)

or:

Combination Group

First Line Treatment:	FOLFOX
Second Line Treatment:	FOLFIRI

Chemotherapy was administered every 2 weeks. The primary endpoint to be measured was progression-free survival after two lines of treatment. 205 patients were randomly assigned to the sequential group and 205 to the combination group. 161 (79%) patients in the sequential group and 161 (79%) in the combination group died during the study. Median progression-free survival after two lines was 10.5 months in the sequential group and 10.3 months in the combination group. All six deaths caused by toxic effects of treatment occurred in the combination group. During first-line chemotherapy, significantly fewer severe hematological adverse events and non-hematological adverse events occurred in the sequential group than in the combination group. Investigators concluded that upfront combination chemotherapy is more toxic and is not more effective than the sequential use of the same cytotoxic drugs in patients with advanced, non-resectable colorectal cancer.

Ducreux, Michel, et al., Sequential versus combination chemotherapy for the treatment of advanced colorectal cancer (FFCD 2000-05): an open label, randomized, phase III trial. The Lancet Oncology. Early Online Publication. Sept. 7, 2011. Doi: 10.1016/S1470-2045(11)70199-1

RADIATION/INTERVENTIONAL RADIOLOGY

6. MRI May Predict Survival In Advanced Rectal Cancer (Aug. 29/11)

This new study has shown that magnetic resonance imaging (MRI) used to evaluate responses to pre-surgery (neo-adjuvant) chemotherapy or radiation may predict survival among patients with advanced rectal cancer.

Source: http://brainimaging.waisman.wisc.edu/facilities/ni_facilities.html

The findings suggest that MRI-assessed tumor responses to neoadjuvant therapy (therapy administered before surgical removal of the primary) can help physicians to better plan their patients' subsequent treatments. MRI prior to surgery could help in the management of patients in a number of ways, including offering more intense therapy or alternative chemotherapy to those patients who appear initially resistant to chemotherapy, or changing the surgical plan. In the study -- called MERCURY -- researchers used MRI to measure tumor shrinkage in 111 patients who had previously undergone preoperative radiotherapy or both chemotherapy and radiation (chemoradiation) for locally advanced rectal cancer. The group -- part of a larger study of MRI use in improving rectal cancer staging begun in 2002 -- was followed for five years. The researchers measured tumor response in terms of "tumor regression grade (TRG)," which measures the degree of tumor shrinkage after therapy, and the involvement of "circumferential resection margin (CRM)," which refers to the remaining cancer at the tumor edges after treatment, or predicted to remain after surgery. Patients were broadly designated either a "good" or "poor" responder to chemoradiation, according to MRI, and researchers compared survival of the two groups. Investigators found that 72% of good responders to chemotherapy/radiation were alive after five years compared to 27% of those who were poor responders. The disease-free survival for those with good responses was 64% versus 31% for the poor responders. In addition, local recurrence rates at five years for those patients for whom there was MRI-predicted CRM involvement was 28% compared to 12% for patients with predicted cancer-free tumor margins. Rectal cancer is commonly found in advanced stages, and as a result, neoadjuvant chemoradiation is frequently given to try to shrink tumors and make them easier to remove. While surgeons attempt to completely remove the cancer in order to minimize the chances of cancer returning, advanced tumors are more difficult to completely remove and more likely to have unseen cancer remaining at the edges of tissue at the surgery site. A positive surgical margin (tumor that remains at the borders of the surgical resection) is considered a strong predictor of local recurrence. Of the 111 patients in the study, 73% (81 patients) were expected to have cancer left in the surgical margins prior to initial treatment. After neoadjuvant therapy, only 42% (47 patients) were predicted to have disease left in the surgery margins, meaning this group was still at risk for recurrence prior to surgery.

***Patel, Uday B. et al.,Magnetic Resonance Imaging–Detected Tumor Response for Locally Advanced Rectal Cancer Predicts Survival Outcomes: MERCURY Experience. Journal of Clinical Oncology*, 2011; DOI**: 10.1200/JCO.2011.34.9068

7. Invendoscopy Deemed to Be Safe and Effective in Colorectal Cancer Screening (Aug.19/11)

According to the results of this study, the invendoscopy system has been found to be safe and effective in the screening of colorectal cancer. The Invendo SC20, a new, self-propelled colonoscope was also found to be helpful in **reducing sedation** (as depicted in the image to the right**)**. Consisting of a sheathed endoscope within an inverted sleeve, the Invendo SC20 has an instrument channel and an electrohydraulic bendable tip and is steered using a handheld device and propelled by a motorized drive unit. A total of 61 volunteers (34 men, 27 women), aged between 50 and 70-years-old, were subjected to total colonoscopy, using carbon dioxide insufflation or water instillation on demand. All procedures were started without sedation. Cecum was reached in 60 volunteers (cecal intubation rate of 98.4%) and the median time to reach the cecum was 15 min. Sedation was given in three participants. On withdrawal, the material for histological evaluation was obtained from 33 polyps in 23 people by biopsy forceps or snare. No device-related complications were encountered. The researchers concluded: "A new computer-assisted colonoscope, controlled using a handheld device, showed excellent cecal intubation rates during screening examinations, with sedation required in only ~5% of participants. Further clinical and comparative studies are warranted."

Groth, Stefan, et al., High cecal intubation rates with a new computer assisted colonoscope: a feasibility study. Amer J of Gastro 2011; 106: p. 1075-1080.

8. Men With Type II Diabetes Require Screening (Sept.4/11)

A major Australian study has for the first time established a significant link between type 2 diabetes and the risk of colorectal cancer in men. The 11 year study involving almost 1,300 people with type 2 diabetes found that men with the lifestyle-related condition were twice as likely to develop potentially fatal bowel cancer as their diabetes-free peers. Researchers who conducted the 'Cancer and Diabetes in Australia' Fremantle Diabetes Study described the results as "highly significant" and said that they should prompt doctors to screen type 2 diabetes patients who are at heightened risk of for colorectal cancer. According to the investigators, checking for fecal blood is one option but a colonoscopy is far more thorough and could become an integral part of diabetes management. While the study revealed an increased risk of all cancers in both men and women with type 2 diabetes, it was the two-fold increase in colorectal cancer among men with type 2 diabetes that alarmed researchers. Presenting the results of the study at the Australian Diabetes Society and Australian Diabetes Educators Association Annual Scientific Meeting in Perth, Professor Davis said that around one in 12 Australians will be diagnosed with bowel cancer before they reach the age of 85 but the risk of developing the condition doubled for men with type 2 diabetes. While the 'Cancer and Diabetes in Australia' study established a link between type 2 diabetes and colorectal cancer, Professor Davis said more research was needed to explain the existence of the link. "It might be that the risk factors for the two conditions, including obesity, are the same and that they develop independently of each other or it may be that factors associated with diabetes trigger bowel cancer," Professor Davis said.

Davis, T.M.E.,* et al*. Cancer and Diabetes in Australia: The Fremantle Diabetes Study.

9. Mailed Educational Reminder to Increase Colorectal Cancer Screening (Aug. 26/11)

According to the authors of this study, colorectal cancer (crc) screening rates are low in many areas and cost-effective interventions to promote CRC screening are needed. Recently in a randomized controlled trial, a mailed educational reminder increased CRC screening rates by 16.2% among U.S. Veterans. The aim of this study was to assess the costs and cost-effectiveness of a mailed educational reminder on fecal occult blood test (FOBT) adherence. In a blinded, randomized, controlled trial, 769 patients were randomly assigned to the usual care group (FOBT alone, n=382) or the intervention group (FOBT plus a mailed reminder, n=387). Ten days after picking up the FOBT cards, a 1-page reminder with information related to CRC screening was mailed to the intervention group. Primary outcome was number of returned FOBT cards after 6 months. At 6 months after card distribution, 64.6% patients in the intervention group returned FOBT cards compared with 48.4% in the control group. The total cost of the intervention was $962 or $2.49 per patient. According to the authors, a simple mailed educational reminder increases FOBT card return rate at a cost many health care systems can afford. Compared to other patient-directed interventions (telephone, letters from physicians, mailed reminders) for CRC screening, this study's intervention was more effective and cost-effective.

Lee, Jeffrey, et al., Cost Effectiveness of a mailed educational reminder to increase colorectal cancer screening. BMC Gastro. 2011, 11:93.

PSYCHOSOCIAL

10. Psychosocial Status of Colorectal Cancer Patients Referred to Outpatient Oncology Clinic (Aug. 24/11)

According to this study, malnutrition and psychological distress are associated with poorer outcomes following treatment for colorectal cancer. Screening for issues such as malnutrition, depression, and anxiety is being adopted in some oncology settings, but its effectiveness or the relationship between these risk factors in this population are not well understood. A retrospective chart review was conducted of 836 health assessment forms provided to colorectal cancer patients referred to an outpatient oncology clinic. Nutritional and psychological screening tools were included in the form. Demographic and screening tool information was obtained from completed forms. The prevalence of nutritional risk, depression, and anxiety were determined based on screening tool scores and clinical cutoffs. The prevalence of nutritional risk, anxiety, and depression were determined to be 29%, 10%, and 7%, respectively. Depression was the most significant predictor, with odds of increased nutritional risk being 5.6 times greater for depressed individuals. The use of nutritional and psychosocial screening tools is warranted and needs to be emphasized more in oncology settings. According to the investigators, there appears to be a relationship between psychosocial issues and increased nutritional risk which should be taken into account when considering cancer care interventions.

Lizardo Daudt, Helena Maria, et al., Nutritional and psychosocial status of colorectal cancer patients referred to an outpatietns oncology clinic. Supp Care in Cancer. doi: 10.1007/s00520-011-1224-7

11. Music Therapy May Ease Anxiety of Cancer Patients (Aug. 22/11)

Separately, music therapy has been found to have beneficial effects on mental health and pain management. As cancer patients often experience anxiety, mood changes, and pain during treatments, researchers have studied the effects that sessions with trained music therapists in this population and found that the addition of a music intervention can bring about significant improvements in quality of life. Music therapy is the clinical and evidence-based use of music to accomplish individualized goals within a therapeutic relationship by a credential professional who has completed an approved music therapy program. The music therapist assesses emotional well-being, physical health and cognitive skills through musical responses and designs sessions based on the evaluated needs. People at all stages of life from childhood to the elderly can benefit from music therapy.

Dr. Joke Bradt, an associate professor at Drexel University's College of Nursing and Health Professions, conducted a systematic review of 30 trials consisting of data gathered from 1,891 participants. In 13 of the trials, music therapy conducted by a trained professional was used and in 17 of the trials, patients listened to prerecorded music. The researchers focused on the results from patients with any kind of cancer for their review. Compared to standard treatments, music overall reduced anxiety considerably based on clinical anxiety scores. Patients who took sessions with music therapists ***showed an improvement in mood and quality of life and a decrease in pain***. Smaller benefits were also seen for heart rate, respiratory rate, and blood pressure. Dr. Bradt concludes that "music interventions may be useful as a complementary treatment to people with cancer" and that "the beauty of music can bring renewed hope for patients and their loved ones." More studies are needed as there is currently not enough evidence to determine if music therapy sessions or listening to pre-recorded music is more effective than the other. Other interventions, such as singing and playing a musical instrument, may also be of benefit as well.

Bradt Joke````,0 et al., Music interventions for improving psychological and physical outcomes in cancer patients. Cochrane Database of Systematic Reviews 2011, Issue 8. Art. No.: CD006911. DOI: 10.1002/14651858.CD006911.pub2.

OTHER

12. Testing Women with Endometrial Cancer to Detect Lynch Syndrome (Aug. 30/11)

Women who have Lynch syndrome have an increased risk of getting endometrial cancer during their lifetime that is as high as 60%. Often endometrial cancer (*cancer of the lining of the uterus)* is the first Lynch-related cancer diagnosed, earlier than colon or rectal cancer. Identifying a mutation in these women can prevent future colorectal cancers and discover ovarian, gastric, and other Lynch cancers early when they can be treated successfully. And not only does this help the woman with endometrial cancer, it helps her family as well if they are tested for the inherited mutation and take steps to reduce their risk of future cancers. A research team has found the most cost-effective way to identify those women with endometrial cancer with Lynch syndrome by screening their tumors for missing Lynch proteins *only if they also have a first-degree relative with a Lynch-related cancer.* Researchers from the University of British Columbia and MD Anderson Cancer Center in Texas built a computer model to study ways to find women with Lynch syndrome among all women diagnosed with endometrial cancer. Their goal was to decide on the best strategy to identify both:

- The most women with Lynch syndrome at risk for future colorectal cancer
- The most cost-effective way of finding those women

The six strategies they considered were:

- Direct referral for genetic testing for women with Amsterdam II family histories.
- Direct referral to genetic testing for women diagnosed under age 50 with at least one first-degree relative with a Lynch-related cancer.
- Immunohistochemical (IHC) triage of tumors in women under age 50 with genetic testing for those positive.
- IHC triage for women under age 60, followed by genetic testing for positive results.
- IHC triage for women diagnosed at any age with one first-degree relative with a Lynch cancer, followed by genetic testing.
- IHC triage for all women with endometrial cancer, with follow-up of positive results with genetic testing.

While using immunohistochemical testing for all women diagnosed at any age with endometrial cancer would find 100% Lynch syndrome, it is extremely expensive with an incremental cost-effectiveness ratio (ICER) of $648,494 for each life-year gained. A better strategy was to use IHC triage for all women diagnosed at any age, but limit the tests to those who had a first-degree relative (parent, child, sibling) with a Lynch-related cancer. The ICER for this plan was **$9,126** — well within the range of cost-effective public health benefits. It would also find more than 91% of women with Lynch syndrome.

- Using the Amsterdam family history criteria would miss about a third of women (35%) who have Lynch syndrome.
- Direct genetic testing without IHC triage for women under 50 with a first-degree relative with a Lynch cancer would also miss 36% of potential Lynch mutations.
- IHC triage of women under 50 and under 60 would miss 38% and 34% of women with Lynch syndrome respectively.

Both women with Lynch syndrome and women with sporadic endometrial cancer benefit from colonoscopy screening to reduce their subsequent risk for colorectal cancer and death from colorectal cancer:

- Lynch syndrome women who have annual colonoscopies have a 15% risk of getting colorectal cancer and a 6% risk of dying from it.
- LS women who don't get the critical annual colonoscopy surveillance have a 40% risk of getting colorectal cancer and a 47% chance of dying.
- Women with sporadic endometrial cancer who have at least one colonoscopy every 10 years cut their risk of colorectal cancer from 5% to 3% compared to women who don't get a colonoscopy. Their chances of dying of colorectal cancer are cut down from 37% to 15%.

Investigators concluded: *Immunohistochemical (IHC) triage of women with endometrial cancer at any age having at least 1 first-degree relative (FDR) with a Lynch-associated cancer is a cost-effective strategy for detecting Lynch syndrome. IHC triage of women with endometrial cancer at any age having at least 1 FDR with a Lynch-associated cancer is a cost-effective strategy for detecting Lynch syndrome.*

Kwon, Janice, et al., Testing Women with endometrial cancer to detect lynch syndrome. J of Clin Onc. Vol. 29, No. 16: pp. 2247-2252.

http://fightcolorectalcancer.org/research_news/2011/08/id-ing_lynch_syndrome_in_women_with_endometrial_cancer_saves_lives_and_is_cost-effective

13. Colon Cleansing Deemed Useless and Dangerous (Sept. 8/11)

Administered either orally as teas, pills, or powders or through the rectum as high-powered enemas or *colonic hydrotherapy*, colon cleansers promise to "detox" the body and eliminate fatigue, weight gain, and headaches. Using infomercials and celebrities, they say they will "boost the immune system" and promote

weight loss. The problem is that there is not a shred of evidence that colon cleansing does any of these things, according to the results of this study. And ***there is*** evidence that it can promote "holes" in the colon requiring surgery, cause serious infections, lead to dehydration and heart and kidney damage, and sometimes fatal. In this study, researchers reviewed the case for colon hydrotherapy and herbal supplements sold to clean the colon and "detoxify" the body. Researchers found little evidence that they were effective and many reasons to avoid them. Some adverse events were mild like cramping and nausea, others life-threatening including bowel perforations, kidney and heart failure, and abdominal abscesses. Several patients died when unsterile hydrotherapy equipment infected them with amebiasis, an intestinal parasite. Devices used for colonic therapy and irrigation are Class III medical devices and must be licensed by the FDA (in the U.S.) and used only for those medical purposes that are approved by the FDA. Colon hydrotherapy is not one of those purposes, and the FDA has issued a number of warning letters to "colon hydrotherapists" who misuse the devices. In the Journal of Family Practice, study authors urge doctors to raise the issue of colon cleansing with their patients and let them know about lack of evidence and potential risks. They conclude with **4 things to tell patients about colon cleansing:**

- Colon irrigation is not wise—particularly if you have a history of gastrointestinal disease (including diverticulitis, Crohn's disease, or ulcerative colitis) or a history of colon surgery, severe hemorrhoids, kidney disease, or heart disease. These conditions increase the risk of adverse effects.
- Side effects of colon cleansing include nausea, vomiting, diarrhea, dizziness, dehydration, electrolyte abnormalities, acute kidney insufficiency, pancreatitis, bowel perforation, heart failure, and infection.
- The devices that practitioners use for the procedure are not approved for colon cleansing by the US Food and Drug Administration. Inadequately disinfected or sterilized irrigation machines have been linked to bacterial contamination.
- Colon cleansing practitioners are not licensed by a scientifically based organization. Rather, practitioners have undergone a training process structured by an organization that is attempting to institute its own certification and licensing requirements.

Mishori, Ranit, et al., The dangers of colon cleansing. The Journal of Family Practice. August 2011. Vol. 60, No. 8: pp. 454-457.

14. Rise in Lymph Node Numbers Not Associated with Node-Positive Cancers (Sept. 15/11)

The results of this study revealed, that the increase in the percentage of patients who have a high number of lymph nodes evaluated during colon cancer operations has increased significantly during the past two decades, however, this improvement is not linked to an increase in the overall proportion of colon cancers that are **node positive**. Among patients surgically treated for colon cancer, several studies have demonstrated better survival for patients with more lymph nodes evaluated. The proposed mechanism behind this association suggests that a more extensive lymph node evaluation reduces the risk of understaging, in which inadequate assessment may incorrectly identify a patient with node-positive disease as node negative, thus failing to identify appropriate treatment. Most organizations and cancer centres currently support the surgical evaluation of 12 or more lymph nodes for acceptable staging of newly diagnosed colon cancer patients. When performing the review, the study authors discovered that lymph node evaluation for colon cancer increased significantly from 1988 to 2008. From 1988 to 1990, 34.6% of patients (n = 3,875) received lymph node evaluation at a level of 12 lymph nodes or more. Between 1994 and 1996, 37.9% of patients (n = 4,362) equaled this evaluation level, increasing to 46.8% in 2000 to 2002 and 73.6% (9,798/13,310) respectively from 2006 to 2008. Although the number of lymph nodes evaluated increased significantly, there is no link to an increase in node-positive cancers over this period (40% in 1988-1990, 42% in 2006-2008). The authors also discovered that even though patients with high rates of lymph node evaluation had only a marginally higher chance of having node-positive disease, they experienced a substantially lower relative risk of 5-year mortality compared with those with fewer nodes evaluated. They concluded: "*When stratified by node positivity, patients with node-positive disease as well as node-negative disease continued to experience lower relative hazard of death when more lymph nodes were evaluated. In conclusion, the number of lymph nodes evaluated for colon cancer markedly increased in the past 2 decades but was not associated with an overall shift toward higher-staged cancers, questioning the upstaging mechanism as the primary basis for improved survival in patients with more lymph nodes evaluated*."

Regional Lymph Nodes

There are between 100 and 150 lymph nodes in the mesentery of the colon. Regional lymph nodes are the nodes along the colon, plus the nodes along the major arteries that supply blood to that particular colon segment.

Segment of Colon	Regional Lymph Nodes (See Diagram Below)
Cecum	Pericolic, anterior cecal, posterior cecal, ileocolic, right colic

Ascending Colon	Pericolic, ileocolic, right colic, middle colic
Hepatic Flexure	Pericolic, middle colic, right colic
Transverse Colon	Pericolic, middle colic
Splenic Flexure	Pericolic, middle colic, left colic, inferior mesenteric
Descending Colon	Pericolic, left colic, inferior mesenteric, sigmoid
Sigmoid Colon	Pericolic, inferior mesenteric, superior rectal, superior hemorrhoidal, sigmoidal, sigmoid mesenteric
Rectosigmoid	Perirectal, left colic, sigmoid mesenteric, sigmoidal, inferior mesenteric, superior rectal, superior hemorrhoidal, middle hemorrhoidal
Rectum	Perirectal, sigmoid mesenteric, inferior mesenteric, lateral sacral, presacral, internal iliac, sacral promontory (Gerota's) superior hemorrhoidal, inferior hemorrhoidal
Anus	Perirectal, anorectal, superficial inguinal, internal iliac, hypogastric, femoral, lateral sacral

Source: ***http://training.seer.cancer.gov/colorectal/anatomy/lymph-nodes.html***

Parsons, Helen, et al., Association between lymph node evaluation for colon cancer and node positivity over the past 20 years. JAMA 2011; 306(10): 1089-1097.

NUTRITION & HEALTHY LIFESTYLE

15. Green Tea May Prevent Colorectal Cancer (Aug. 23/11)

Based on the results of this study, drinking green tea, which is more popular in Asia, may help reduce risk of colorectal cancer in men. The study found men drinking green tea were 46% less likely to suffer colorectal cancer, compared with those who did not drink the beverage. For the study, researchers followed 60,567 men aged 40 to 74 for five years during which 243 cases of colorectal cancer were identified. The participants were enrolled in the Shanghai Men's Health Study. The researchers found drinking green tea and risk of colorectal cancer were inversely associated; meaning high intake of green tea was linked with lower risk of colorectal cancer. Green tea has been demonstrated in lab and animal studies to have anti-cancer properties. Epigallocatechin gallate (EGCG), the main ingredient in green tea, was found to promote apoptosis, programmed death of cells, which is missing in cancerous tumors. The current study also quantified the effect of green tea on colorectal cancer risk - intake of additional two grams of dry green tea leaves was correlated with a 12% reduction in the risk. But these green tea benefits were not found among **smokers**. Previous studies have linked drinking green tea or extract to enhanced weight loss and reduced risk of Alzheimer's disease or dementia, heart disease, thyroid cancer, chronic lymphocytic leukemia, prostate cancer, glaucoma and breast cancer. It is also linked to boosted immunity, better vision, lowered cholesterol and blood pressure.

Yang, Gong, et al., Green tea consumption and colorectal cancer risk: a report from the Shanghai men's health study. Carcinogenesis. Doi: 10.1093/carcin/bgr186. First published online: august 19/11

16. Folate Tied to Lower Colon Cancer Risk (Sept. 2/11)

People who eat plenty of folate had a lower risk of colon and rectal cancers in a new study that examined the effects of folic acid fortification in the United States. In addition, the study did not find any extra cancer-related danger at very high levels of folate -- as some researchers have worried -- over close to a decade. The benefit and possible harm of folate is "definitely still an open question," though according to study author. But, he claims that there seems to be an association between people who report higher folate with those people who have a lower risk of colorectal cancer. In the late 1990s, the U.S. and Canadian governments began requiring that folic acid (a synthetic form of folate) be added to grain products in order to prevent some birth defects that had been linked to low folate levels in pregnant women. While previous studies have generally suggested that a diet rich in folate decreases the risk of colorectal cancer as well, most of those were done before fortification started, according to study author. To see if the government mandate affected that link, the researchers used data from a diet survey started in 1995 that included more than 500,000 middle-aged and older U.S. adults. At the start of the study, participants filled out a questionnaire about their normal eating habits and any supplements they took regularly. From that, the researchers were able to calculate how much folate they got on a typical day before and after fortification started. For the next ten years or so, they tracked cancer registries to see which participants were diagnosed with colorectal cancer. They found a total of approximately 7,200

cases in their original sample, including approximately 6,500 that were diagnosed after the start of the fortification program. People who ate the highest amount of folate each day (at least 900 micrograms post-fortification) were 30% less likely to get colorectal cancer than those who got less than 200 micrograms each day, the researchers reported. That was after taking into account weight, smoking, physical activity, and certain other aspects of diet. Still, the study author claims that the findings can't prove that increased folate drove the cancer benefits, because "people who report high levels of folate tend to be healthy in other ways," possibly including some the researchers didn't record. The recommended daily allowance for folate is **400 micrograms** for most adults and **600 micrograms** for pregnant women. Along with fortified cereals and other grains, vegetables and beans are good sources of folate, a type of B vitamin. As a result of fortification, the average person's folate intake through foods increased by about 100 micrograms. The study did not find any upticks in cancer rates at folate levels far above that recommended daily allowance. Apparently, concern over the possibility that too much folate could raise cancer risk had mostly come from studies in animals. Those studies suggested that "in normal tissues, giving folate or folic acid can ensure DNA replicates and cells are grown properly". "But once cells are pre-cancerous, giving folate can increase the progression of these cancer cells." ***In other words, it's possible that if someone already had cell changes that are precursors of colorectal cancer, too much folate could make the cancer grow faster.*** The current findings are "reassuring" that fortifying grains with folate did not seem to lead to a spike in colorectal cancers. However, "there's still a concern that those taking really high levels of folic acid (in supplements) may be detrimental." The new report doesn't close the door on that possibility, especially because some cancers take many years to develop. More studies will have to look at the risk of colorectal cancer over longer periods of time. But, so far "we don't see any evidence of increased risk," he added. To be safe, people who do have colon cancer should not take extra folate, and that others shouldn't see any need to overdo it. "If people take 400 micrograms a day, it should be sufficient to meet health benefits from folate". Based on the current study, "people don't need to change their current activities" with respect to folate. Most people are getting what is considered the adequate amount."

Gibson, Todd, et al., Pre- and post fortification intake of folate and risk of colorectal cancer in a large prospective cohort study in the United States. The Amer J of Clin Nutrition. Published online Aug. 3, 2011. Doi: 10.3945/ajcn.11.002659.

17. Alcohol Consumption and Colorectal Cancer (Sept. 13/11)

This study consisted of a meta-analysis wherein 61 studies were retrospectively reviewed on the association of alcohol consumption with colorectal cancer (22 studies from Asia, 2 from Australia, 13 from Western Europe, and 24 from North America). The paper provides evidence that alcohol, at least at higher levels of consumption, is associated with an increase in the risk of colorectal cancer. Overall, there was no increase in the risk for consumers reporting an average intake of up to 1 drink per day, but an increase (of 21%) for what the authors defined as "moderate drinking" (averaging up to 49.9 g of alcohol – far in excess of all responsible drinking guidelines). The increase in risk was greater (52%) for consumers of 50 or more grams of alcohol per day. The study results indicate that alcohol intake, especially heavier drinking, is associated with an increase in the risk of colorectal cancers. Future studies are needed to help determine if there is a threshold level of alcohol that increases the risk, if there are differences by type of beverage, and if the pattern of drinking (regular versus binge drinking) affects the risk.

Fedirko V, et al. Alcohol drinking and colorectal cancer risk: an overall and dose–response meta-analysis of published studies. Annals of Oncology 22: 1958, 2011, doi:10.1093/annonc/mdq653