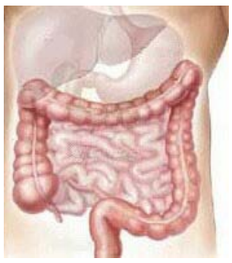
COLORECTAL CANCER RESEARCH

Month Ending November 13, 2009



The following colorectal cancer research update extends from October 17 – November 13, 2009 inclusive and is intended for informational purposes only.

CONTENT

NUTRITION / HEALTHY LIFESTYLE

DRUGS / SYSTEMIC THERAPIES

1. Tel Aviv University Uses Antibiotic For Gene Repair & Slow Polyp Growth (Oct. 17/09)

A new Tel Aviv University drug, based on an older generation antibiotic, may provide doctors with an effective and innovative method of treating colon cancer in both its incipient and full-blown stages - and minimize the need for painful, uncomfortable colonoscopies and surgical polyp removal. Researchers have shown in preclinical studies that a common antibiotic can suppress the growth of colon cancer polyps in mice. The aim is to reformulate the drug for use as a preventative therapy - or, in stronger doses, in combination with chemotherapy and radiation to fight existing cancers until they're gone. The current formulation reduced the size of the polyps in about 80% of the mice studied, and on average the animals lived 30% longer than those who were not given the antibiotic. The antibiotic acts in a genetic fashion. In diseases like cystic fibrosis (CF) and muscular dystrophy, antibiotics from the **aminiglycoside** family can repair damaged or mutated DNA. For the purposes of the study, researchers looked at a closely-related but less toxic family of antibiotics from the **Macrolide** family that achieves the same therapeutic results. The study focused on a gene associated with colorectal cancer, the APC gene, and noticed that the mutation types in colorectal cancer are similar to those in the CF gene. Noting that old generation antibiotics are effective in fighting CF, researchers studied its effects on colon cancer as well. They found that the drug partially repaired faulty genes in mice with colon cancer. Benefits from using old generation and out of circulation antibiotics means that the new therapy will not interfere with current antibiotics used for today's bacterial infections. At first they thought about using the antibiotic as a preventative therapy, but later investigated its efficacy in treating full-blown cancer and found it similarly effective.

www.medicalnewstoday.com/articles/167349.php

2. Treatment Options for Advanced Colon Cancer – Capox or Capiri In The Elderly (October 17/09)

The outlook for people with advanced or metastatic colon cancer continues to improve with advent of new therapies. And the latest research on how best to manage advanced disease points to a combination of medications that may lengthen life, and do so with fewer symptoms and side effects. The chemotherapy medication capecitabine or xeloda has improved treatment for advanced disease and researchers continue to study how to best combine it with other chemotherapy options to maximize the benefit to patients. This study conducted in 94 elderly patients, 70 years of age or older, compared capecitabine combined with oxaliplatin (CAPOX) and capecitabine combined with irinotecan (CAPIRI). Researchers found that the two treatment options, CAPOX and CAPIRI, were similarly effective at treating advanced colon cancer in elderly patients, but CAPOX seemed to be better tolerated, with patients experiencing fewer and less severe side effects. The group receiving CAPOX had a median survival time of 19.3 vs. 14 months with CAPIRI. This study highlights the importance of clinical trials in identifying the best treatment options for different groups of patients.

Rosati, G., et al, Capecitabine in combination with oxaliplatin or irinotecan in elderly patients with advanced colorectal cancer: results of a randomized phase II study. Annals of Oncology. Advance Access Published online. DOI: 10.1093/annonc/mdp359

3. Metals May Be Used in New Cancer Drug (Oct. 19/09)

Drugs made using unusual metals could form an effective treatment against colon cancer, including cancerous cells that have developed immunity to other drugs, according to research at the University of Warwick and the University of Leeds. The study, published in the Journal of Medicinal Chemistry, showed that a range of compounds containing the two transition metals Ruthenium and Osmium, which are found in the same part of the periodic table as precious metals like platinum and gold, cause significant cell death in ovarian and colon cancer cells. Dr Patrick McGowan, one of the lead authors of the research from the School of Chemistry at the University of Leeds, explains: "Ruthenium and Osmium compounds are showing very high levels of activity against ovarian cancer, which is a significant step forward in the field of medicinal chemistry. Sabine H. van Rijt, lead researcher in the laboratory of Professor Peter Sadler in the Department of Chemistry at the University of Warwick, said: "Most interestingly, cancerous cells that have shown resistance to the most successful transition metal drug, Cisplatin, show a high death rate with these new compounds." Professor Sadler, at the University of Warwick, commented that he is "excited by the novel design features in these compounds which might enable activity to be switched on and off". Cisplatin was discovered in the 1970s and is one of the most effective cancer drugs on the market. Since the success of Cisplatin, chemists all over the world have been trying to discover whether other transition metal compounds can be used to treat cancer. In this

type of anti cancer drug, transition metal atoms bind to DNA molecules which trigger apoptosis, or programmed cell death, in the cancerous cells.

www.medicalnewstoday.com/articles/167836.php

4. Casopitant For The Prevention of Chemo-Induced Nausea and Vomiting (Oct. 20/09)

This phase II study evaluated the neurokinin-1 receptor antagonist casopitant mesylate in combination with ondansetron/dexamethasone for the prevention of chemo-induced nausea and vomiting related to moderately emetogenic (causing nausea) chemo. Chemotherapy-naïve patients who were receiving a moderately emetogenic chemo, were randomized to receive either oral placebo or casopitant plus ondansetron and dexamethasone. The endpoints measured were rates of complete response (consisting of no vomiting, retching, rescue therapy, or premature discontinuation) and significant nausea. All casopitant doses that were tested significantly increased the proportion of patients with complete response. Rates of significant nausea did not differ among treatment arms. Casopitant appeared to be well tolerated with no notable differences in overall adverse event frequency. Researchers concluded that casopitant plus ondansetron and dexamethasone was more effective than ondansetron plus dexamethasone alone for the prevention of chemo-induced nausea and vomiting.

Arpornwirat, Wichit, et al., Phase II trial results with the novel neurokinin-1 receptor antagonist casopitant in combination with ondansetron and dexamethasone for the prevention of chemotherapy-induced nausea and vomiting in cancer patients receiving moderately emetogenic chemotherapy. J Cancer. Published online Oct. 15, 2009.

5. Helping to Improve Cancer Treatments (Oct. 25/09)

Cancer patients don't have time to waste, yet many must endure a tedious process of elimination as physicians try several different treatments until identifying the one that is most effective against their particular type of tumor. In this study, researchers at the University of Virginia Health System have developed a breakthrough method that could one day eliminate this trial and error approach to treating many cancers, including colorectal cancer. Their discovery is a novel algorithm, called COXEN (co expression extrapolation), that rapidly sorts molecular information about a patient's particular tumor and matches this information to a precise drug treatment. The most exciting aspect of this research is that in addition to predicting patient responses to therapy, the COXEN algorithm can be used to discover effective compounds for many forms of cancer. Because COXEN examines both cancer cells and drug activity at the molecular level, these newly discovered drugs should prove to be more effective in patients. This pre-screening for effectiveness should greatly lower the failure rate of clinical trials that test new compounds and also should decrease drug discovery timelines. The study evaluated gene expression models (GEMs) and resultant scores for their ability to predict tumor response or patient survival. Gene expression models provided effective prediction of tumor response and patient survival, while offering additional help to established clinical and pathologic tumor variables. The multidisciplinary team led by Theodorescu and Lee involved collaboration with colleagues in several departments. The team is currently planning several national and international clinical trials, based on COXEN-derived gene expression models, for personalized medicine approaches using both new and established compounds against bladder and ovarian cancer.

Theodorescu, Dan, et al., Concordant Gene Expression Signatures Predict Clinical Outcomes of Cancer Patients Undergoing Systemic Therapy. Cancer Research, 69, 8302, November 1, 2009. Published Online First October 20, 2009; doi: 10.1158/0008-5472.

6. Kras & Other Markers To Be Considered When Choosing Anti-EGFR Treatments (Oct. 26/09)

The highest standard of care dictates to test colon tumors in people with metastatic colon cancer for a biomarker called Kras, before using Anti-EGFR treatments such as erbitux and vectibix. KRAS refers to a gene that can be altered (mutated) in colon cancer cells. Studies show that if this alteration (mutation) is present, the anti-EGFR medications cetuximab (Erbitux) and panitumumab (Vectibix) are not effective and should not be used. New research generated out of Italy, published in the medical journal PLoS ONE, suggests that in addition to testing for KRAS, physicians should test for three other tumor markers, called **BRAF, PIK3CA, and PTEN**. By testing patients for these three markers *before* treating them with anti-EGFR medications, doctors can reduce the likelihood of giving potentially toxic and very expensive therapy that isn't going to help the patient. Combining testing for KRAS, BRAF, PIK3CA, and PTEN tumor markers with other new advances in cancer care, such as better ways to determine effective treatments without trial and error (as described in article #5 above) and surgeries and chemotherapies to improve survival (as described in article #2 appearing above), brings us closer to the day when ***all*** cancer care is personalized, highly effective, and less toxic. Kras mutations occur in 35-45% of the metastatic colorectal cancer population. However, less than 20% of patients displaying wild-type kras tumors (lack of kras mutation) achieve objective response. Researchers believe that alterations (mutations) in other biomarkers such as the BRAF, PIK3CA and PTEN, have independently been found to give rise to resistance in anti-egfr therapies. This study retrospectively analyzed objective tumor response, progression-free and overall survival together with the mutational status of kras, braf, pik3ca and expression of pten in 132 tumors from erbitux and vectibix treated mcrc patients. Among the 106 non-responsive patients, 74 had tumors with at least one molecular alteration in the four markers.

Accordingly, progression-free survival and overall survival were increasingly worse for patients with tumors harboring none, 1, or ≥ 2 molecular mutations. The researchers concluded that up to 70% of mcrc patients are unlikely to respond to anti-EGFR therapies when expression of pten and mutations in kras, braf and pik3ca are determined and recommend that comprehensive molecular dissection of the egfr signaling pathways should be considered when selecting mcrc patients for erbitux and vectibix-based therapies.

DiNicolantonio, Federica, et al., Multi-determinants analysis of molecular alterations for predicting clinical benefit to egfr-targeted monoclonal antibodies in colorectal cancer. PLoS ONE 4(10): e7287.doi:10.1371/journal.pone.0007287

7. NSAIDS Tied to Reduced Death After Colon Cancer Diagnosis (Oct. 29/09)

This study indicates that women who regularly use nonsteroidal anti-inflammatory drugs (NSAIDs) have better survival after a colorectal cancer (CRC) diagnosis. Apparently, a wide body of evidence links use of NSAIDs to a reduced risk of CRC. Until now, however, potential survival benefits associated with NSAID use had not been established. To investigate, the researchers analyzed data from 621 women in the California Teachers Study, all with a first primary invasive CRC. Prior to their CRC diagnosis, roughly 64% did not use NSAIDs regularly, 17% used them 1 to 6 days per week prior, and 20% reported daily use. Overall, roughly 17% of the group had regularly taken NSAIDs for less than 5 years and approximately 18% reported regular use extending back 5 years or more. Outcomes were tracked from the date of CRC diagnosis until death or December 31, 2005. Pre-diagnosis regular NSAID use (defined as 1 to 3 times per week, 4 to 6 times per week, or daily use) was associated with a 42% reduced risk of death from colorectal cancer compared to no regular NSAID use. In addition, compared with no regular NSAID use, regular pre-diagnosis use was associated with improved overall survival and regular use for 5 years or more was associated with improved overall survival. When patients were analyzed by the site of their cancer, women with colon cancer and at least 5 years of NSAID use prior to diagnosis had a significant reduction in CRC-specific mortality but not overall mortality. No such effect was observed in the subset of patients with rectal cancer, however.

Zell, Jason A., et al., Nonsteroidal anti-inflammatory drugs. Effects on mortality after colorectal cancer diagnosis. Cancer. Published online Oct. 13, 2009.

8. Antidepressants Show Inhibition of Colorectal Tumor Cell Growth (Oct.29/09)

Use of antidepressants, particularly selective serotonin reuptake inhibitors (SSRI) and possibly tricyclic antidepressants (TCA), is associated with a reduced risk of colorectal cancer, according to this research. But researchers caution it's too soon to make specific recommendations on how to harness the potential value of these drugs in cancer prevention. But the finding is consistent with other studies that suggest a reduced risk of colorectal cancer with use of SSRIs. SSRIs have been linked to hematosis (the formation of blood cells in the body) and to inhibition of growth of colorectal tumor cells that are dependent on serotonin for their growth. This led to the hypothesis of a reduced risk of colorectal cancer associated with their use. The researchers looked at antidepressant use in the 10 years before a diagnosis of colorectal cancer was made. Patients who first used an SSRI or a TCA in the year before they received a diagnosis of colorectal cancer were excluded to control for any possible bias that they may have started using an antidepressant because of their disease. Antidepressant use was associated with a 30% reduction in the risk of colorectal cancer, after adjusting for the confounders of smoking, NSAID and aspirin use, and diabetes. This result is consistent with other studies suggesting a reduced risk of colorectal cancer with SSRIs, and also with TCAs. The goal now is to translate the finding into clinical practice, starting with making sure that the benefits of antidepressants are well characterized. Researchers wish to determine not only that antidepressant use in general might reduce the risk of colorectal cancer, but to find out which antidepressants specifically.

www.searchmedica.com/resource.html?rurl=http%3A%2F%2Fwww.cancernetwork.com%2Fdisplay%2Farticle%2F10165%2F1482016&q=colorectal+tumor&cq=s%3Anci%5C.006S6&c=on&ss=defLink&p=Convera&fr=true&ds=0&srid=8

9. Erbitux Therapy in Patients With Absent EGF Receptor (Nov. 2/09)

Some colorectal cancer patients whose tumors do not express the epidermal growth factor receptor (EGFR) were still able to respond to treatment with erbitux when given as a single drug (monotherapy), according to testing performed with immunohistochemical staining. 7 of 85 patients had tumors shrink. For the group, median time to cancer progression was 2.1 months with median overall survival of 10 months. About 40% of patients were alive one year after treatment began. Study results were similar to other clinical trials of erbitux monotherapy restricted to patients with EGFR positive tumors. The patients who were enrolled were patients with refractory metastatic colorectal cancer (patients whose disease had progressed after receiving at least one standard, fluoropyrimidine-containing chemotherapeutic regimen) with lack of specific membrane immunostaining for the epidermal growth factor receptor. The study was actually performed prior to results of studies linking erbitux sensitivity to kras mutation status. Nevertheless, the researchers concluded that erbitux therapy produces objective antitumor activity in patients with mcrc that does not express egfr.

Wierzbicki, Rafal, et al., A phase II, multicenter study of cetuximab monotherapy in patients with refractory, metastatic colorectal carcinoma with absent epidermal growth factor receptor immunostaining. Investigational New drugs. Published ahead of print. DOI:10.1007/s10637-009-9341-6

10. The Impact of CEA Flare In Patients with Advanced Colorectal Cancer Receiving First-Line Chemo (Nov. 3/09)

Carcinoembryonic antigen (CEA) flare may have a favorable response to chemotherapy, but its impact on survival is unknown. Colorectal cancer patients have been known to have their CEA blood tests rise at the beginning of chemotherapy and then fall (CEA flare). Others have been known to experience a consistently rising CEA. Studies have shown that CEA flares don't necessarily predict worsening cancer. This study aimed to evaluate the incidence of CEA flare and its impact on objective response rate (ORR) – tumour shrinkage, progression-free survival (PFS) – time before the cancer got worse, and overall survival (OS) – survival time. Patients with histologically proven advanced colorectal cancer undergoing first-line chemotherapy with three or more blood CEA measurements (one at baseline and two or more during treatment) were included. Patients were grouped according to CEA kinetic as either:

- flare (F),
- decreasing CEA,
- normal baseline CEA,
- stable CEA and
- increasing CEA.

From January 2000 to February 2008, 837 patients were screened of whom 670 were eligible. CEA flare occurred in 78 (11.6%) patients. Compared with patients with increasing CEA, patients with CEA flare had a significantly better ORR [Increasing versus Flare: 11% versus 73%], PFS (median 3.1 versus 8.3 months) and OS (median 10.9 versus 17.7 months). Compared to patients with consistently rising CEA, patients who had a CEA flare had more tumor shrinkage, longer time before their cancer got worse, and longer survival time. Researchers concluded that compared with patients with rising CEA, flare was an independent favorable predictive and prognostic factor for tumour response and survival.

Strimpakos, AS, et al., The impact of carcinoembryonic antigen flare in pateitns with advanced colorectal cancer receiving first-line chemotherapy. Annals of Oncology.

11. Vectibix Failed to Meet Secondary Endpoint (Nov. 5/09)

The biotechnology company Amgen Inc. announced its KRAS wild-type metastatic colorectal cancer or mCRC experimental drug Vectibix in combination with Folfox failed to meet secondary endpoint of overall survival in its prime 203 trial. The analysis of the company's prime 203 trial showed that Vectibix in addition to a Folfox chemotherapy regimen in patients with metastatic colorectal cancer, or mCRC, resulted in a median overall survival of 23.9 months compared with 19.7 months for patients treated with Folfox alone, the difference of 4.2 months did not reach the statistical significance. Previously, they announced that the 203 study met its primary endpoint of progression-free survival in the first-line treatment of patients with KRAS wild-type metastatic colorectal cancer. The results showed overall survival appeared to be reduced in patients with KRAS mutant tumors receiving Vectibix. Though not statistically significant, the result emphasizes the importance of ensuring that patients receiving Vectibix do not bear tumors containing KRAS mutations. Vectibix is the first human anti-EGFR antibody, approved for the treatment of mCRC. Patients in the trial were randomized to receive either 6 mg per kg of vectibix and folfox4 once every two weeks or folfox alone once every two weeks.

www.rttnews.com/ArticleView.aspx?Id=1119992

12. Diabetic Patients Not More Likely to Develop Chemo-Induced Neuropathy (Nov. 7/09)

According to this study, diabetic patients have no more risk of developing peripheral sensory neuropathy when they are treated with oxaliplatin than do patients without diabetes. A pooled analysis looked at three studies totaling almost 1,600 patients. Of those, 135 or 8.5% had diabetes. The percentage of patients without diabetes and with diabetes who developed neuropathy was almost identical for each grade: 45.0%/46.7% (grade 1), 28.6%/26.7% (grade 2), and 13.0%/12.6% (grade 3). Diabetic patients who had neuropathy before beginning treatment with oxaliplatin were not included in the study.

Ramanathan, RI., et al., Incidence and evolution of oxaliplatin-induced peripheral sensory neuropathy in diabetic patients with colorectal cancer: a pooled analysis of three phase III studies. Annals of Oncology. Advance Access published online on November 3, 2009.

13. New Nano-Drug Brings Hope to Cancer Patients in Taiwan (Nov. 10/09)

The Institute of Nuclear Energy Research under the Cabinet-level Atomic Energy Council is developing a new drug which uses nanotargeted therapy to cure colorectal cancer. The drug, which targets cancer

cells with radioactive isotopes, is applied via IV injection to the blood vessels undergoing angiogenesis where the tumor cells reside. The drug can effectively cut off nutrition routes for the problem cells as well as radiates beta rays to kill the cells. The potential therapeutic drug, which treats late-stage colorectal cancer, has completed trials on animals and phase 1 clinical trials on humans are expected to begin in Taiwan in 2011.

www.chinapost.com.tw/health/cancer/2009/11/10/232102/New-nano-drug.htm

SURGICAL THERAPIES

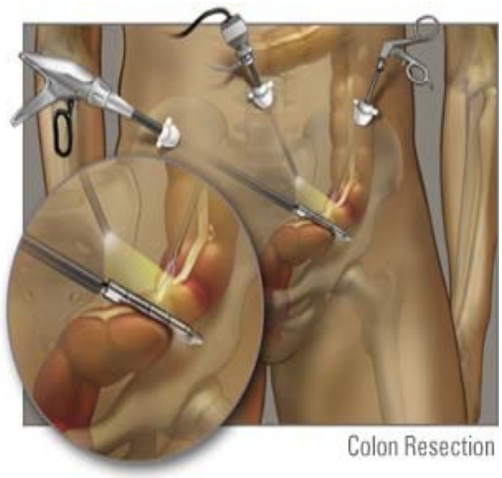
14. Genes Identified That Could Prevent Rectal Cancer Surgery (Oct. 15/09)

A set of 87 genes one day may be used to routinely determine which patients can be successfully treated for advanced rectal cancer without undergoing a surgical procedure. The genes were identified in a study of 46 patients who had locally advanced rectal cancer and were far more commonly expressed in patients who had a complete pathological response to chemotherapy and radiotherapy [there were no living cancer cells in a pathologically examined surgical specimen] than those who did not have a pathological response to treatment. The panel of genes may be the first reliable way of finding patients whose rectal cancer completely responds to chemotherapy and radiotherapy, which precedes an operation in the standard treatment of locally advanced rectal cancer. Typically, patients need chemotherapy, radiation therapy, and surgery to get the best outcomes. The upfront chemotherapy and radiation therapy helps shrink tumors down so they can be more easily removed surgically and decreases the chance that the tumor will come back in the pelvis. The combination of preoperative chemotherapy and radiotherapy is also highly effective in and of itself. Approximately 20% of patients have no signs of rectal cancer after the combination treatment. However, surgeons have not had a way of finding these patients until they operated upon them and removed a surgical specimen for pathological analysis. Findings from this study suggest that we may have a new tool to say to a patient whose tumor has a specific DNA profile and who has had a complete clinical response to chemotherapy and radiation therapy that he may not need radical surgery. Researchers from M.D. Anderson Cancer Center are planning to validate findings from this study in an independent data set and then assess whether the genes are able to accurately predict ahead of time which patients will have a pathologically complete response to chemoradiation. Once these results have been validated, they can start to explore clinical trials that use the information from the genetic analysis to make decisions regarding patient management. They will propose to take patients who have a positive DNA profile and put them in a study where they don't undergo surgery. They would follow the patients to see if they have as good cancer-related outcomes as patients who underwent the traditional approach of chemoradiotherapy plus surgery. The hope is that, in the future, researchers would be able to show that specific patients who have a complete pathological response, that is those who have complete eradication of the tumor with preoperative chemoradiation, can safely forego surgery.

www.medicalnewstoday.com/articles/167424.php

15. Special Colectomy for Transverse Colon Cancer (Oct.19/09)

Laparoscopic assisted colectomy (LAC) is commonly performed on cancer-stricken colons, but LAC for transverse colon cancer is a complex procedure, even in the hands of experts. In particular, laparoscopic take-down of the splenic and/or the hepatic flexure (splenic flexure: the sharp bend of the colon under the spleen where the transverse colon joins the descending colon ; hepatic flexure**:** the right-angle bend in the colon on the right side of the body near the liver that marks the junction of the ascending colon and the transverse colon) and dissection of the lymph nodes around the middle colic vessels are extremely complicated maneuvers compared to the complexity of these procedures during open surgery. This study describes a simple and less-invasive technique for performing hybrid hand-assisted laparoscopic colectomy (hybrid-HALC). This procedure combines the established convenient and safe techniques of open surgery with the less invasive hand-assisted laparoscopic approach. From 2000 to 2007, 22 patients with transverse colon cancer underwent hybrid-HALC. Short-term outcomes of hybrid-HALC were retrospectively compared with those of LAC over the same period and with those of conventional open surgery as a historical control. The intraoperative and postoperative data indicating the short-term outcomes of the hybrid-HALC group were better than those of conventional open surgery and similar to those of the LAC group; the average operative time for hybrid-HALC was 40 min shorter than that for LAC. Furthermore, the reduction in the operative time in the hybrid-HALC group was more prominent in the case of non-expert surgeons. Researchers concluded that hybrid-HALC for transverse colon cancer is a feasible, convenient, and less-invasive technique, and that it is a useful alternative, especially for non-expert laparoscopic surgeons.



In selected patients, laparoscopic surgery is used to remove parts or in some cases the entire colon through small incisions with proven benefits compared with open surgery.

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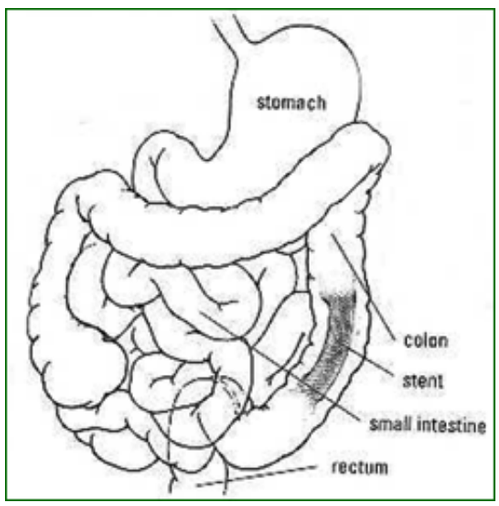
Takakura, Yuji, et al., Hybrid Hand-Assisted Colectomy for Transverse Colon Cancer: A Useful Technique for Non-Expert Laparoscopic Surgeons. World Journal of Surgery. Published online. DOI: 10.1007/s00268-009-0244-7 October 13, 2009

16. Stent Or Surgery for Incurable Obstructive Colorectal Cancer (Oct. 29/09)

In the setting of stage-IV obstructive colorectal cancer, self-expanding metallic stents (SEMS) placement and palliative surgery may be appropriate options. The aim of this study was to evaluate the long-term results of surgery compared with stent implantation and to identify patients in whom one of these options can provide more benefit. From November 2000 to November 2008, 98 patients with incurable stage-IV colorectal cancer were treated with palliative surgery or SEMS. Data were recorded with respect to age, gender, tumor location, carcinoembryonic antigen (CEA), presence of metastatic disease in one or multiple organs, volume of liver metastases, urgency of the procedure and treatment with chemotherapy. Comparison between surgery and stent placement was performed for all groups and for patients who received and did not receive chemotherapy. Both groups were comparable regarding age, chemotherapy treatment, tumor location and presence of metastatic disease in one or multiple organs but not in gender, rate of urgent procedures, abnormal CEA and of volume of liver metastases >25%. Survival in the surgical group was significantly higher (11.9 vs 7.3 months). SEMS group had lower early morbidity, hospital stay and stoma creation. For patients who received chemotherapy, surgery provided benefit in survival (6.8 vs 3.9 months); in this subgroup, long-term complications from the primary tumour were more common in the stented group, and time to chemotherapy was longer in the group of surgery. No differences in survival were shown in patients who did not receive chemotherapy. Researchers concluded that **stent placement offers advantages regarding early morbidity, hospital stay and stoma creation. Surgery on the other hand, offers a benefit in survival in patients who receive chemotherapy but not in non-candidates to chemotherapy.**



A colonic stent is a self-expanding wire mesh tube that is designed to hold open a blockage in the bowel. A medical specialist trained in the technique implants the stent via the rectum. Once implanted the stent will expand into a 20mm wide support structure, which is intended to stay in place permanently. The symptoms of blockage - bloating, nausea, constipation and pain - should be relieved by the treatment. Most people cannot feel the stent once it is in. It will not rust, nor interfere with daily activities.

Source:
http://images.google.com/imgres?imgurl=http://www.adhb.govt.nz/gastroenterologyhepatology/images/general/colonic_diagramme.gif&imgrefurl=http://www.adhb.govt.nz/gastroenterologyhepatology/colonic_stent.htm&usg=__0RfwJWEEpb7Ijko0aG4DeAT7T8Y=&h=251&w=250&sz=28&hl=en&start=1&sig2=MVQPpZt7rgql9f5l8emvjq&um=1&tbnid=diMuGKHhgpl6QM:&tbnh=111&tbnw=111&prev=/images%3Fq%3Dcolonic%2Bstent%26hl%3Den%26sa%3DX%26um%3D1&ei=BdgCS6r4EoKCMYDFjdcP

Suarez, Javier, et al., Stent or surgery for incurable obstructive colorectal cancer: an individualized decision. Published online. DOI:10.107/s00384-009-0814-z

17. Repeated Resection for Recurrent Pulmonary Mets from Colorectal Cancer (Oct. 3009)

It remains controversial whether metastasectomy (surgical removal of colorectal cancer mets) is still feasible in patients with pulmonary recurrence from colorectal cancer, after initial metastasectomy. The aim of this study was to evaluate outcomes of repeated metastasectomy in these patients. According to the results, it appears that patients who have had one operation to remove lung tumors that have spread from cancer in their colon or rectum can have good outcomes with a second and even third lung surgery. Surgeons in Seoul, South Korea reviewed outcomes for 202 patients who had surgery to remove a colorectal cancer metastasis in their lungs *(pulmonary metastasectomy).* After a median follow-up of 28.9 months, 48 patients had a second lung surgery. Of those, 28 patients had cancer return in their lungs again, and 10 had a third operation to remove lung tumors.

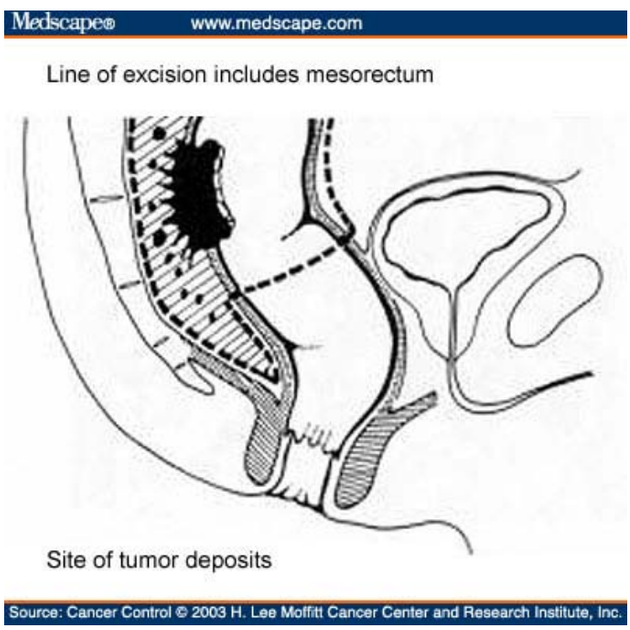
- For the 48 patients who had a second lung surgery, overall survival at five years was 79%, with 49% of patients having no sign of cancer at that time.
- For the 10 patients with a third surgery, overall survival five years later was 78%.

Researchers concluded that **repeated resection after initial metastasectomy can be carried out safely and provides long-term survival in patients with recurrent pulmonary metastasis from colorectal cancer.** The findings indicate that close follow-up for the early detection of recurrence and parenchyma-saving resection can improve the results after repeated resection.

Park, JS., et al., Outcomes after repeated resection for recurrent pulmonary metastases from colorectal cancer. Annals of Oncology. Advance Access published online on October 27, 2009. DOI:10.1093/annonc/mdp475

18. Quality of Rectal Cancer Surgery: Comparing Open and Laparoscopic Approaches (Nov. 3/09)

Macroscopic evaluation of a tumor specimen is an independent prognostic factor of oncologic outcome after total mesorectal excision (TME) for rectal cancer. This study sought to assess macroscopic quality of specimens acquired after laparoscopic vs. open TME in patients with low rectal cancer. 72 patients with low rectal cancer underwent TME either by open or laparoscopic approach. In all specimens, all areas of the surgery were macroscopically assessed. Colorectal anastomoses (surgical connection of resected colon ends) were located significantly lower in the laparoscopic than in the open group. A significantly more complete TME was performed after laparoscopy compared with open surgery. Researchers concluded that laparoscopy offers a macroscopically more complete specimen after TME for rectal cancer than the open approach because it offers a better view in the pelvis.



This image refers to a patient with a distal mesorectal deposit

Source; http://images.google.com/imgres?imgurl=http://www.medscape.com/content/2003/00/45/60/456036/art-cc456036.fig1.jpg&imgrefurl=http://www.medscape.com/content/2003/00/45/60/456036/456036_fig.html&usg=__XTAvdw0EAZOQf3lASl5pb1pd2I=&h=395&w=400&sz=36&hl=en&start=12&sig2=mx9O-COmWfSp99Z0Q8PkAw&um=1&tbnid=-FHNCQTZWyZrpM:&tbnh=122&tbnw=124&prev=/images%3Fq%3Drectal%2Bcancer%2Bsurgery%26hl%3Den%26um%3D1&ei=ldoCS_OiOMOGkAW9pPRG

Gouvas, Nikojaos, et al., Quality of surgery for rectal carcinoma: comparison between open and laparoscopic approaches. The American Journal of Surgery. Vol. 198, Issue 5, pp. 702-708. November 2009.

RADIATION / INTERVENTIONAL RADIOLOGY

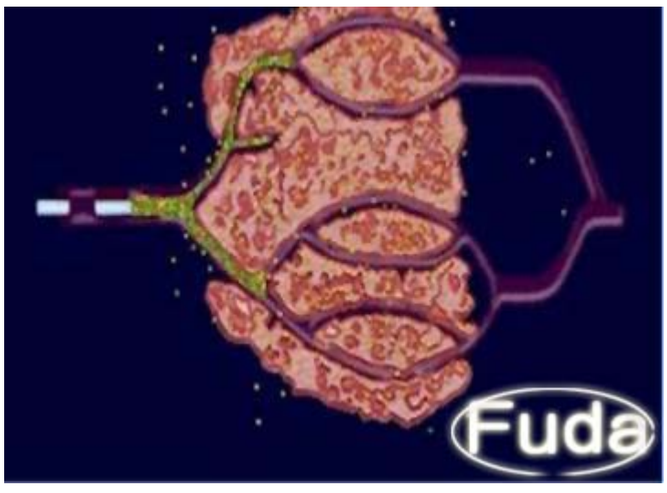
19. Outcomes of Dose-Escalated Image-Guided Radiotherapy for Spinal Mets (Nov. 1/09)

The purpose of this study was to evaluate the outcomes after dose-escalated radiotherapy (RT) for spinal metastases and paraspinal tumors was administered. A total of 14 patients, 12 with spinal metastases and a long life expectancy and 2 with paraspinal tumors, were treated for 16 lesions with intensity-modulated, image-guided RT. A median biologic effective dose of 74 Gy10 in an average of 20 fractions was prescribed. The spinal canal was treated to 40 Gy in 20 fractions using a second intensity-modulated RT dose level in the case of epidural involvement (located on or over the dura mater) . After median follow-up of 17 months, one local recurrence was observed, for a local control rate of 88% after 2 years. Local control was associated with rapid and long-term pain relief. Of 11 patients treated for a solitary spinal metastasis, 6 developed systemic disease progression. The overall survival rate for metastatic patients was 85% and 63% after 1 and 2 years, respectively. Acute Grade 2-3 skin toxicity was seen in 2 patients with no late toxicity greater than Grade 2. No radiation-induced myelopathy (disturbance in the spinal chord) was observed. Researchers concluded that dose-escalated irradiation of spinal metastases was safe and resulted in excellent local control. Oligometastatic patients (refers to patients whose metastases are limited in number and location and are amenable to regional treatment) with a long life expectancy and epidural involvement are considered to benefit the most from fractionated RT.

Guckenberger, J Goebel, et al., Clinical outcome of dose-escalated image-guided radiotherapy for spinal metastases. International Journal Radiation Oncology & Biological Physics. 2009 Nov. 1; Volume 75, Issue 3: pp. 828-835

20. Transarterial Chemoembolization of Liver Mets (Nov. 2/09)

Hepatic metastasis of colorectal cancer (MCC) is quite common occurring at some time in 23% of all colorectal patients diagnosed each year. While systemic chemotherapy can slow growth and even cause regression of the size of the hepatic metastases, long-term survival without local therapy is unlikely. Surgical resection of hepatic metastases continues to remain the optimal first line treatment for hepatic colorectal metastases. Other therapies that have been used are transarterial chemotherapy, ethanol injection, cryotherapy, radiofrequency ablation, and microwave ablation. The role of hepatic transarterial therapy of hepatic colorectal metastases continues to evolve as the technology evolves and experience with this technique matures. The purpose of this study was to evaluate the patient tolerance and efficacy of delivering locoregional chemotherapy to metastatic colorectal (MC) hepatic metastases via **hepatic trans-arterial** approach using **irinotecan loaded drug eluting beads**. This open-label, multi-center, single arm study included 30 MC patients, who had failed first line therapy. Of the 57 total embolization sessions, 12 (21% of sessions) were associated with adverse reactions during or after the treatment. After a median followup of 9 months, response rates were 75% at 3 months and 66% at 6 months. Researchers concluded that hepatic trans-arterial therapy using Irinotecan loaded DC Beads was safe and effective in the treatment of MCC as demonstrated by a minimal complication rate and acceptable tumor response.



Transarterial Chemoembolization (TACE): Liver mets derive its blood supply exclusively from the hepatic artery in contrast with the rest of the liver, which is also served by the portal vein. The branch of the hepatic artery supplying the tumor is occluded (blocked) at the time of arteriography (Examination of the arteries using x-rays following injection of a radiopaque dye), by injection of lipiodol or/and gelatin-sponge particles, which results in necrosis of the tumor (tumour death). Chemotherapeutic agents, which are often mixed with lipiodol, are simultaneously given

Source;
http://images.google.com/imgres?imgurl=http://www.orienttumor.com/english/t%26t/liver/002.jpg&imgrefurl=http://www.orienttumor.com/english/t%26t/liver_therapy.htm&usg=__NiU9J_B76zW-Ovx8QFLiivcm1uo=&h=260&w=360&sz=54&hl=en&start=1&sig2=02nkGrSeHyGbcl2uUNHMrw&tbnid=PwJ8paYSWfq9TM:&tbnh=87&tbnw=121&prev=/images%3Fq%3Dtransarterial%2Bchemoembolization%26gbv%3D2%26ndsp%3D20%26hl%3Den%26sa%3DN&ei=Vt4CS8SrN5fm7APcpuFn

Martin, Robert, et al., Transarterial chemoembolization of metastatic colorectal carcinoma with drug-eluting beads, irinotecan (debiri): multi-institutional registry. Journal of Oncology. Volume 2009, Article ID 539795, doi: 10.1155/2009/539795

21. ASCO Calls For More Research Into RFA of Hepatic Mets from CRC (Nov. 5/09)

After a comprehensive systematic review of literature published from 1996 to 2007, an American Society of Clinical Oncology panel concluded that there is not enough clinical evidence to construct a guideline for the use of radiofrequency ablation for patients with extrahepatic colorectal cancer. A clinical evidence review was published online Oct. 19 in the *Journal of Clinical Oncology.* The panel reviewed 245 articles to develop the evidence review for the use of radiofrequency ablation in colorectal cancer. The following three clinical issues were considered by the panel: the efficacy of surgical hepatic resection versus RFA for resectable tumors; the utility of RFA for unresectable tumors; and RFA approaches (open, laparoscopic, or percutaneous). Evidence suggests that hepatic resection improves overall survival (OS), particularly for patients with resectable tumors without extrahepatic disease. Careful patient and tumor selection is discussed at length in the literature. RFA investigators report a wide variability in the 5-year survival rate (14% - 55%) and local tumor recurrence rate (3.6% - 60%). The reported mortality rate was low (0% - 2%), and the major complications rate was commonly reported to be between 6% and 9%. RFA is currently performed with all three approaches. The panel's recommendations were based on evidence from single-arm, retrospective and prospective trials. No randomized controlled trials were included in the review because radiofrequency ablation has not undergone such a trial. The panel concluded that "there are no compelling data to guide use of radiofrequency ablation in patients with viable extrahepatic disease" and "radiofrequency ablation in the setting of known extrahepatic disease is not supported by data at this time." ASCO did not go so far as to discourage use of radiofrequency ablation for it would be difficult to phase out a treatment that has been in use for years.

Wong, SL, et al., American Society of Clinical Oncology 2009 Clinical Evidence Review on Radiofrequency Ablation of Hepatic Metastases From Colorectal Cancer Journal of Clinical Oncology. 2009; doi:10.1200/JCO.2009.23.4450

SCREENING

22. ColoMarker May Be New Tool Used for Detection (Oct. 15/09)

Colonoscopy remains the gold standard for colon cancer detection, but researchers are always on the look out for less-invasive ways to screen for this disease. And despite the fact that colonoscopy is not as bad as you may imagine, a simple blood test for colon cancer would be a welcome development for many. This type of test may soon be a reality. EDP Biotech Corporation has developed a blood test, called ColoMarker, which in preliminary studies detected a very high percentage of stages I, II, and III colon cancers in people with the disease. The ColoMarker test looks for a substance in blood called CA1-18. In tests of 2,370 blood samples, ColoMarker showed an overall accuracy rate for detecting colon cancer of 93%. In another early trial, researchers tested for the presence of ColoMarker in 243 blood samples from patients who had symptoms of colon cancer. They compared the results of these blood tests to results from the Fecal Occult Blood Test (FOBT). ColoMarker had a false positive rate of 11% compared with a false positive rate of 30% for FOBT. This means that ColoMarker is much less likely to identify people as having colon cancer, when they do not have the disease. In this same group of 243 patients, ColoMarker detected 100% of Stage I (early stage) colon cancers, while FOBT identified only about 40% of early stage disease. ColoMarker is not proven to identify people with polyps, growths in the colon that if left untreated, may develop into colon cancer. Ideally, a colonoscopy will find polyps and your doctor can remove them, long ***before*** they turn into colon cancer.

www.medicalnewstoday.com/articles/164201.php

23. Colonoscopic Perforations (Oct. 16/09)

This study showed that patients over 75 are 6 times more likely to experience a colon perforation during a colonoscopy or sigmoidoscopy. Doing a treatment intervention during the endoscopy, such as removal of polyps, triples the risk for all patients. Researchers reviewed nearly 9000 colonoscopies and 1,100 sigmoidoscopies done in a large GI training center in Bangkok. They found 15 perforations (1.5/1000). Gender, experience of the endoscopist, or method of sedation didn't affect perforations. Researchers concluded that their *findings have indicated that special precautions should be made during therapeutic endoscopy and while performing colonoscopic examination in the elderly, particularly in patients over 75 years. Non-invasive investigation of the colon such as CT colonography, if applicable, might be considered in such advanced age patients.*

Lohsiriwat, Varut, et al., What are the risk factors of colonoscopic perforation? BMC Gastroenterology. 2009, Volume 9, p.71. doi: 10.1186/1471-230X-9-71

24. Colonoscopy Improves Survival After Colorectal Cancer Diagnosis in Inflammatory Bowel Disease (Oct. 16/09)

Colonoscopic surveillance provides the best practical means for preventing colorectal cancer in inflammatory bowel disease patients. Strong evidence for improved survival from surveillance programmes is sparse, however. This study sought to determine if improved survival from surveillance could be determined. Results from this study revealed that regular colonoscopy surveillance of patients with inflammatory bowel disease (IBD) finds colorectal cancer at an earlier stage and prevents deaths from colorectal cancer. Researchers in the Netherlands compared outcomes for IBD patients who were part of a surveillance program before a colorectal cancer diagnosis with IBD patients who were not. Five year colorectal cancer specific survival for the surveillance group was 100% compared to 75% of those who didn't have surveillance before cancer diagnosis. Only one surveillance patient died of colorectal cancer compared to 29 in the non-surveillance group.

Lutgens, MWMD, et al., Colonoscopic surveillance improves survival after colorectal cancer diagnosis in inflammatory bowel disease. British Journal of Cancer. Advance Online Publication. October 13, 2009. doi: 10.1038/sj.bjc.6605359

25. Camera Improves Colonoscopy (Oct. 27/09)

The screening test , colonoscopy, is getting more accurate, thanks to better techniques and equipment, such as a camera that helps detect polyps and other lesions lurking behind the folds of the intestines. A routine colonoscopy, a visual inspection of the colon using a special flexible scope, is generally recommended at age 50 to detect cancer and precancerous growths, and earlier if there is a family history or for certain ethnic groups. But the test isn't foolproof, and researchers have been trying to improve the technology. One improvement in colonoscopy is a disposable device that is passed through the instrument channel of a standard colonoscope, called the Third Eye Retroscope (TER), which gives physicians a better look at the lesions they may miss with standard screening equipment. 'The third eye is a camera on the end of a probe. It allows physicians to inspect the colon backward as they withdraw the scope. The image is not quite as clear [as the forward image]. Still, the idea is to help physicians detect the lesions -- polyps and adenomas -- behind the many folds and turns in an intestine, which has remained difficult despite other advances in equipment. Nearly 300 patients underwent colonoscopies using the third eye camera. By using a split screen monitor, researchers were able to detect which growths were observed due to the camera that wouldn't have been detected with traditional colonoscopy alone. The overall increased detection rate for all adenomas using the third eye device was 16%, with an even greater detection rate for larger growths than smaller

www.webmd.com/colorectal-cancer/news/20091027/new-techniques-cameras-improve-colonoscopy

26. Videos Improve Colonoscopy Performance (Oct. 28/09)

According to this study, when endoscopists knew that their colonoscopies were being recorded on video, their overall performance increased significantly. They spent more time on each exam and average quality judged on a 1 to 5 scale improved from 2.9 to 3.8. In a quality improvement program, experienced doctors were not told at first that their colonoscopies were being taped, but digital recordings were made of 8 to 10 tests. After being told they would be recorded another 10 cases were taped. Both sets of "pre" and "post" awareness tapes were randomly shuffled, reviewed and scored by an expert endoscopist who didn't know which gastroenterologist did the exam or whether the doctor was aware or not of being recorded. Researchers concluded that video recording of colonoscopy dramatically changed process quality indicators of colonoscopist behavior toward longer examination time and better technique. Systematic video recording of colonoscopy may support quality performance of colonoscopy.

American College of Gastroenterology Abstract 11, Rex et al., Video recording Impacts Colonoscopy Performance.

27. Colon Cancer & Genetic Testing (Oct.. 29/09)

In the past decade, the identification of defective genes (mutations) associated with colon cancer in families where colon cancer is common has taken place. When a defective gene can be identified, it is possible to examine other members of the family to see if they also carry the defective gene. Those individuals who carry the defective gene are at a very high risk (75%-100%) for developing colon cancer. However, if an individual is found to have the defective gene, his or her colon can be removed before the cancer occurs. Only 5% of all colon cancers occur in families with a history of colon cancer and identifiable genetic defects. Therefore, genetic testing as it exists today is useful for only a minority of the population who are destined to develop colon cancer. Nevertheless, genetic testing is important because the risk is so extremely high among individuals who are found to have the genetic defect. In addition, more defective genes are likely to be found during the next few years, and this will make genetic testing valuable for an increasing number of individuals who will develop colon cancer. At present, there are two types of familial colon cancer in which defective genes can be identified. One type of cancer is associated with a strong family history of colon polyps. The other type of colon cancer is not associated with a family history of colon polyps. The polyp-associated cancerous disease is called familial adenomatous polyposis (FAP). (Adenomatous polyps are a type of polyp that have the potential to become cancerous.) The

nonpolyp-associated cancerous disease is called hereditary nonpolyposis colorectal cancer (HNPCC). An individual is likely to belong to a family with FAP if he or she has more than 100 adenomatous colon polyps or is a first-degree relative (parent, sibling, or child) of a person who has more than 100 adenomatous colon polyps. The number of polyps is less in some families, a condition referred to as attenuated FAP. Therefore, individuals who have between 20 and 100 adenomatous colon polyps or are first-degree relatives of individuals with 20 to100 adenomatous colon polyps also may belong to a family with FAP. An individual is likely to belong to a family with HNPCC and require genetic testing if

(1) three or more relatives have had colon cancer (or another cancer associated with HNPCC such as uterine, small bowel, urethral, or renal pelvic cancer) and at least one of the relatives is a first-degree relative,

(2) two or more generations of the family have colon cancer, or

(3) one or more relatives were diagnosed with colon cancer before age 50.

These criteria for identifying HNPCC are referred to as the Amsterdam II Criteria. The Amsterdam II Criteria have been modified in order to identify additional individuals who should undergo genetic testing for HNPCC. These include people with

(1) two or more colon cancers,

(2) colon cancer and a first-degree relative with colon cancer or another cancer associated with HNPCC before age 50, or an adenomatous colon polyp before the age of 40,

(3) colon or uterine cancer before age 50, and

(4) an adenomatous colon polyp before age 50.

The expanded Amsterdam II Criteria are referred to as the modified Bethesda Criteria. Almost all mutations that cause FAP occur in one gene, referred to as the APC gene. If an individual has FAP, that family member should have their APC gene examined for mutations. If a mutation is found, the same mutation can be sought in other family members. If a family member has the same mutation, then he or she will probably develop colon cancer. If that person does not have the mutation, he or she is not at an increased risk for colon cancer. If there is no member in the family who clearly has FAP and can undergo genetic testing, then genetic testing has little value for other family members. Mutations that cause HNPCC occur in several different genes. If an individual in a family suspected of being in an HNPCC family has colon cancer, tissue from the cancer can be examined to determine if a mutation is present. If there is a mutation, then other family members can be examined for the mutation. If they have the mutation, then they probably will develop colon cancer. If they do not have the mutation, they are not at increased risk for colon cancer. If there is no member in the family with colon cancer and an identifiable mutation, then genetic testing of family members has little value.

www.emedicinehealth.com/script/main/art.asp?articlekey=18472

28. High Definition Colonoscopy Superior (Nov. 2/09)

Colonoscopy is the gold standard for detecting colon cancer. There is no doubt that colonoscopy saves lives. Even so, researchers are always looking for ways to make this test even better. This is because the more effectively colonoscopy screening can detect the smallest tumors or pre-cancerous colon growths, the more likely it is that these growths will be caught and removed early, before they have spread. New research has found that a type of colonoscopy testing called high-definition colonoscopy is superior to regular colonoscopy for finding colon growths that can develop into colon cancer. Results from the largest head-to-head comparison of regular vs. high-definition colonoscopy screening are clear: High-def colonoscopy should be the screening of the future. If a patient is at average risk for colon cancer, health experts recommend that they begin colonoscopy screening at age 50. If a patient is at above-average risk, for example because of inflammatory bowel disease, (IBD) or a genetic condition that increases risk, they will likely need to begin colonoscopy screening much earlier and undergo it more often. Here are some steps one can take to take control of their colon health:

- Do not use these latest study results on high-def colonoscopy as an excuse to avoid getting this test altogether. Your doctor may not have access to this sort of test quite yet, but regular colonoscopy is still the single best way to detect colon cancer early, before it has spread and when it is easiest to treat and cure.
- Learn what you need to do to prepare for a colonoscopy. A little planning will help you have a sense of control over your health and your health care choices.
- Learn what happens during a colonoscopy. Knowing what to expect can ease your fears significantly. L
- earn how to remove the dread and fear of colonoscopy. Nobody looks forward to getting a colonoscopy, but it likely is not as bad as you may think.

- Focus on the future. Focusing on the fact that getting a colonoscopy can save your life and keep you cancer-free can make it easier to pick up the phone and call your doctor to ask about this important screening.

/www.newswise.com/articles/view/558015/

29. NCCN Guidelines Including Additional Primary Screening Modality (Nov. 2/09)

Although colonoscopy remains the preferred colorectal cancer screening method, the recently updated NCCN Guidelines for Colorectal Cancer Screening have added annual immunohistochemical stool testing with or without a flexible sigmoidoscopy every five years as an alternate screening option for average risk individuals. Additional updates include guidelines for individuals with three rare syndromes putting them at greater risk for developing the disease. The updated NCCN Guidelines continue to emphasize the importance of screening in order to detect the disease at an early stage or prevent cancer through polypectomy (removal of polyps). For those at average risk of developing colorectal cancer, annual immunohistochemical-based stool testing with or without a flexible sigmoidoscopy every five years has been added as a primary screening option in the updated NCCN Guidelines. **Average risk** is defined as those individuals who are 50 years or older with no history of adenoma, colorectal cancer, or inflammatory bowel disease, and with no family history of colorectal cancer. Compared to colonoscopy, stool tests (guaiac-based or immunohistochemical) and flexible sigmoidoscopy requires no sedation and less preparation, which may be more appealing to some individuals; however the NCCN Guidelines Panel notes that colonoscopy remains the preferred screening method if available. Colonoscopy is also required to confirm any positive findings from other tests. Another noteworthy update to the NCCN Guideline for Colorectal Cancer Screening is the addition of definitions and surveillance recommendations for Peutz-Jeghers Syndrome, Juvenile Polyposis Syndrome, and Hyperplastic Polyposis Syndrome. These conditions are all relatively rare, but they do pose an increased risk of colorectal cancer over the general population and those with the condition should consider following the screening guidelines noted in the updated NCCN Guidelines.

www.nccn.org/about/news/newsinfo.asp?NewsID=227

30. Screening Finds Polyps in People From 40-49 (Nov. 4/09)

Current ACG guidelines call for screening people with a first-degree relative (parents, siblings, children) with colorectal cancer to have screening colonoscopies beginning at age 40. Doctors at the University of Michigan reviewed colonoscopies done only for screening in their patients from 40 to 49 who had a first-degree relative with colorectal cancer. They found adenomatous polyps in 1 in 5, and advanced adenomas in 4 out of 100. There was no significant difference in either polyps or advanced adenomas depending on whether the relative had been diagnosed with colorectal cancer before or after the age of 60. However, diabetes did have a significant impact on finding polyps. Researchers concluded that based upon 21.7% prevalence of adenomas and 3.6% prevalence of advanced adenomas, the data supports current guideline recommendations to begin screening colonoscopy at age 40 among individuals with a family history of colorectal cancer.

American College of Gastroenterology. Abstract 16A: Gupta et al., Prevalence and Risk Factors for Adenomas in 40-49 year old individuals with a family history of colon cancer.

31. Early Morning Colonoscopies Detect More Polyps (Nov. 11/09)

Researchers have reported that a greater number of polyps was detected among patients seen early in the morning than among those patients seen later in the day. The reasons for this are uncertain, but it's possible that the lower rate of polyp detection later in the day is the result of provider fatigue or less complete bowel preparation. Colonoscopy is accepted as the optimal method for detecting colorectal adenomas and cancers. There is emerging evidence that the skill of the endoscopist is an important factor in determining the accuracy of colonoscopy. For example, researchers from the University of Illinois have previously reported that gastroenterologists who perform a screening colonoscopy in less than six minutes detect significantly fewer adenomas than gastroenterologists who take six minutes or more to perform the procedure. Researchers from the University of Indiana have also reported that the individual performing the colonoscopy is a more important predictor for detecting adenomas than age or male gender. **Researchers from Canada have reported that colonoscopies performed in an office or performed by an internist or family physician carry a higher risk of missing colorectal cancers compared with colonoscopies performed in a hospital setting or performed by a gastroenterologist.** To explore whether polyp detection varies by time of day, researchers in this study evaluated the medical records of 477 patients who received colonoscopies. Early colonoscopies were defined as those that occurred at or before 8:30 am.

- 20% more polyps per patient were detected among patients who received colonoscopies early in the day than among patients who received colonoscopies later in the day.
- The number of polyps detected decreased hour by hour as the day progressed.

The reasons for the differences in polyp detection by time of day are uncertain, but the researchers speculate that provider fatigue later in the day may be one contributing factor. It's also possible that better bowel preparation the night before contributes to more complete polyp detection among patients seen in the morning.

Chan MY, et al., Fewer polyps detected by colonoscopy as the day progresses at a Veteran's Administration teaching hospital. **Clinical Gastroenterology and Hepatology.** ***2009;7:1217-1223.***

PSYCHOSOCIAL

32. Helping to Deal With Chemobrain (Oct. 16/09)

The American Cancer Society has tips and resources for coping with foggy thinking during and after chemotherapy and links to puzzle sites where patients can give their brain a workout. Besides using a detailed daily planner with everything one might need to remember in one place, the ACS recommends having one place to put things that can be easily lost like keys and glasses. Talking to friends and going to a support group also helps as do good health habits including enough sleep and a nutritious diet.

www.newconnections-cancer.org/issue_29/pos/03.html

OTHER

33. Early Circulating Tumour Cells Predict Survival in Advanced Colon Cancer (Nov. 2/09)

Early predictive markers for treatment response are needed for advanced colorectal cancer (ACC) patients. This study assessed the value of circulating tumour cells (CTC) in ACC patients treated with chemotherapy plus targeted agents (CAIRO2 phase III trial) and compared the results with CT imaging. CTC were determined at baseline and at different time points during treatment. Patients were grouped into **low** (less than three CTC per 7.5 ml of blood) or **high** CTC (three or more CTC per 7.5 ml of blood). A total of 467 patients were assessable for CTC analysis. Among them, 129 patients (29%) with **high** baseline CTC had a **significantly decreased progression-free survival** or PFS [time till disease got worse] and overall survival or OS compared with 322 patients with low baseline CTC. Researchers found that the combined analysis of CTC and CT imaging provided a more accurate outcome assessment than either modality alone. The CTC count before and during treatment independently predicts PFS and OS in ACC patients treated with chemotherapy plus targeted agents and provides additional information to CT imaging.

Tol, J., et al., Circulating tumour cells early predict progression-free and overall survival in advanced colorectal cancer patients treated with chemotherapy and targeted agents. **Annals of Oncology. 2009. October 27. Epub ahead of print. Doi:10.1093/annonc/mdp463**

NUTRITION & HEALTHY LIFESTYLE

34. Folic Acid and Colon Cancer (Oct. 30/09)

A Harvard Study is reporting that supplements of folic acid may reduce the recurrence of colorectal cancer in people with low levels of the nutrient, but not in people who already have adequate amounts. And contrary to other studies, the Harvard researchers found *"no evidence for an increased risk of advanced or multiple adenomas"*. The study may go some way to weakening the arguments of opponents of folic acid fortification who cite studies with reported potential increases in colorectal cancer risk associated with folic acid. Epidemiological evidence suggests a slight increase in colorectal cancer rates following the introduction of fortification. Such associations have been noted in the US, Canada, and Chile. However, over 30 case-control and prospective cohort studies have reported colorectal cancer risk *reduction* associated with folate. Folate is found in foods such as green leafy vegetables, chick peas and lentils, while folic acid is the synthetic, bioavailable form of the vitamin used in fortification programmes worldwide, as well as in supplements and other fortified foods. A possible explanation for the contradictory results of studies with the vitamin and colorectal cancer may be the difference between the synthetic and natural forms of the vitamin. "*The fact that folic acid, which is not a naturally occurring form of the vitamin, is used by food and pharmaceutical industries for fortification and supplementation is potentially of importance,"* cite researchers. On passage through the intestinal wall, folic acid is converted to 5-methyltetrahydrofolate, the naturally circulating form of folate. However, some studies have suggested that oral doses of folic acid in high doses may overwhelm this conversion pathway, leading to measurable levels of folic acid in the blood. According to researchers, some studies have shown that high folate levels in certain people who harbour pre-cancerous or cancerous tumours may actually promote cancer but the new study represents randomised clinical trial evidence of no risk for folic acid. Furthermore, the researchers, led by Kana Wu, found a protective effect of supplements in people with low levels of the B vitamin at the start of the study. Wu and co-workers conducted a double-blind, randomised trial of the effects of folic acid supplementation (1 milligram per day) or placebo on recurrent colorectal tumours over three to six and a half years. Overall, no beneficial or detrimental effects were observed as a result of folic acid supplementation. However, among participants with plasma folate

levels below 7.5 nanograms per millilitre, folic acid was found to decrease the risk of tumour recurrence by 39%. Researchers concluded: "*Our results do not support an overall protective effect of folic acid supplementation on adenoma recurrence. Folic acid supplementation may be beneficial among those with lower folate concentrations at baseline".*

Wu, K., et al., A randomized trial on folic acid supplementation and risk of recurrent colorectal adenoma. American Journal of Clinical Nutrition. Published online ahead of print, doi:10.3945/ajcn.2009.28319

35. Yoga Benefits Cancer Patients (Nov. 2/09)

Some of the major cancer centers, including MD Anderson, Memorial Sloan-Kettering, and Dana-Farber Cancer Institute, now offer their patients yoga as a complementary therapy in an effort to provide a more integrative approach to cancer care. In addition, some physician-directed programs educate patients in yoga techniques. Yoga is a form of nonaerobic exercise that involves a program of precise postures, breathing exercises, and meditation. Yoga can be a useful method to help relieve some symptoms of chronic diseases such as cancer and can lead to increased relaxation and physical fitness. Recent scientific studies do not support yoga as an effective stand-alone treatment for cancer or any other disease; however, it may enhance quality of life by relieving the stress and anxiety associated with disease progression or treatment. Alyson Moadel of the Albert Einstein College of Medicine studied the effects of yoga in breast cancer patients and published her findings in a 2007 issue of the Journal of Clinical Oncology. She found that patients who did yoga saw improvements in social and emotional well-being compared with those who didn't. Most studies on yoga and cancer have focused on breast cancer patients, but recently studies have begun to incorporate other cancer patients, including those with lung cancer and **colorectal cancer.** Results from recent studies on yoga and cancer show that the complementary therapy can have many benefits for patients, both mentally and physically. Some of the benefits include:

- Combating the side effects of treatment
- Anxiety Relief
- Reduction of stress and cortisol levels
- Immune System Response
- Improve Coping Mechanism
- Decrease insomnia
- Improve depression symptoms
- Relief of Chronic Pain
- Provide gentle exercise

People with cancer should speak to their doctor before starting any type of therapy that involves movement of joints and muscles.

www.emaxhealth.com/1506/51/34310/yoga-benefits-cancer-patients.html

36. Excess Body Weight Linked to New Cancer Diagnoses (Nov. 9/09)

According to estimates from the American Institute for Cancer Research (AICR), excess body weight may be responsible for more than 100,000 new cancer diagnoses each year in the United States. Excess body weight is increasingly recognized as a risk factor not only for cancer development but also for worse outcomes after cancer treatment. Links have been established between excess body weight and cancers of the endometrium, esophagus, pancreas, kidney, breast (in postmenopausal women), and colorectum. There is also a probable link between excess body weight and gallbladder cancer. Body mass index (BMI) is a commonly used (though imperfect) measure of body size. It involves a comparison of weight to height (weight in kilograms divided by height in meters squared). A BMI between 18.5 and 24.9 is generally considered healthy, a BMI between 25 and 29.9 is considered overweight, and a BMI of 30 or higher is considered obese. A report released by AICR estimated the number of cancers that could be prevented each year in the United States if everyone maintained a healthy body weight:

Cancer	Estimated percentage of cases due to excess body fat[1]	Approximate number of cases preventable by maintaining low body fat, per year[2]
Esophagus	35%	5,800
Pancreas	28%	11,900
Gallbladder	21%	2,000
Colorectum	**9%**	**13,200**
Breast	17%	33,000
Endometrium	49%	20,700
Kidney	24%	13,900
TOTAL		**100,500**

These results suggest that over 100,000 cancer diagnoses could be prevented each year in the United States if everyone maintained a healthy body weight. Accordingly, excess body weight increases the risk of several common types of cancer as depicted above.

AICR. New estimate: excess body fat alone causes over 100,000 cancers in US each year. Researchers present data linking obesity/overweight to higher cancer risk, poorer cancer survival. Available at:

http://www.aicr.org/site/News2/1028460841?abbr=pr_&page=NewsArticle&id=17333&news_iv_ctrl=1102.

37. Coffee Compound Protects Against Colon Cancer (Nov. 13/09)

A compound in coffee called trigonelline (or "trig") may have a role in estrogen-dependent breast cancer but also be helpful against the development of colon cancer. The bottom line at this point is that trigonelline can act like a hormone. During the last century, more than 19,000 studies have been conducted on the health pros and cons of coffee. In a 2006 study conducted at Vanderbilt University's Institute for Coffee Studies, Tomas DePaulis, PhD, a research scientist, noted that one reason "coffee is far more healthful than it is harmful" is the presence of the antioxidant trigonelline, which also gives coffee its bitter taste and aroma. According to researchers, trigonelline is a natural compound that is used in traditional Indian culture for post-menopausal women. Its chemical structure is not similar to estradiol (a type of estrogen), hence researchers did not believe the coffee compound would demonstrate estrogenic effects. But it did. Just because trigonelline has a link to cancer "in the sense that we are looking at estrogen-dependent cancer cells," noted researcher Dr. Allred "that doesn't suggest that it would actually cause the disease." He does not believe consumers should be worried about drinking coffee. "It is way too early to say that drinking a cup of coffee is exposing you to something that is definitely going to be estrogenic." Dr. Allred also noted that the amount of trigonelline in coffee varies depending on the variety of coffee bean. The two main types of coffee beans used in the United States both contain the antioxidant. The more coffee beans are roasted, the less trigonelline remains in the bean. The other side of the coffee compound is its possible use against colon cancer. The study's authors are interested in exploring whether this phytoestrogen can prevent the formation of colon cancer. If it does, it may be possible to develop a drug that could target colon cancer cells only and so spare the rest of the body from any estrogenic effects. Dr. Allred noted that "It's really important for us to come up with strategies that we can have the benefits in the colon without the risks associated with (estrogenic compounds)."

www.emaxhealth.com/1275/16/34431/coffee-compound-may-have-breast-and-colon-cancer-link.html