

## SIDE EFFECTS OF COLORECTAL CANCER TREATMENTS

Treatment-induced side effects may cause inconvenience, discomfort, pain and occasionally fatalities. One of the more disturbing facts associated with unwanted side effects is the interruption or discontinuation of the treatment as well as a possible dosage reduction. This can clearly limit a patient's ability to achieve the best outcome from treatment by preventing the delivery of therapy at its optimal dose and time.

In the past fifteen years, improvements and progress have been made in the development of treatments that aid in the prevention and control of unwanted side effects resulting from therapies. These agents have led to vast improvements in the management of symptoms associated with cancer therapies, allowed for greater accuracy and consistency concerning the administration of cancer treatment, and have made many cancer therapies more widely available to patients throughout the world.

To assist patients throughout their management of treatment-induced side effects, Colorectal Cancer Canada has developed the following list of treatment-induced side effects arranged alphabetically providing information relating to:

- **Description/Symptoms**
- **Cause**
- **Remedy/Treatment and**
- **Prevention**

Simply click on one of the letters below to access a wide range of side effects appearing therein.

Additionally, a link to each colorectal cancer **drug side effects monograph** has been provided at the end of the document to assist patients in the understanding of the respective drug's toxicity profile.

The information in this section is not medical advice. It is a general description of some possible side effects produced from specific features through the administration of colorectal cancer therapies. Other sources of information are the patient's healthcare team and the drug manufacturer's product package. Always consult with your healthcare provider for information related to drug treatment or side effects.

**A/B/C/D/E/F/G/H/I/J/K/L/M/N/O/P/Q/R/S/T/U  
/V/W/X/Y/Z**

A/

## Abdominal Pain

Description/Symptoms: Abdominal pain may present as a dull ache, cramping or sharp pain in the abdominal area. Dull aches and cramping are often associated with some chemotherapy drugs. Chemotherapeutic agents cause these abdominal pains by changing the rate of intestinal activity.

Cause: Chemotherapeutic drugs such as oxaliplatin, irinotecan, mitomycin c, xeloda as well as other agents such as avastin, erbitux, vectibix and decadron can cause either an increase or decrease in the activity of the intestines. Specifically, the normal wave-like action of the intestines that moves stool through the bowel may be faster or slower than usual. An increase in intestinal activity may cause stool to travel faster and be less formed, resulting in cramping and/or diarrhea. Conversely, a decrease in intestinal activity may cause stool to travel slower, becoming hard and dry and more difficult to pass, a condition generally recognized as constipation. Chemotherapy may also alter the bacterial flora that is present in the intestines. Under normal conditions, the intestines are populated with a variety of “good” bacteria that help with digestion. Chemotherapy may kill these bacteria, resulting in an imbalance in the intestines that allows “bad” bacteria to flourish. The result is poor digestion, increased flatulence (gas) and abdominal cramping.

Remedy/Treatment: Management of abdominal pains depends on their cause. Colorectal cancer drug-induced abdominal pain can be remedied. For mild abdominal pain related to digestive problems, over-the-counter medications, including Maalox, Mylanta, Pepto-Bismol and TUMS, may provide some relief. However, these only treat the symptoms of abdominal pain, not the cause. For lasting relief, an alteration in diet in a way that helps either slow or speed the intestinal activity is recommended.

Prevention: Changes in the diet are sometimes helpful in not only controlling but preventing abdominal cramps. Dairy, soy, fat or wheat gluten products are not tolerated well by patients following treatment for colorectal cancer. A modification in diet, with the doctor’s approval, can assist in helping to prevent colorectal cancer drug-induced abdominal pain.

## Abscess

Description/Symptoms: An abscess is a localized collection of pus in any part of the body, usually caused by an infection. Abscesses develop when an area of tissue becomes infected and the body is able to prevent the infection and keep it from spreading. During this process ‘pus’ forms, which is an accumulation of fluid, living and dead white blood cells, dead bacteria or other foreign invaders or materials. Following radiation therapy for rectal cancer,

abscesses within the pelvis may develop. This usually occurs as a late effect if at all, but may develop earlier in certain people. Abscesses are oftentimes accompanied with pronounced pain, fever, nausea, difficulty with bowel movements, or the appearance of pus from the vagina or rectum. Your doctor should be contacted immediately.

Cause: The causative agent in the development of rectal abscesses is usually external beam radiation therapy.

Remedy/Treatment: The primary treatment of abscesses is to drain them. However, it is also important to not attempt to drain an abscess yourself. This can lead to trauma of the surrounding tissue and potentially help spread the underlying infection. Draining the abscess is done by making a cut in the lining and providing an escape route for the pus, either through a drainage tube or by leaving the cavity open to the skin. The area around the abscess will be numbed before draining. Most people feel immediately better after the draining.

Prevention: The promotion and practice of hygiene is strongly recommended in the prevention of abscesses resulting from rectal cancer radiotherapy but radiotherapy-induced abscesses may be difficult to prevent in light of their site of origin.

## Acid Reflux (Heartburn)

Description/Symptoms: Heartburn is an irritation of the esophagus which causes burning discomfort in the chest just behind the breastbone. The burning sensation results when harsh stomach juices come in contact with and irritate the delicate lining of the esophagus, which is the tube-like structure that connects the mouth to the stomach. Heartburn may feel like:

- A burning chest pain that begins at the breastbone that moves up toward the throat
- Food or liquid is coming back into the mouth or throat
- An acid or bitter taste at the back of the throat
- A worsening pain/burning behind the breastbone when lying down or bending over

Cause: Heartburn is caused when harsh stomach juices come in contact with and irritate the delicate lining of the esophagus, which is the tube that connects the mouth to the stomach. Stomach juices help break down food in the stomach and contain a strong acid, called hydrochloric acid. While the stomach is naturally protected from the harmful qualities of acid, the esophagus is not. Stomach juices come into contact with the esophagus when the muscle that separates the stomach from the esophagus, called the lower esophageal sphincter, does not work properly. When working normally, this muscle works like a natural valve, letting food into the stomach but keeping stomach juices out of the esophagus. When not functioning properly, this muscle relaxes and allows stomach juices to flow upward into the esophagus. Your doctor may call this backward movement of stomach juices **gastroesophageal reflux**.

The hydrochloric acid damages the lining of the esophagus causing heartburn and its associated symptoms. Heartburn can occur in association with eating certain foods or taking certain drugs, including chemotherapy drugs used to treat colorectal cancer. Examples are: xeloda, oxaliplatin, 5FU, irinotecan, and the biologic avastin.

Treatment/Remedy: Avoiding things that cause heartburn can help, but if lifestyle changes are not enough to prevent heartburn, medication may be prescribed. Effective over-the-counter and prescription medications are available. **Over the counter antacids** work by neutralizing the acid in the stomach. They may contain the following compounds alone or in combination: calcium carbonate, aluminum hydroxide, magnesium hydroxide and magaldrate. Examples are Maalox, Mylanta, Roloids, or Tums. **H2 blockers** decrease stomach acid by blocking histamine from binding to the H2 receptors on cells in the stomach lining. Histamine, a natural substance produced by the body, stimulates cells in the stomach lining to release acid into the stomach. H2 blockers decrease gastric acid secretions. A few examples of these drugs that may be prescribed include Tagamet, Pepcid, Axid or Zantac. Pepcid and Zantac are now available over the counter. **Proton-pump inhibitors** inhibit the final step in the production of gastric acid. Examples include Prilosec, Prevacid, Nexium, Protonix or Aciphex. If it is determined that an ulcer is the underlying cause of the heartburn, these medications may be prescribed for short-term treatment of the ulcer. However, an ulcer is caused by the *H. pylori* bacteria and must be treated with a combination of medication and antibiotics for long-term results. Colorectal cancer therapy-induced heart burn requires the use of the above noted medications for as long as the condition persists or until your doctor deems appropriate.

Prevention: In general, there are a number of lifestyle changes that can be made to prevent or lower the risk of experiencing heartburn. These may include:

- Smoking Cessation
- Limit or eliminate alcohol
- Limit your caffeine intake (coffee, soda, tea)
- Lose some weight if you are overweight
- Avoid fatty foods (deep fried foods)
- Do not eat 2-3 hours before going to bed
- Avoid foods that cause you to have heartburn

## Allergic Reactions

Description/Symptoms: It is possible to have an allergic reaction to virtually any drug, depending on a host of poorly understood factors. Allergic reactions are more likely to occur with high doses of a drug that is administered rapidly. In the past, most allergic reactions were detected in the hospital chemo clinic as chemotherapy was being administered through an IV

line, by drip bag or bolus push (a bolus is the back end of a syringe, the reservoir that holds the medication). With the advent of the continuous infusion pump, however, it is possible to have an allergic reaction at home, hours or days after the pump was disconnected. Allergic reactions are highly individualized to substance type, but the symptoms are similar and include any of the following: hives, itching, difficulty breathing, tightness in chest or throat, sore throat, fever or chills.

Cause: Any of the following colorectal cancer agents may cause an allergic reaction: Oxaliplatin, irinotecan, 5FU, methotrexate, leucovorin, xeloda, avastin, erbitux, vectibix, mitomycin c and decadron. Immediate attention is required.

Remedy/Treatment: Generally, medications such as antihistamines, epinephrine and steroids are the treatment of choice after the allergen (agent causing the allergic reaction) is removed. Very severe reactions may require other therapy, such as oxygen for breathing difficulties or intravenous fluids to boost blood pressure in anaphylactic shock. Patients with very severe reactions usually require hospitalization.

Prevention: It is difficult to predict which patients will develop an allergic reaction to their colorectal cancer therapies and therefore prevention is difficult. However, remedies are available to treat the onset of a drug-induced allergy.

## **Alopecia (Hair Loss)**

Description/Symptoms: Radiotherapy and many chemotherapeutic agents employed in the treatment of colorectal cancer can cause hair loss – alopecia – although there is a wide range of individual responses to treatment in this regard. Some people lose just a little hair; others lose all hair, including body hair, eyebrows and eyelashes, facial hair, pubic hair, underarm hair and leg hair. Others report losing grey hair earlier than hair that contains pigment. Those receiving radiation therapies may lose hair only on the spots irradiated, such as pubic hair.

Cause: Chemotherapy damages rapidly dividing cells, such as cancer cells. Some healthy cells also divide rapidly, such as hair follicles. Chemotherapy damages these cells, leading to hair loss. Hair loss will typically begin two or three weeks after your first treatment. The amount of hair that you lose will depend on the type of chemotherapy drug you are taking. Hair typically begins to grow back approximately 2-3 weeks after treatment is finished. The hair may grow back differently than it was before treatment. For example, color or texture (curly or straight) may be different. Those colorectal cancer therapies capable of causing hair loss are: irinotecan, 5FU, mitomycin c, xeloda, methotrexate, and avastin. Conversely, Interferon sometimes used for colorectal cancer may cause excessive growth of hair.

Treatment/Remedy: New hair should regrow in the weeks or months after treatment. In some

instances, it might not regrow, although this is more common after radiotherapy than after chemotherapy. Importantly and generally, you should remember that hair loss associated with chemotherapy is temporary and the hair WILL grow back. In the meantime, here are a few suggestions to help you cope with the hair loss:

- You may wish to cut your hair before it starts falling out. The experience of losing the hair is sometimes worse than dealing with it once it's gone.
- For women, planning ahead may be helpful; shop for a wig before your hair is gone, especially if you wish to match your natural color.
- Try hats or head scarves; these are good alternatives or a compliment to a wig.
- Remember to cover your head or use sunscreen on your scalp. Skin that has been covered with hair may be particularly sensitive to UV rays of the sun.
- Ask your insurance company if they cover the cost of the wig.
- Treat your new hair gently once it grows back. Avoid chemicals, bleach, peroxide or colors.
- Get involved in a "Look Good... Feel Better" program, a community-based, free, national service that teaches female cancer patients beauty techniques to help restore their appearance and self-image during chemotherapy and radiation treatments. For more information go to [www.lookgoodfeelbetter.org](http://www.lookgoodfeelbetter.org).

Methods to spare the scalp from exposure to chemotherapeutic agents, such as ice-packing or tourniquets are not recommended, because small amounts of cancer may be sequestered in the skin or blood vessels of the scalp. Denying chemotherapy the opportunity to kill all colorectal cancer cells may result in failed treatment or relapse.

Prevention: It is difficult to prevent the loss of hair resulting from colorectal cancer therapies. But remedies can be taken to deal with it quite effectively.

## Anemia

Description/Symptoms: Anemia is an inadequate supply of red blood cells, resulting in a decrease in the oxygen carrying capacity of the blood. Red blood cells contain the protein hemoglobin, which carries oxygen to all parts of the body. Low levels of red blood cells, and thus hemoglobin, cause a reduction in the amount of oxygen that can be carried to the various body parts and tissues. The decreased delivery of oxygen causes the following symptoms: fatigue or tiredness, trouble breathing, rapid heartbeat, dizziness, light-headedness, inability to concentrate, or headache.

Cause: Anemia commonly occurs in colorectal cancer patients, either as a direct result of the cancer or as a side effect of cancer treatment. Chemotherapies such as irinotecan, oxaliplatin,

xeloda, 5FU, methotrexate and mitomycin C, biologics such as avastin and erbitux, and radiation therapy and blood loss during surgery are all common causes of anemia in colorectal cancer patients. Chemotherapy drugs kill rapidly dividing cells in the body, including cancer cells and normal cells, such as cells in the bone marrow responsible for red blood cell production (a process called *erythropoiesis*). Over 60% of colorectal cancer patients treated with chemotherapy develop anemia. A careful evaluation is necessary to determine the cause of anemia so that the most appropriate treatment is administered.

Treatment/Remedy: Erythropoiesis is controlled by red blood cell growth factors. Erythropoietin is the major blood cell growth factor that increases red blood cell production in the bone marrow. Erythropoietin is produced by cells in the kidney. When kidney cells detect a decrease in tissue oxygen, erythropoietin is released into the circulation. The end result is increased red blood cell production in the bone marrow. Anemia can be treated by increasing the hemoglobin level with blood transfusions or with erythropoietin (epoetin alfa or Procrit/Epogen and darbepoetin alfa or Aranesp), a blood cell growth factor that increases red blood cell production. **The two objectives for treating anemia are to first correct the underlying cause of the anemia and secondly treat the symptoms of the anemia.** Successful management of anemia may require erythropoietin, transfusions or both. Although erythropoietin has been shown to reduce the need for blood transfusions in patients with chemotherapy-induced anemia, some studies have reported serious adverse effects of erythropoietin in certain groups of patients wherein disease progression was evident. In response to these reports, and based on the advice of two advisory committees, the FDA in the US released an updated Advisory on the use of erythropoietin in November 2007. Hence, patients should discuss the risks and benefits of anemia treatment with their doctor. More information about the FDA Advisory can be found at: <http://www.fda.gov/cder/drug/infopage/RHE/default.htm>. Blood transfusions rapidly replace the oxygen-carrying capacity of the blood. The goal of a blood transfusion is to increase oxygen and carbon dioxide exchange between the tissues and reduce the symptoms of anemia. However, transfusions are associated with complications, including the risk of disease progression. Patients should carefully consider whether to undergo a transfusion and the benefits should outweigh the risk or complications of the procedure. Patients with chemo-induced anemia may be prescribed an iron supplement to help compensate for the reduced oxygen-carrying capacity of red blood cells. Natural sources of iron may also be obtained from the following: beef and other animal foods, green leafy vegetables, fruit, grains, nuts/seeds, cooking with cast-iron, taking vitamin C which helps the body absorb iron from food, limit calcium intake which makes it more difficult for iron absorption, limit coffee, tea and soda which make it difficult to absorb iron, and limit high-fiber cereals. Consulting the advice of your physician regarding the treatment of anemia is always recommended.

Prevention: Anemia can be prevented or corrected by using erythropoietin, or by giving a blood transfusion, both of which have been determined to advance disease progression. Carefully-managed anemia will be overseen by the treating physician so as to either prevent or

quickly treat the cause. It may be difficult to prevent chemo-induced anemia but remedies are available for treatment.

## **Appetite or Taste Changes (Early Satiety)**

Description/Symptoms: Early satiety is the feeling of being full after you have only eaten a small amount, perhaps only a few bites. This condition may also be described as having a poor appetite.

Cause: Early satiety as well as taste changes are common side effects resulting from chemotherapies such as 5FU, Xeloda, Irinotecan, Mitomycin C, Methotrexate, biologics such as avastin as well as radiotherapy, but may also be a complication of the cancer itself. Chemotherapy and radiotherapy can affect the taste buds to the extent that food can no longer be tasted, or that it tastes metallic or even unpalatable.

Remedy/Treatment: Early satiety may be treated with nutritional support or appetite stimulants. Since early satiety can compromise your ability to get adequate nutrition through food sources, you may benefit from treatment with nutritional support. All cancer patients should meet with a nutritionist or registered dietician prior to and throughout their treatment to help maintain their health through appropriate alterations to their diet. The nutritionist may recommend that you focus on eating higher calorie foods, such as protein-rich foods which include the following:

- Protein drinks (powdered protein supplement mixed with fruit, milk and/or yogurt)
- Milk
- Dairy products
- Eggs
- Meat
- Sauces or gravies
- Oil

In some situations, caloric supplementation is required which may be administered into the veins through Parenteral Nutrition, or directly into the intestines with enteral nutrition. Appetite stimulants may help you to maintain adequate calorie and nutrient intake from food sources. These include Marinol, megestrol acetate and dexamethasone. The doctor may also recommend vitamin supplements and liquid supplements such as Ensure to provide the much needed nutritional benefits during and after therapy.

Prevention: Prevention of therapy-induced early satiety may be difficult but adhering to the

recommendations of the doctor is important in helping to avoid food aversion. Also, adhering to a well balanced high calorie diet before beginning therapy can help in diminishing this unwanted side effect during therapy.

## Ascites

Description/Symptoms: Ascites is the accumulation of protein-containing (ascetic) fluid in the abdominal cavity. Inside the abdomen is a membrane called the peritoneum, which has two layers. One layer lines the abdominal wall and the other layer covers the organs inside the abdominal cavity. The peritoneum produces a fluid that acts as a lubricant and allows the abdominal organs to glide smoothly over one another. Sometimes too much of this fluid can build up between the two layers and this is what is commonly known as ascites. Ascites can be a symptom of colorectal cancer and its therapies. The symptoms of ascites can be very distressing. The abdomen becomes very swollen and distended, which can be uncomfortable or painful. It can also cause difficulty in getting comfortable, sitting up or walking. It can make one feel very tired (lethargic) and breathless due to pressing up on the lungs. It may cause feelings of sickness (nausea) or make you sick (vomiting). You may also suffer indigestion and a reduced appetite. There may also be changes in bowel function, satiety after eating only small amounts of food, increased abdominal girth, and low back pain.

Cause: There may be several reasons for the build-up of ascites:

- If cancer cells have spread to the lining of the abdomen (peritoneum), they can irritate it and cause fluid to build up
- If the liver is affected by cancer cells, this may block the circulation of blood through the liver, which can lead to a build-up of fluid in the abdomen
- If the liver is damaged, it may produce less blood protein. This may upset the body's fluid balance, which causes fluid to build up in the body tissues, including the abdomen. The liver may become damaged as a result of accessing chemotherapeutic agents such as oxaliplatin, irinotecan, 5FU, methotrexate, mitomycin c, and xeloda which can lead to liver toxicity.
- Cancer cells can block the lymphatic system. The lymphatic system is a network of fine channels which run throughout the body. One of its functions is to drain off excess fluid, which is eventually cleared in the urine. If some of these lymphatic channels are blocked, the system cannot drain efficiently and fluid can build up.
- The accumulation of fluid in the abdominal cavity can be associated with portal hypertension, which means there is an increased blood pressure in the veins draining the liver. The higher pressure can be caused by liver damage.

Treatment/Remedy: The treatment of ascites involves slowing the build-up of the fluid and

putting a tube into the fluid to drain it, in order to relieve symptoms. This procedure is known as paracentesis. Doctors may prescribe a water tablet (diuretic) called spironolactone which can make the patient want to pass more urine than normal but will slow the build-up of the ascetic fluid. A peritoneo-venous shunt (sometimes called a LeVeen shunt) may sometimes be considered. This is a permanent shunt that has been put into the peritoneal cavity and drains the ascetic fluid directly into a large vein. Bed rest and a salt-restricted diet are usually recommended as well. Fluid restriction of 1 liter per day is advised. Some patients may require a transjugular intrahepatic portosystemic shunt, also called TIPS, which is a mesh tube that is passed through the skin of the neck and into the jugular vein and advanced into the liver, pushed into the portal vein, which drains into the liver. The shunt reduces pressure and ascites formation.

Prevention: If the condition is a result of disease progression, very little can be done if conventional therapies have been exhausted. However, the condition can be treated with the above-noted remedies.

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### **Blood Clots**

Description/Symptoms: A blood clot is a mass of thickened blood. Clotting is a mechanism used by the body to stop bleeding. A blood clot becomes harmful when it blocks an artery or vein and stops blood flow. Common signs of a blood clot that can occur in the lungs or in the legs include:

- Pain in the calf or leg muscle
- Swelling
- Tenderness
- Discoloration
- Prominent veins
- Coughing up blood
- Shortness of breath
- Chest pain

Less common symptoms may include pain in the back, shoulder or upper abdomen; dizziness; fainting; painful respiration; new onset of wheezing; and any new heart arrhythmia.

Cause: At the beginning of treatment, a large abdominal tumor (as can be found in the liver) may shrink rapidly in response to colorectal cancer therapy, and may dislodge a pre-existing blood clot. Blood clots also may form around a central catheter at any time during treatment.

Anti-clotting agents are affected by poor diet and liver malfunction, which may be common problems in colorectal cancer patients, thereby producing blood clots. Colorectal cancer drugs such as avastin, can cause the creation of blood clots in the body.

Remedy/Treatment: If blood clots are diagnosed or you are considered to be at risk of forming blood clots, anti-coagulant drugs that prevent clotting will be administered. A commonly used anti-coagulant drug is **warfarin**, which is administered as an oral agent. **Heparin** is another anti-coagulant drug. It is administered intravenously or subcutaneously and immediately blocks the clotting process.

Prevention: If blood clots are diagnosed or you are considered to be at risk of forming blood clots, drugs that prevent clotting, referred to as anti-coagulants, may be administered to decrease your risk of forming blood clots. Common anti-coagulant drugs include warfarin and heparin.

## Bone Pain

Description/Symptoms: Bone pain may be hard to differentiate from ordinary low back pain or arthritis. Usually the pain due to bone metastasis is fairly constant, even at night. It can be worse in different positions, such as standing, which may compress the cancer in a weight bearing bone. Bone metastases generally occur in the central parts of the skeleton, although they may be found anywhere in the skeletal system. Common sites for bone metastases are the back, pelvis, upper leg, ribs, upper arm, and skull. More than 90% of all bone metastases are found in these locations.

Cause: A cause of bone pain may be due to metastatic colorectal cancer. The spread of cancer from the colorectum to another location in the body is called metastasis. Though bone metastasis arising from colorectal cancer is rare, it has been known to occur. Bone metastasis usually occurs by way of the bloodstream. A cancer cell may break away from the original location in the body and travel in the circulatory system until it gets lodged in a small capillary network in bone tissue. Cancer may also spread to bone by erosion from the adjacent cancer, though this occurs less frequently than spread by the bloodstream. The pain occurs with bone mets because the cancer disrupts the balance of normal cellular activity in the bones, causing damage to the bone tissue. Normal bone is constantly being remodeled, or broken down and rebuilt. Cancer cells that have spread to the bone disrupt this balance between the activity of osteoclasts (cells that break down bone) and osteoblasts (cells that build bone), resulting in either weakened or excessively built-up bone. This damage can either stretch the periosteum (thick membrane that covers bone) or stimulate nerves within the bone, causing pain. Bone pain should always be reported promptly as colorectal cancer can travel to and lodge in bone, and can affect abdominal and pelvic nerves that cause pain in the spine. The colony

stimulating factor G-CSF (found in neupogen) for the treatment of neutropenia (low white blood cell count) can cause aching bones as well. Though, bone pain associated with G-CSF is temporary and has a tendency to affect approximately 30% of the patient population.

Remedy/Treatment: The goal of treatment for bone pain caused by bone metastases is to relieve the pain, treat fractures, reduce the risk of fracture, and prevent or delay additional bone complications. Treatment options for bone metastases include pain medications, bisphosphonate drugs, radiation therapy, and/or surgery. Cancer-related bone pain can be managed with various pain medications. The severity of a patient's pain, rated on a scale of 1-10, will dictate what type of pain medication is used. Pain medications may have side effects, including sleepiness, constipation, dizziness, nausea, and vomiting. Relief from pain medications is temporary and the pain may return in a short time; thus, medications are best used at the onset of pain or at regular intervals. Bisphosphonate drugs can effectively prevent loss of bone that occurs from metastatic lesions, reduce the risk of fractures, and decrease pain. Bisphosphonate drugs work by inhibiting bone resorption, or breakdown. Bisphosphonates have been shown to prevent or delay bone destruction and related pain in clinical trials involving patients with bone metastases related to breast, prostate, lung, multiple myeloma, and renal cell cancer. There currently is no indication for bisphosphonate treatment of bone metastases arising from colorectal cancer but there is anecdotal evidence attesting to off-label use in colorectal cancer. For metastatic lesions that do not represent an immediate risk of fracture, radiation is effective for reducing bone pain and progression of the cancer. Radiation is especially useful when metastatic lesions are limited to a single area. When there is an immediate or significant risk of fracture, surgery may be necessary to stabilize the weakened bone. Metal rods, plates, screws, wires, nails, or pins may be surgically inserted to strengthen or provide structure to the bone damaged by metastasis. Ice packs may relieve bone pain caused by G-CSF and if this is not helpful, consulting the physician for a dose reduction in the G-CSF may end up helping. Bone mets are also being addressed through the use of magnetic resonance guided ultrasound or Ex-Ablate accessible in the clinical setting in Canada – a one time therapy for the treatment of bone metastases arising from colorectal cancer .

Prevention: It is difficult to prevent bone pain arising from metastatic colorectal cancer unless regular screening is pursued so that colorectal cancer can be treated early as well as prevented but remedies can be administered to alleviate the pain resulting from the metastases, as noted above. Bone pain resulting from G-CSF is also difficult to prevent but remedies are available to help treat the side effect.

## **Bowel Obstruction**

Description/Symptoms: A bowel obstruction is a mechanical or functional obstruction of the

intestines, preventing the normal transit of the products of digestion. Following surgery or radiation therapy for colon or rectal cancer, one or more bowel obstructions may develop and persist over time. Bowel obstruction is a painful, life-threatening event. The doctor should be contacted if difficult or absent bowel movements, pain, fever, or a small amount of diarrhea are in the presence of these symptoms: Cramping and belly pain that comes and goes. The pain can occur around or below the belly button, vomiting, bloating, constipation and a lack of gas, if the intestine is completely blocked, and diarrhea, if the intestine is partly blocked.

Cause: Surgery or radiation therapy may be the causative agent for bowel obstructions. Obstruction may be due to causes within the bowel lumen, within the wall of the bowel, or external to the bowel (such as compression, entrapment or volvulus). Bowel obstruction may be complicated by the following: dehydration and electrolyte abnormalities due to vomiting; respiratory compromise from pressure on the diaphragm by a distended abdomen, aspiration of vomitus; bowel ischemia, perforation from prolonged distension or pressure from a foreign body. In small bowel obstruction, the pain tends to be colicky (cramping and intermittent) in nature, with spasms lasting a few minutes. The pain tends to be central and mid-abdominal. Vomiting occurs before constipation. In large bowel obstruction, the pain is felt lower in the abdomen and the spasms last longer. Constipation occurs earlier and vomiting may be less prominent. Right sided obstruction of the large bowel may present as small bowel obstruction. Tumors, scar tissue (adhesions), or twisting or narrowing of the intestines can cause a bowel obstruction. These are called mechanical obstructions. In the small intestine, scar tissue is most often the cause. Other causes include hernias and Crohn's disease, which can twist or narrow the intestine, and cancer, which can cause tumors. A blockage also can happen if one part of the intestine folds like a telescope into another part, which is called intussusception. In the large intestine, cancer is most often the cause. Other causes are severe constipation from a hard mass of stool and twisting or narrowing of the intestine caused by diverticulitis or inflammatory bowel disease. Colorectal cancer drugs can also cause bowel obstructions which tend to worsen over time. Drugs such as irinotecan, oxaliplatin, 5FU, xeloda and mitomycin c.

Remedy/Treatment: Most bowel obstructions are treated in the hospital. A partial blockage may go away on its own, or you may need treatments that don't require surgery (nonsurgical treatments). These treatments include using liquids or air (enemas), small mesh tubes (stents), or medicine to open the blockage. You will stay in the hospital while waiting to see if the blockage goes away. If these treatments don't work, you'll need surgery to remove the blockage. Surgery is almost always needed when the intestine is completely blocked or when the blood supply is cut off and is often done laparoscopically. This means that the surgeon uses a lighted scope and tools inserted through a few small cuts rather than making a large cut. If your blockage was caused by another health problem, such as diverticulitis, the blockage may come back if you don't treat that health problem.

Prevention: You may be able to reduce your risk of drug-induced bowel obstruction by modifying your diet and lifestyle, wherein you are consuming a diet high in fiber. To help

prevent colorectal cancer recurrence, eat a balanced diet low in fat with plenty of vegetables and fruits. To help prevent hernias, avoid heavy lifting, which increases pressure inside the abdomen and may force a section of intestine to protrude through a vulnerable area of your abdominal wall. If you develop an abnormal lump under the skin of your abdomen, especially near your groin or near a surgical scar, contact the doctor. There is no proven way to prevent obstruction caused by diverticular disease, but some doctors believe that people with diverticular disease should follow a high-fiber diet and avoid foods that may become lodged in the diverticula, such as seeds and popcorn.

## Breathing Problems

Description/Symptoms: Lung damage is a side effect of some cancer treatments. This damage may include inflammation, which reduces the amount of oxygen you can absorb, and/or scarring, which reduces the amount of air you can breathe. Both of these result in uncomfortable symptoms, including shortness of breath and fatigue. Symptoms that you may experience if you have damage to your lungs are breathlessness during exercise, fatigue, dry cough, shortness of breath, discomfort or worsening symptoms when lying on your back. Treatment for lung damage is primarily aimed at relieving symptoms.

Causes: Many treatments for colorectal cancer that affect the heart can cause difficulty breathing. And chemotherapies such as oxaliplatin, xeloda, irinotecan, 5FU, mitomycin c, methotrexate, and radiation therapy may both all cause lung toxicity. Biological therapies such as erbitux, vectibix and avastin may also cause difficulty breathing. One of the ways that radiation and chemotherapy drugs damage cells is by forming free radicals. Free radicals are unstable molecules which are formed during many normal cellular processes that involve oxygen, such as burning fuel for energy. They are also formed from exposure to elements in the environment, like tobacco smoke, radiation and chemotherapy drugs. The free radical damage from radiation and chemotherapy is worse in the lungs because of the high concentration of oxygen.

Remedy/Treatment: While there is no specific treatment to reverse lung damage, physicians may prescribe medications or therapies to help manage the symptoms of lung toxicity; therapies such as corticosteroids, oxygen therapy, narcotics, and pulmonary rehabilitation. And there are things you can do everyday to help manage the symptoms of lung toxicity:

- Try relaxation techniques to control your breathing, such as meditation, yoga, or deep breathing exercises.
- Promote oxygenation (air circulation) throughout your lungs, especially the bottom, to prevent infection and pneumonia. This can be done with breathing exercises or physical activity.

- Use an incentive spirometer, a device that makes you breathe slowly and deeply, to maintain oxygenation.
- Find a kind of exercise that you can tolerate and do it daily.
- Avoid smoking and smoke-filled environments. Smoking or second-hand smoke can further damage your lungs.
- Reduce anxiety and manage stress.

Prevention: It may be difficult to avoid lung damage that is the result of colorectal cancer therapies but every effort should be made to recognize the symptoms so that remedies may be administered as quickly as possible.

## **Bruising and Bleeding**

Description/Symptoms: Bleeding is loss of blood outside the body or into a body cavity. A bruise, also called a hematoma, is bleeding into the skin from damaged blood vessels, causing a black and blue appearance. The following are indications that you may have a problem with bleeding or bruising:

- You bleed excessively and even a small cut bleeds for a long time.
- You have excessive bruising, including many purplish spots under the skin even when you haven't had an injury.
- You may have frequent nose bleeds.

Causes: Bruising and bleeding are usually caused by some kind of trauma or injury. However, certain underlying conditions may cause you to bruise or bleed more easily than normal. The most common reason for this in colorectal cancer patients is a low platelet count, a condition also referred to as thrombocytopenia. Platelets, also called thrombocytes, are fragments of blood cells which are found in the circulating blood and are critical for stopping bleeding. Platelets plug the small holes that form in blood vessels daily and work with other blood factors to form a blood clot, which stops bleeding in larger blood vessel injuries. Also, if chemotherapy is administered directly to the liver via portable infusion pump, then the result may be gastrointestinal bleeding, which should be reported to the doctor immediately. Drugs that tend to cause thrombocytopenia are avastin, erbitux, vectibix, irinotecan, oxaliplatin, xeloda, 5FU, mitomycin c, and methotrexate.

Remedy/Treatment: If the bruising and bleeding is determined to be a consequence of a low platelet count, the doctor may prescribe a blood cell growth factor. Blood cell growth factors are substances produced by the body to stimulate the bone marrow to produce more platelets. Examples of blood cell growth factors are Neumega approved by the FDA in the US. If you have a severely low platelet count, you may require treatment with platelet transfusions and

occasionally, admission to the hospital until the platelets return to sufficient levels in the blood to prevent bleeding.

Prevention: It is difficult to prevent chemo-induced thrombocytopenia but physicians in the US have noticed that the administration of neumegea has been somewhat successful at preventing the condition.

## C/

### **Cognitive Changes/Forgetfulness**

Description/Symptoms: Chemotherapy has been associated with causing cognitive deficits, such as forgetfulness and an inability to concentrate. Cognitive deficits are problems with thinking, learning and memory. If you have cognitive deficits, you may be forgetful or have difficulty concentrating.

Causes: Research has demonstrated that chemotherapies such as those administered in the treatment of colorectal cancer can have a negative impact on cognitive functioning. The patients who receive chemotherapy report greater problems with working memory. Furthermore, some survivors may experience long-term cognitive deficits associated with systemic chemotherapy. The way in which chemotherapy causes cognitive deficits is not clear at this time. It may be related to anemia or a direct effect of chemotherapy on brain function. Problems with memory and concentration may improve once chemotherapy is complete; but there is also a possibility that these will be long-term problems. Those colorectal cancer drugs reported to cause cognitive changes are: xeloda, 5FU, oxaliplatin, irinotecan, mitomycin c, methotrexate, erbitux, vectibix and avastin.

Treatment/Remedy: At this time, there are no proven treatments for cognitive deficits associated with colorectal cancer chemotherapies. However, research is ongoing to find a treatment that may help relieve this side effect. Some researchers have suggested that the herbs *Ginkgo biloba* and ginseng can improve cognition and mood and the North Central Cancer Treatment Group (NCCTG) is conducting a randomized placebo-controlled trial testing the effects of *Ginkgo biloba* on cognitive function in patients with early-stage breast cancer receiving adjuvant chemotherapy.

Prevention: Prevention is difficult. However, the best way to deal with this unpleasant side effect of chemotherapy is to take steps to minimize the impact of forgetfulness and difficulty concentrating on your daily life.

## Constipation

**Description/Symptoms:** Constipation is difficulty passing stools or a decrease in number of stools. It may be accompanied by gas, abdominal cramping or pressure in the lower abdomen. Constipation may lead to stool impaction, a severe form of constipation where the stool will no longer pass through the colon or rectum. Some symptoms of constipation include:

- A sustained change in frequency of bowel movements from your normal.
- Hard, difficult to pass bowel movements. You may pass small, marble-like pieces of stool without a satisfactory elimination.
- Cramping and/or flatulence (gas).

**Causes:** Constipation is caused by a slowing of the intestinal activity. The normal wave-like action of the intestines, called peristalsis, serves to continually move stools out of the body. When peristalsis slows, the stools become hard, dry and difficult to pass. Constipation can have a number of causes including: tumour regrowth; pain medications; antidepressants; antihistamines; chemotherapy drugs such as irinotecan, xeloda, 5FU; biological therapies such as avastin, erbitux, and vectibix; decreased activity; poor diet; and inadequate fluid intake. Chemotherapy drugs can cause either an increase or decrease in peristalsis. An increase in intestinal activity may cause stools to travel faster and be less formed, resulting in cramping and/or diarrhea. A decrease in intestinal activity may cause stool to travel slower, becoming hard and dry and more difficult to pass, thereby resulting in constipation.

**Remedy/Treatment:** The doctor may prescribe laxatives for the treatment of chemotherapy-induced constipation. Laxatives are available in liquid, tablet, gum, powder and granule forms. There are several different kinds that work in different ways. Laxatives should only be used for a short period of time to retrain the bowel to pass stools naturally. If used continually, you may become dependent on laxatives. In most people, slowly stopping use of the medication will restore the colon's natural ability to contract. For constipation caused by opioid pain medications (such as morphine, codeine, oxycodone, and fentanyl), laxative use often continues for as long as the patient is taking the pain medication.

**Prevention:** For patients who develop constipation because of opioid pain medications, an agent is available for the treatment of the condition. Relistor, developed in the US, acts by blocking the activity of opioids in the gastrointestinal tract without blocking the pain-relieving effects of opioids in the central nervous system thereby preventing the onset of constipation. Not surprisingly, it is easier to prevent constipation with lifestyle changes than to treat it once it happens. Here are some recommendations to help in the prevention of constipation you may wish to discuss with your treating physician:

- Increased fluid intake (6-8 glasses of fluid daily)
- Regular exercise
- Increased dietary fiber (fruits, vegetables and beans stimulate the movement of the intestine)
- Warm or hot drinks
- Privacy and quiet time in the bathroom
- Easy access to toilet or bedside commode
- Stool softeners
- Avoid cheese, meat, processed food and other low fiber foods

***D/***

## **Dehydration**

**Description/Symptoms:** Cancer patients must have adequate fluid to remove toxins from the body as well as proteins released by dying cells. The lack of appropriate fluid in the body is referred to as dehydration. Quantities of electrolytes and minerals such as phosphorus, calcium, potassium, magnesium and sodium may be disrupted in the colorectal cancer patients, both by disease and by treatment. Dehydration exacerbates this imbalance. The most reliable symptom of dehydration is thirst. Other signs include the inability to urinate about once an hour, the production of very little urine, or the production of urine that is both dark and low in volume. Other symptoms, such as faintness, dry lips, thick saliva, or loss of appetite resemble the side effects of some chemotherapies too closely to be reliable indicators of dehydration.

**Cause:** Colorectal cancer therapies such methotrexate, irinotecan, oxaliplatin, mitomycin c, 5FU, and xeloda can cause dehydration. Also, dehydration is a very serious side effect resulting from vomiting or excessive diarrhea brought on by the aforementioned drugs.

**Remedy/Treatment:** Physicians recommend taking in as much fluid as possible, but do not drink products containing electrolytes (such as the products marketed for sports enthusiasts) unless instructed to do so by a physician who has determined that that your kidneys are in good condition and therefore able to address excess electrolytes. Severe dehydration may be addressed with the administration of hydration therapy through intravenous in the hospital setting. Hydration therapy can reverse the onset of dehydration by supplying the body with the much-needed fluids it requires as well as restoring electrolyte balance.

**Prevention:** Dehydration may be prevented by ingesting regular amounts of fluids on a daily basis.

## Depression

Description/Symptoms: Depression is a persistent sadness that interferes with your ability to complete daily activities. The symptoms of major depression include:

- Depressed mood for most of the day and on most days
- Nervousness or sluggishness
- Feelings of worthlessness
- Changes in eating and sleeping habits
- Guilt
- Loss of pleasure and interest in most activities
- Poor concentration
- Tiredness
- Constant thoughts of death or suicide
- Feeling dissatisfied

For colorectal cancer patients, the most common symptoms of depression are:

- Guilt
- Worthlessness
- Hopelessness
- Thoughts of suicide
- Loss of pleasure

If you exhibit these symptoms for at least 2 weeks, you may be diagnosed with depression. However, it is sometimes difficult to separate the symptoms of depression from the side effects of treatment or the symptoms of the cancer itself.

Cause: While the actual causes of depression in cancer patients are not known, there are a variety of factors that can increase your likelihood of becoming depressed. These may include:

- Physical condition
  - Poorly controlled pain
  - An advanced stage of cancer
  - Increased physical impairment or pain
- History
  - Personal history of depression or attempted suicide
  - Family history of depression or suicide

- History of alcoholism or drug abuse
- Lack of family support
- Other life events that produce stress
- Pessimistic personality

Medications commonly prescribed for management of your cancer may have depression as a side effect, such as:

- Colorectal Cancer Chemotherapy drugs (ie. irinotecan, oxaliplatin, xeloda, 5FU and mitomycin c)
- Steroids (ie decadron)

Treatment/Remedy: Depression is most often treated with a combination of counseling and anti-depressant drugs. Medication is often used to ease symptoms so that other therapies can continue. **Anti-depressant drugs** (such as Effexor, Prozac, Zoloft, Paxil, Amytriptyline, Imipramine, and nortriptyline) take 3 to 6 weeks to begin working and may be associated with some side effects. Even after you feel better, your doctor may recommend that you continue to take the medication for 6-9 months. **Counseling** also known as “talk therapy”, can be an effective treatment for depression. There are several approaches to psychotherapy that have been used to relieve symptoms of depression. These involve working with a trained therapist to identify the thoughts or behaviors that are contributing to the depression and figure out ways to solve these problems and cope with depression. In general, psychotherapy takes weeks to months to complete. Ensure you are getting enough sleep and try to exercise daily. Being well rested will help you cope with difficult events and emotions. Exercise increases the release of natural chemicals in your body called endorphins, which promote a feeling of well-being. A daily exercise program can be as simple as 20-30 minutes of walking. Also, **cancer support groups** may be helpful in treating depression. Support groups have been shown to improve mood, encourage the development of coping skills, improve quality of life and improve immune response. **Support groups** affiliated with Colorectal Cancer Canada can be found on the website at [www.colorectal-cancer.ca](http://www.colorectal-cancer.ca) under the heading “Support”. The **Cancer Coach Program** may also be accessed under the same heading. You may also wish to try **relaxation techniques** to help you cope with your depression, such as:

- Meditation
- Yoga
- Deep breathing

Prevention: Treatment-induced depression may be difficult to prevent as might be the depression resulting from the cancer, but remedies are available upon request so that patients do not need to suffer alone or in perpetuity.

## Diarrhea

Description/Symptoms: Diarrhea is defined as loose or watery stools lasting for more than one day and occurring more frequently than normal. It is not only an inconvenient side effect of cancer treatment, but also can be life-threatening if not adequately managed. It may lead to dehydration; electrolyte imbalance; low immune function; malnutrition due to reduced absorption of nutrients; and inflammation, pain and/or bleeding because of the increased frequency of bowel movements. Diarrhea can be severe enough such that you are unable to tolerate your prescribed chemotherapy treatments. Commonly, chemotherapy treatments are delayed if diarrhea persists. A disruption or delay in treatment may diminish the effect of therapy.

Causes: Removal of most or all of the large intestine frequently results in diarrhea as does radiotherapy targeting the abdomen. Chemotherapy also causes diarrhea, as dying cells are shed from the intestine. Administration of the drug CPT-11 or irinotecan can cause immediate diarrhea in some people. Chemotherapy damages rapidly dividing cells. Cancer cells tend to divide rapidly and uncontrollably. However, some healthy cells also divide rapidly, such as those that line the interior of the digestive tract. Chemotherapy also damages these cells, leading to a disruption in the delicate fluid balance that they maintain. Specifically, absorption of fluid from the gastrointestinal (GI) tract back into the body is decreased and secretion of fluid and electrolytes in the stool is increased. This causes watery bowel movements which, as stipulated above, are the definition of diarrhea. Other colorectal cancer therapies such as xeloda, oxaliplatin, 5FU, mitomycin c, leucovorin, erbitux, vectibix, floxuridine, methotrexate and avastin may also cause the unwanted side effect. Some factors may make chemotherapy-related diarrhea worse. For example, damage to the intestines because of surgery or radiation may make the GI system more susceptible to irritation. Other medications, such as antibiotics, diabetes, irritable bowel syndrome, reduced pancreas function or other conditions, may also worsen diarrhea. If you have certain biochemical characteristics, you may be more sensitive to chemotherapy drugs.

Treatment/Remedy: Physicians can recommend anti-diarrheal drugs such as Imodium, which must be balanced carefully with drugs such as stool softeners to control constipation. Therefore, experimenting with small amounts of different foods until you have a sense for what will maintain a balance between constipation and diarrhea is recommended. Foods that irritate the GI system should be avoided, such as greasy, spicy or fried foods. You should also avoid milk and milk products because diarrhea may lead to a loss of the enzyme lactase which breaks down lactose, the sugar found in milk, resulting in temporary lactose-intolerance. Because of their high fiber content, vegetables tend to be difficult to digest and should be avoided during episodes of diarrhea. Cruciferous vegetables, such as cabbage, brussel sprouts and broccoli can be particularly problematic. Your diet should be limited to simple, easy to digest foods, and then expanded as the diarrhea begins to subside. A diet consisting of bananas, rice, applesauce, toast (called the BRAT diet) and clear liquids is a good starting

point. Eventually, pasta without sauce, white-meat chicken without skin, scrambled eggs and other easily digested foods can be added, as tolerated. Staying hydrated is very important in the management of diarrhea. You must consume enough clear liquids to make up for the volume of fluids lost due to the diarrhea. This amount is in addition to the usual daily intake. You may need to take in 3-4 liters or more of fluid per day. In addition to plain water, you should include fluids that contain some sugar and salt, such as broth. Replacement of fluids with plain water alone can lead to low levels of salt or calcium in the blood. These can be life-threatening conditions. If severe diarrhea results after therapy, inform your physician who will be able to prescribe tablets to take with your next cycle of chemotherapy which will slow down the churning of your digestive tract and so help reduce the diarrhea. Inquire about soothing creams to apply around the anus which can become very sore and even broken with severe diarrhea.

Prevention: It may be difficult to prevent the onset of chemo-induced diarrhea but following the physician's advice once diarrhea does come on is crucial to the management and reduction of the unpleasant side effect. Adhering to a special diet (BRAT Diet) may actually safeguard against the onset of the unwanted side effect.

## Dry Mouth

Description/Symptoms: Colorectal cancer therapies can at times cause dry mouth. Saliva is necessary for taste, swallowing and speech. Therefore, a dry mouth can significantly impact daily activities and quality of life. Dry mouth treatment consists of symptomatic relief through stimulation of salivary flow, oral aids to decrease discomfort or intervention with medications. Symptoms of a dry mouth are:

- A small amount of thick or stringy saliva
- A sore or burning feeling (especially on the tongue)
- Changes in the surface of the tongue
- Taste changes
- Cracked lips
- Cuts or cracks at the corners of the mouth
- Changes in your ability to articulate or speak clearly
- Difficulty wearing dentures

In addition to aiding in taste, swallowing and speech, saliva is also important for protecting your teeth against tooth decay. Eating sugary foods leaves acid in your mouth, which causes minerals to be lost from your teeth, leading to tooth decay. Saliva protects your teeth by neutralizing this acid. Because saliva is a lubricant, it also acts to protect the cells that line your mouth. Without enough lubricant, the lining of your mouth becomes more susceptible to

damage. Simply brushing your teeth or eating certain foods can damage the lining of your mouth. Once you get a small cut, it may not heal normally and can develop into a mouth sore that can be very uncomfortable and may make it difficult to eat.

Causes: Mouth sores are a side effect of many chemotherapy drugs, and this condition is sometimes called mucositis. Once you have mouth sores, you may also develop symptoms of a dry mouth. Most chemotherapy drugs can cause mouth sores, but this side effect is more frequent in patients who have been treated with the following chemotherapy agents: Irinotecan, 5FU, methotrexate, xeloda and mitomycin c.

Treatment/Remedy: Treatment for a dry mouth is aimed at either relieving symptoms or preventing the damage before it happens. Your doctor may recommend oral aids to relieve dry mouth symptoms such as sipping water, gargling with a salt and soda mouthwash, and artificial saliva spray. The drug pilocarpine stimulates salivary flow from the minor salivary glands that are known to be rich in mucin, a component of saliva that acts as a lubricant and protects the lining of the mouth and throat. Pilocarpine appears to be moderately effective in relieving symptoms of a dry mouth and is currently being developed in the U.S.

Prevention: Symptomatic relief from dry mouth can be achieved by sucking ice chips when the chemotherapy drug is most concentrated in the body. This technique, called cryotherapy, works by decreasing blood flow to the cells in the mouth, reducing exposure to the drug and decreasing the risk of developing mouth sores and therefore dry mouth. If you are suffering from a dry mouth, it is very important to maintain good oral hygiene in order to prevent infection or tooth decay. Try to maintain the following:

- Gently brush your teeth 2-3 times per day. Use a soft bristle brush and warm water to avoid damaging your gums.
- Rinse 4-6 times per day with a solution of salt and baking soda. Avoid mouthwashes that contain alcohol.
- Avoid foods and liquids that contain a lot of sugar. Having a dry mouth increases your susceptibility to cavities and sugar causes tooth decay.

Also, the following suggestions have proven helpful in the prevention of dry mouth:

- Drink plenty of water.
- Eat moist foods with extra sauces, gravies, butter or margarine.
- Suck on hard candy or try chewing gum.
- Eat frozen desserts (such as frozen grapes and ice pops) or ice chips.
- Use a straw to drink liquids.

**E/**

## **Early Satiety (Appetite or Taste Changes)**

Description/Symptoms: Early satiety is the feeling of being full after you have only eaten a small amount, perhaps only a few bites. This condition may also be described as having a poor appetite.

Cause: Early satiety as well as taste changes are common side effects resulting from chemotherapies such as 5FU, Xeloda, Irinotecan, Mitomycin C, Methotrexate, biologics such as avastin as well as radiotherapy, but may also be a complication of the cancer itself. Chemotherapy and radiotherapy can affect the taste buds to the extent that food can no longer be tasted, or that it tastes metallic or even unpalatable.

Remedy/Treatment: Early satiety may be treated with nutritional support or appetite stimulants. Since early satiety can compromise your ability to get adequate nutrition through food sources, you may benefit from treatment with nutritional support. All cancer patients should meet with a nutritionist or registered dietician prior to and throughout their treatment to help maintain their health through appropriate alterations to their diet. The nutritionist may recommend that you focus on eating higher calorie foods, such as protein-rich foods which include the following:

- Protein drinks (powdered protein supplement mixed with fruit, milk and/or yogurt)
- Milk
- Dairy products
- Eggs
- Meat
- Sauces or gravies
- Oil

In some situations, caloric supplementation is required which may be administered into the veins through Parenteral Nutrition, or directly into the intestines with enteral nutrition. Appetite stimulants may help you to maintain adequate calorie and nutrient intake from food sources. These include Marinol, megestrol acetate and dexamethasone. The doctor may also recommend vitamin supplements and liquid supplements such as Ensure to provide the much needed nutritional benefits during and after therapy.

Prevention: Prevention of therapy-induced early satiety may be difficult but adhering to the recommendations of the doctor is important in helping to avoid food aversion. Also, adhering to a well balanced high calorie diet before beginning therapy can help in diminishing this unwanted side effect during therapy.

## Extravasation

Description/Symptoms: Sometimes, chemotherapy that is administered by IV or catheter can leak out of the vein into surrounding tissue, an adverse event called extravasation. The reaction of the body to a high concentration of chemotherapy in the skin or other tissue can be serious and painful. The artery or vein may be unusable for chemotherapy thereafter; the skin may die, slough off, and fail to regrow. Symptoms of extravasation include pain, redness, swelling or burning at the IV or catheter site, during or after the administration of chemotherapy. The medical staff should be notified immediately if these symptoms are experienced during or just after treatment.

Cause: Extravasation injuries are a potentially serious consequence of all types of intravenous therapy. Factors that can increase your risk of having extravasation include:

- your age and medical condition - elderly people and most cancer patients have very fragile veins
- repeated injections - having repeated intravenous therapy can damage your veins and reduce the number of optimal injection sites if a central line is not established
- type and concentration of fluid – chemotherapeutic agents tend to weaken the veins (this includes all colorectal cancer agents)
- cannula site - certain areas of the body such as the hand, foot and joint spaces are more prone to injury because they have little protection

Remedy/Treatment: Extravasation injuries must be treated as quickly as possible to prevent serious tissue damage. If extravasation is suspected, the drip is stopped and the area is immediately flushed with hyaluronidase and saline (salt water). This is done to remove as much of the leakage as possible from the area. Corticosteroids, painkillers and antihistamines may be used to treat symptoms such as inflammation, pain and stinging. You may be given an antidote if it's available for the type of drug you are having. You may also have hot and cold compresses placed on the area three or four times during the day. If treatment is delayed it can lead to permanent tissue damage and may require surgery to remove the damaged tissue and clean the area. Sometimes a skin graft is required.

Prevention: The following steps are usually taken by medical staff to reduce the risk of extravasation:

- Medicines likely to cause extravasation are usually given through a central line or drum catheter (port).
- The fluid is passed into your bloodstream very slowly.
- Injection area is checked at regular intervals.

- Patients are asked to report any feelings of pain or burning immediately.
- For repeat intravenous therapy the injection site is regularly changed unless a central line is established.

## Eye Changes

Description/Symptoms: Some colorectal cancer treatments may cause problems with your eyes, such as **conjunctivitis** (also known as pink eye resulting from a suppressed immune system), **cataracts** (cloudy area in the lens of the eye that prevents light from passing through), **dry eyes** (results from the lack of production of tears), **photophobia** (sensitivity to light causing eye pain when moving from a dark space to a light one), and watery eyes (the production of too many tears).

Cause: Colorectal cancer drugs that may cause eye problems are listed in the following table.

Eye problem	Drug(s)
<b>Conjunctivitis</b>	capecitabine (Xeloda) methotrexate oprelvekin (Neumega)
<b>Cataracts</b>	Dexamethasone (decadron) hydrocortisone methylprednisone prednisone
<b>Dry eyes</b>	5FU (fluorouracil)
<b>Photophobia</b>	Fluorouracil (5FU)
<b>Watery eyes</b>	capecitabine (Xeloda) fluorouracil (5FU) Irinotecan (Camptosar or CPT-11)

Treatment/Remedy: How your eye problems are treated depends on your diagnosis and how severe your condition is. Medicine for eye problems is often administered in eye drops. If the

drops do not remedy the situation, an ophthalmologist who is a lacrimal (tear) specialist may be consulted. If you have symptoms of eye problems, notify your doctor immediately.

Prevention: It is difficult to predict which patients will respond to therapy with eye problems, therefore, prevention of chemo-induced eye problems is also difficult. Symptoms of eye problems should not be ignored; notify your doctor immediately if you have cloudy/blurred vision, sensitivity to light, severe eye pain or a sudden loss of vision so as to prevent further advancement of the condition.

## **F/**

### **Fatigue (Tiredness)**

Description/Symptoms: Fatigue is a general tiredness or an overwhelming lack of energy. It may be associated with an increasing need for rest, an inability to regain energy with rest, difficulty concentrating, or a disinterest in activities or events. 95% of those being treated for colorectal cancer report fatigue as a major side effect of therapy. Compared with symptoms such as nausea or pain, fatigue can be very difficult to identify and discuss. Sensations such as weakness, dizziness, difficulty thinking, being worn out, drained, and tiredness may be part of the feeling. Other symptoms associated with fatigue are leg pain, difficulty climbing stairs or walking short distances, and shortness of breath after light activity. People sometimes think they are just being lazy or depressed. They may tell themselves, "I can snap out of this if I really try." Sudden changes in feelings of fatigue may mean there is a serious problem. Slower, gradual development of fatigue may lead to a decreased ability to perform everyday activities. There are no medical tests to measure fatigue; however, fatigue can be treated in many circumstances. Patients experiencing fatigue should report this feeling to their nurse or physician in order to determine whether a treatable cause of fatigue exists and to develop a strategy to reduce the amount of fatigue. Symptoms usually start out mild and become progressively worse such that you are unable to perform everyday activities.

Cause: The reasons that colorectal cancer patients experience fatigue are many and complex. In fact, fatigue often results from more than one cause and may require the use of many strategies for effective treatment. Generally, however, patients treated by surgery, radiation or chemotherapies experience such side effects as fatigue as a consequence of the therapy itself. All of the following can contribute to fatigue by decreasing the body's ability to produce energy or by consuming the limited energy produced. **Anemia** is an inadequate supply of red blood cells, resulting in a decrease in the oxygen-carrying capacity of the blood. A common reason that colorectal cancer patients experience anemia is as a side effect of systemic therapies (**irinotecan, oxaliplatin, methotrexate, 5FU, xeloda, mitomycin c, avastin,**

**erbitux, and vectibix**). Anemia is important because it may cause unwanted symptoms, such as fatigue, tiredness or shortness of breath, and may exacerbate or cause other medical problems, such as a heart condition. The presence of **infections** in the body utilizes extra energy to fight the infection which can contribute to fatigue. Many drugs, including those used for the treatment of nausea (**antiemetics**), pain (**analgesics**), anxiety (**anti-depressants**), and other conditions, can cause fatigue as a side effect. Cancer or cancer treatments may also cause you to lose your appetite, or feel full early (early satiety). **Insufficient intake of calories** and vitamins reduces the body's ability to produce energy and may cause anemia. **Bed rest** or even restriction of activity for 1 or 2 days can decrease the body's ability to produce energy. Researchers have not identified how much rest is required for recovery versus how much rest contributes to low energy production. However, it appears that extended rest may contribute to fatigue and modest amounts of activity and movement can improve fatigue. Pain, anxiety, or depression can cause **stress** or result in sleep deprivation, causing increased fatigue.

Treatment/Remedy: Because fatigue can have so many causes, - nutritional deficit, colorectal cancer drugs, drug interactions, tumor activity, tumor death, inability to exercise, depression, changed sleep patterns – it is difficult to treat fatigue with other than trial-and-error methods. Fatigue has so many different causes and patterns that it may require the use of many strategies for effective treatment. For these reasons, it is important that you discuss your symptoms with your nurse or physician in order to devise an individual plan that will work. While there are no standard medical treatments for fatigue, new tools exist for evaluating and coping with fatigue. The following suggestions may also help you to cope with fatigue and have more energy:

- **Anemia** is the most common cause of fatigue in cancer patients. It is also very treatable. Treatment of anemia may involve the use of red blood cell boosters such as Procrit or Aranesp, a longer-acting form of erythropoietin that allows patients to receive fewer injections but these agents have been reported to promote cancer progression. Patients should discuss the risks and benefits of treatment with a red blood cell booster or blood transfusion with their doctor.
- Maintaining good **nutritional intake** with vitamin/mineral supplementation during treatment is especially important because cancer treatments increase the nutritional demands of the body. However, treatments may also cause you to lose your appetite, or feel full early (early satiety). Work with a dietician or nutritional specialist to ensure that you are getting proper nutrition. Conserve your energy by being realistic about how much energy you have and what you can and can't do. Only do the things that are most important and ask friends or family for help. It is important to recognize which activities create the most fatigue and also note the frequency, degree, and duration of fatigue so that you can report these to your doctor. If you're having difficulty managing fatigue, you may wish to ask your nurse or doctor to help family members understand how they can help.
- Maintaining normal **rest and sleep patterns** is important for ensuring quality rest. Plan

your daily activities carefully, and schedule rest times between activities throughout your day. Try to rest when you feel the worst and do your activities when you feel better.

- Review your **medications** with your doctor, pharmacist, or nurse to ensure that the medications are not causing or contributing to your symptoms. While conserving energy is important, it is equally important to understand that too much rest or inactivity can actually decrease the body's ability to produce energy and can worsen fatigue.
- Moderate **daily exercise**, such as walking, may help to increase your energy level.
- Counseling, support services, and medications can all play a role in **reducing stress** and thereby alleviating fatigue. The literature shows that even psychological counseling can help to alleviate fatigue.

A web site staffed by oncology nurses for cancer survivors suffering from post-treatment fatigue can be found at [www.cancerfatigue.org](http://www.cancerfatigue.org) . A discussion group for those suffering from cancer fatigue exists on the internet as well. Visit [www.acor.org](http://www.acor.org) to enroll in the cancer-fatigue discussion group. Support Groups affiliated with Colorectal Cancer Canada may be accessed at [www.colorectal-cancer.ca/en/find-support/colorectal-groups/#](http://www.colorectal-cancer.ca/en/find-support/colorectal-groups/#)

Prevention: It may be difficult to prevent the onset of fatigue brought on by colorectal cancer therapies, but the management may be more easily achievable than patients believe by adhering to the recommendations above.

## Feeling Faint/Dizziness/Lightheadedness

Description/Symptoms: Dizziness is a sensation often described as lightheadedness or feeling woozy. Most people notice dizziness when they change positions or move their heads. You might feel like the room is spinning around you, or that you are spinning, a sensation known as vertigo. You may also feel "faint" or dizzy when you rapidly change from lying or sitting to a standing position. As a colorectal cancer patient, dizziness may be a fleeting sensation or the prolonged symptom of a more serious health problem brought on by colorectal cancer treatments.

Cause: There are many possible causes for dizziness resulting from colorectal cancer therapies and some are:

- Nausea and vomiting produced from the colorectal cancer therapies such as irinotecan, oxaliplatin, 5FU, Xeloda, methotrexate, mitomycin c, erbitux, avastin and vectibix
- Anemia
- Dehydration
- Medications to control high blood pressure or heart rate
- Problems with the balance mechanism in your inner ear

- Low blood pressure when you stand up (orthostatic hypotension)

Most of the colorectal cancer therapies administered systemically can cause dizziness and the feeling of fainting.

Treatment/Remedy: Some medications may help to decrease the feelings of unsteadiness or imbalance associated with dizziness. These medications are also known as “motion sickness” drugs. Examples include:

- Meclizine
- Dimenhydrinate
- Scopolamine patch

Prevention: The following are recommended for the prevention of dizziness:

- Stay hydrated by drinking plenty of fluids. Aim for 2-3 liters of fluid per day in the form of fruit juices, water, non-caffeinated drinks and non-alcoholic beverages.
- Change positions slowly. Allow your body a chance to adapt to the position change. For some people, lying down until the dizzy episode passes may be the best solution.
- Avoid medications that have caused dizziness in the past.

Prevention of nausea and vomiting associated with chemotherapy through the use of antiemetic drugs may also decrease feelings of dizziness. Go to the “Nausea and Vomiting” section for more information on the treatment of this side effect.

## **Fever/Infection**

Description/Symptoms: Fever is an abnormally high body temperature. The average human body temperature is 37°C (98.6°F); however, each individual person is different and normal may range from 36.0°C to 38°C. Even under normal conditions, the human body temperature varies throughout the day — it is lower in the morning and higher in the late afternoon and evening. Fever is the body’s natural response to infection. A part of the brain called the hypothalamus raises the body temperature to create an environment that is unfavorable for the bacteria or viruses that cause infectious disease. For example, the viruses that cause colds and other respiratory infections thrive at cool temperatures. One way the body works to eliminate a virus is by producing a fever. Fever can be the first symptom of life-threatening infection when white blood cells have been destroyed by therapy. Unattended fever in the absence of sufficient white blood cell numbers can be fatal, and is a medical emergency requiring immediate attention. Depending on what is causing your fever, your signs and

symptoms may include:

- Sweating
- Shivering
- Headache
- Muscle aches
- Lack of appetite
- Dehydration
- General weakness
- Burning or pain while urinating
- Neck stiffness
- Coughing
- Trouble breathing

Very high fevers, between 40°C and 42°C, may cause hallucinations, confusion, irritability and even convulsions.

Cause: For a cancer patient, fever may be a sign of a dangerous infection. An infection may be particularly serious when your white blood cell count is low or is expected to be low (leucopenia). This is because white blood cells are the body's normal defenses against infection, and when their numbers are low, the body's ability to fight infection is reduced. Additionally, many cancer patients develop a fever in which a definite source of infection cannot be identified. Fever is a side effect of some biological therapies, and may occur in patients who are receiving chemotherapy and biological therapy as part of the "flu-like syndrome". A fever associated with "flu-like syndrome" usually peaks at 40°C and often spikes after a severe chill. Those colorectal cancer systemic therapies known to cause a diminished white blood cell count and therefore the potential to develop infections resulting in fevers are: irinotecan, oxaliplatin, mitomycin c, methotrexate, 5FU, xeloda, avastin, erbitux, and vectibix. The danger period for most patients is five to ten days after treatment. In general, chemotherapy is more likely to cause leucopenia than radiotherapy, but radiotherapy is also a known cause of diminished white blood cell count.

Treatment/Remedy: Medical treatment for a fever depends on the cause. If the fever is determined to be related to an infection, treatment will be prescribed for the infection. For a bacterial infection, such as pneumonia or tonsillitis, antibiotics are usually prescribed. For viral infections, including stomach flu (gastroenteritis), the best treatment is often rest and plenty of fluids, although anti-viral drugs may be used to treat some viruses. If an infection-related fever is tolerable, then doctors may not treat the infection but monitor it closely because the fever contributes to eliminating the bacteria or virus. If a cancer patient develops a low white blood count and fever, it is assumed that an infection is present and antibiotics are then given until the fever is resolved and white blood cell count recovered. If an infection-related fever is very high, over-the-counter medications may be prescribed to reduce the fever and associated

discomfort. Non-steroidal anti-inflammatory drugs (NSAIDs), such as acetaminophen or ibuprofen, are often used for this purpose. Adults may also use aspirin to reduce a fever. If you have a bleeding disorder, you should avoid NSAIDs, as well as aspirin. These drugs may prolong bleeding by interfering with the activity of blood platelets. Use of such drugs to treat fever should be discussed first with your healthcare professional. NSAIDs or aspirin are also used if the source of the fever is related to flu-like syndrome associated with biologic therapy or certain types of chemotherapy and not infection. If an infection develops, you may be admitted to the hospital, placed in an isolation room, and given a combination of immunoglobulin therapy, antibiotics, antiviral, or antifungal agents.

Prevention: It may be difficult to prevent the onset of fevers resulting from infections that have been brought on by diminished white blood cell counts. However, diminished white blood cell counts may be prevented through the use of such agents as neupogen or neulasta. Please see the section on neutropenia. Preventive measures may also include: avoiding scratches and cuts via gentle handling of the skin, frequent hand-washing, patting skin dry rather than rubbing, thorough cooking of food, reducing human contact so as to reduce the potential of contracting an infection, and avoiding gardening and handling pet litters.

## H/

### **Hair Loss (Alopecia)**

Description/Symptoms: Radiotherapy and many chemotherapeutic agents employed in the treatment of colorectal cancer can cause hair loss – alopecia – although there is a wide range of individual responses to treatment in this regard. Some people lose just a little hair; others lose all hair, including body hair, eyebrows and eyelashes, facial hair, pubic hair, underarm hair and leg hair. Others report losing grey hair earlier than hair that contains pigment. Those receiving radiation therapies may lose hair only on the spots irradiated, such as pubic hair.

Cause: Chemotherapy damages rapidly dividing cells, such as cancer cells. Some healthy cells also divide rapidly, such as hair follicles. Chemotherapy damages these cells, leading to hair loss. Hair loss will typically begin two or three weeks after your first treatment. The amount of hair that you lose will depend on the type of chemotherapy drug you are taking. Hair typically begins to grow back approximately 2-3 weeks after treatment is finished. The hair may grow back differently than it was before treatment. For example, color or texture (curly or straight) may be different. Those colorectal cancer therapies capable of causing hair loss are: irinotecan, 5FU, mitomycin c, xeloda, methotrexate, and avastin. Conversely, Interferon sometimes used for colorectal cancer may cause excessive growth of hair.

Treatment/Remedy: New hair should regrow in the weeks or months after treatment. In some instances, it might not regrow, although this is more common after radiotherapy than after chemotherapy. Importantly and generally, you should remember that hair loss associated with

chemotherapy is temporary and the hair WILL grow back. In the meantime, here are a few suggestions to help you cope with the hair loss:

- You may wish to cut your hair before it starts falling out. The experience of losing the hair is sometimes worse than dealing with it once it's gone.
- For women, planning ahead may be helpful; shop for a wig before your hair is gone, especially if you wish to match your natural color.
- Try hats or head scarves; these are good alternatives or a compliment to a wig.
- Remember to cover your head or use sunscreen on your scalp. Skin that has been covered with hair may be particularly sensitive to UV rays of the sun.
- Ask your insurance company if they cover the cost of the wig.
- Treat your new hair gently once it grows back. Avoid chemicals, bleach, peroxide or colors.
- Get involved in a "Look Good... Feel Better" program, a community-based, free, national service that teaches female cancer patients beauty techniques to help restore their appearance and self-image during chemotherapy and radiation treatments. For more information go to [www.lookgoodfeelbetter.org](http://www.lookgoodfeelbetter.org).

Methods to spare the scalp from exposure to chemotherapeutic agents, such as ice-packing or tourniquets are not recommended, because small amounts of cancer may be sequestered in the skin or blood vessels of the scalp. Denying chemotherapy the opportunity to kill all colorectal cancer cells may result in failed treatment or relapse.

Prevention: It is difficult to prevent the loss of hair resulting from colorectal cancer therapies. But remedies can be taken to deal with it quite effectively.

## Hand & Foot Syndrome

Description/Symptoms: Hand & Foot Syndrome, known medically as palmar-plantar erythrodysesthesia or PPES, is a collection of symptoms of tingling or burning, redness, pain, soreness, loss of feeling, swelling, small blisters, and small sores on the palms of the hands or soles of the feet, as well as skin peeling on the fingers and on the soles of the hands and feet. This is a common side effect of Capecitabine (xeloda) therapy. Hand-foot syndrome results when a small amount of drug leaks out of the smallest blood vessels in the palms of the hands and soles of the feet. The amount of drug in the capillaries of the hands and feet increases due to the friction and subsequent heat that is generated in those extremities. As a result, more drug may leak out of capillaries in these areas. Once out of the blood vessels, the chemotherapy drug damages surrounding tissues. This side effect usually recedes when therapy ends. Occasionally therapy is halted if the symptoms become very severe.

Cause: Hand and foot syndrome is often brought on by the use of xeloda, floxuridine and 5FU therapy.

Treatment/Remedy: Hand-foot syndrome is first treated by reducing the dose or stopping treatment with the chemotherapy drug that is causing it. Other approaches to managing hand-foot syndrome include: **Corticosteroids** which are steroids that work by reducing inflammation. Your doctor may recommend a systemic corticosteroid (administered as an oral agent) to help relieve the symptoms of hand-foot syndrome; **Dimethyl-sulfoxide (DMSO)** is a topical treatment which has been shown to treat leakage of chemotherapy drugs into tissues; **Vitamin B6 (pyridoxine)** is a treatment capable of reducing the symptoms of hand-foot syndrome. For relief of symptoms associated with hand-foot syndrome, the following is recommended:

- Cool with ice packs for 15-20 minutes at a time
- Elevate hands and feet
- Apply antibiotic ointment on open sores
- Apply moisturizers sparingly
- Avoid constrictive clothing

Prevention: Changes to your normal, daily activities after receiving intravenous (through a vein) chemotherapy (5FU) or during treatment with oral chemotherapy (xeloda) can reduce your chances of developing hand-foot syndrome. Reduce exposure of hands and feet to friction and heat by avoiding the following:

- Hot water (washing dishes, long showers, hot baths)
- Impact on your feet (jogging, aerobics, walking, jumping)
- Using tools that require you to squeeze your hand on a hard surface (garden tools, household tools, kitchen knives)
- Rubbing (such as applying lotion, massaging)

## Heartburn (Acid Reflux)

Description/Symptoms: Heartburn is an irritation of the esophagus which causes burning discomfort in the chest just behind the breastbone. The burning sensation results when harsh stomach juices come in contact with and irritate the delicate lining of the esophagus, which is the tube-like structure that connects the mouth to the stomach. Heartburn may feel like:

- A burning chest pain that begins at the breastbone that moves up toward the throat
- Food or liquid is coming back into the mouth or throat
- An acid or bitter taste at the back of the throat

- A worsening pain/burning behind the breastbone when lying down or bending over

Cause: Heartburn is caused when harsh stomach juices come in contact with and irritate the delicate lining of the esophagus, which is the tube that connects the mouth to the stomach. Stomach juices help break down food in the stomach and contain a strong acid, called hydrochloric acid. While the stomach is naturally protected from the harmful qualities of acid, the esophagus is not. Stomach juices come into contact with the esophagus when the muscle that separates the stomach from the esophagus, called the lower esophageal sphincter, does not work properly. When working normally, this muscle works like a natural valve, letting food into the stomach but keeping stomach juices out of the esophagus. When not functioning properly, this muscle relaxes and allows stomach juices to flow upward into the esophagus. Your doctor may call this backward movement of stomach juices **gastroesophageal reflux**. The hydrochloric acid damages the lining of the esophagus causing heartburn and its associated symptoms. Heartburn can occur in association with eating certain foods or taking certain drugs, including chemotherapy drugs used to treat colorectal cancer. Examples are: xeloda, oxaliplatin, 5FU, irinotecan, and the biologic avastin.

Treatment/Remedy: Avoiding things that cause heartburn can help, but if lifestyle changes are not enough to prevent heartburn, medication may be prescribed. Effective over-the-counter and prescription medications are available. **Over the counter antacids** work by neutralizing the acid in the stomach. They may contain the following compounds alone or in combination: calcium carbonate, aluminum hydroxide, magnesium hydroxide and magaldrate. Examples are Maalox, Mylanta, Roloids, or Tums. **H2 blockers** decrease stomach acid by blocking histamine from binding to the H2 receptors on cells in the stomach lining. Histamine, a natural substance produced by the body, stimulates cells in the stomach lining to release acid into the stomach. H2 blockers decrease gastric acid secretions. A few examples of these drugs that may be prescribed include Tagamet, Pepcid, Axid or Zantac. Pepcid and Zantac are now available over the counter. **Proton-pump inhibitors** inhibit the final step in the production of gastric acid. Examples include Prilosec, Prevacid, Nexium, Protonix or Aciphex. If it is determined that an ulcer is the underlying cause of the heartburn, these medications may be prescribed for short-term treatment of the ulcer. However, an ulcer is caused by the *H. pylori* bacteria and must be treated with a combination of medication and antibiotics for long-term results. Colorectal cancer therapy-induced heartburn requires the use of the above noted medications for as long as the condition persists or as recommended by the physician.

Prevention: In general, there are several lifestyle changes that can be made to prevent or lower the risk of experiencing heartburn. These may include:

- Smoking Cessation
- Limit or eliminate alcohol
- Limit your caffeine intake (coffee, soda, tea)
- Lose some weight if you are overweight

- Avoid fatty foods (deep fried foods)
- Do not eat 2-3 hours before going to bed
- Avoid foods that cause you to have heartburn

## High Blood Pressure (Hypertension)

Description/Symptoms: If the following symptoms are noticed, it is recommended that the treating physician be contacted: rapid pulse, fluid retention, headache, or other symptoms of high blood pressure. High blood pressure can develop temporarily because of accessing colorectal cancer drugs. Blood pressure is the force of blood pushing against the walls of arteries as it flows through them. Arteries are the blood vessels that carry oxygenated blood from the heart to the body tissues. Hypertension or high blood pressure is a repeatedly elevated blood pressure exceeding 140 over 90 mmHg – a systolic pressure above 140 with a diastolic pressure above 90.

Cause: The colorectal cancer therapies that have been reported to cause elevated blood pressure are 5FU, xeloda and avastin.

Treatment/Remedy: The treatment of elevated blood pressure consists of anti-hypertensive medications designed to lower blood pressure. Your physician may wish to take a wait and see approach but if the blood pressure is excessively elevated, anti-hypertensives may be prescribed to lower blood pressure. Hypertension is also treated with regular aerobic exercise, weight reduction (if overweight) and salt restriction.

Prevention: It is difficult to prevent the onset of drug-induced hypertension but treatment is readily available upon consulting the advice of the physician overseeing the treatment of your colorectal cancer.

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## Infection/Fever

Description/Symptoms: Fever is an abnormally high body temperature. The average human body temperature is 37°C (98.6°F); however, each individual person is different and normal may range from 36.0°C to 38°C. Even under normal conditions, the human body temperature varies throughout the day — it is lower in the morning and higher in the late afternoon and evening. Fever is the body's natural response to infection. A part of the brain called the hypothalamus raises the body temperature to create an environment that is unfavorable for the bacteria or viruses that cause infectious disease. For example, the viruses that cause colds and other respiratory infections thrive at cool temperatures. One way the body works to

eliminate a virus is by producing a fever. Fever can be the first symptom of life-threatening infection when white blood cells have been destroyed by therapy. Unattended fever in the absence of sufficient white blood cell numbers can be fatal, and is a medical emergency requiring immediate attention. Depending on what is causing your fever, your signs and symptoms may include:

- Sweating
- Shivering
- Headache
- Muscle aches
- Lack of appetite
- Dehydration
- General weakness
- Burning or pain while urinating
- Neck stiffness
- Coughing
- Trouble breathing

Very high fevers, between 40°C and 42°C, may cause hallucinations, confusion, irritability and even convulsions.

Cause: For a cancer patient, fever may be a sign of a dangerous infection. An infection may be particularly serious when your white blood cell count is low or is expected to be low (leucopenia). This is because white blood cells are the body's normal defenses against infection, and when their numbers are low, the body's ability to fight infection is reduced. Additionally, many cancer patients develop a fever in which a definite source of infection cannot be identified. Fever is a side effect of some biological therapies, and may occur in patients who are receiving chemotherapy and biological therapy as part of the "flu-like syndrome". A fever associated with "flu-like syndrome" usually peaks at 40°C and often spikes after a severe chill. Those colorectal cancer systemic therapies known to cause a diminished white blood cell count and therefore the potential to develop infections resulting in fevers are: irinotecan, oxaliplatin, mitomycin c, methotrexate, 5FU, xeloda, avastin, erbitux, and vectibix. The danger period for most patients is five to ten days after treatment. In general, chemotherapy is more likely to cause leucopenia than radiotherapy, but radiotherapy is also a known cause of diminished white blood cell count.

Treatment/Remedy: Medical treatment for a fever depends on the cause. If the fever is determined to be related to an infection, treatment will be prescribed for the infection. For a bacterial infection, such as pneumonia or tonsillitis, antibiotics are usually prescribed. For viral infections, including stomach flu (gastroenteritis), the best treatment is often rest and plenty of fluids, although anti-viral drugs may be used to treat some viruses. If an infection-related fever is tolerable, then doctors may not treat the infection but monitor it closely because the fever

contributes to eliminating the bacteria or virus. If a cancer patient develops a low white blood count and fever, it is assumed that an infection is present and antibiotics are then given until the fever is resolved and white blood cell count recovered. If an infection-related fever is very high, over-the-counter medications may be prescribed to reduce the fever and associated discomfort. Non-steroidal anti-inflammatory drugs (NSAIDs), such as acetaminophen or ibuprofen, are often used for this purpose. Adults may also use aspirin to reduce a fever. If you have a bleeding disorder, you should avoid NSAIDs, as well as aspirin. These drugs may prolong bleeding by interfering with the activity of blood platelets. Use of such drugs to treat fever should be discussed first with your healthcare professional. NSAIDs or aspirin are also used if the source of the fever is related to flu-like syndrome associated with biologic therapy or certain types of chemotherapy and not infection. If an infection develops, you may be admitted to the hospital, placed in an isolation room, and given a combination of immunoglobulin therapy, antibiotics, antiviral, or antifungal agents.

**Prevention:** It may be difficult to prevent the onset of fevers resulting from infections that have been brought on by diminished white blood cell counts. However, diminished white blood cell counts may be prevented through the use of such agents as neupogen or neulasta. Please see the section on neutropenia. Preventive measures may also include: avoiding scratches and cuts via gentle handling of the skin, frequent hand-washing, patting skin dry rather than rubbing, thorough cooking of food, reducing human contact so as to reduce the potential to contract an infection, and avoiding gardening and handling pet litters.

## L/

### **Liver or Gallbladder Dysfunction**

**Description/Symptoms:** Mild liver or gallbladder problems sometimes develop when you are fed only by IV line (TPN, total parenteral nutrition). These problems usually go away when you resume eating normally. Scarring of the liver, called biliary sclerosis, can occur when an infusion pump delivers chemotherapy directly to the liver. Transient liver problems might result. Thus, if chemotherapy is being delivered directly to the liver (through hepatic arterial infusion or HAI) via pump, the following side effects are particularly germane: nausea, jaundice, swollen abdomen, pain in the upper abdomen, or mental confusion. Some researchers believe that concurrent administration of corticosteroids such as prednisone can reduce scarring of the liver. Because liver problems can be a sign of relapse, report the concern immediately if you notice any combination of symptoms of liver dysfunction: nausea, jaundice, swollen abdomen, pain in the upper abdomen, or mental confusion. Liver damage, also known as hepatotoxicity, causes this critical organ to under function, or to function irregularly. The liver is the largest organ in the body and serves many vital functions. The liver's most important task is to filter toxic substances from your body, including alcohol and

many different medications, such as chemotherapy drugs, antibiotics and Tylenol. Other important functions that the liver performs include:

- Works with the spleen to remove old or damaged red blood cells from the blood
- Produces bile, a substance that is released into the intestine to aid in the absorption and digestion of fats, and provides a way for the liver to excrete waste products
- Produces clotting factors that are critical for forming a clot to stop bleeding
- Processes and stores vitamins, minerals, proteins, fats and glucose (sugar) from your diet

When the liver is damaged, it may not be able to perform these functions optimally. Notably, it may not be able to excrete bile, the primary way that the liver disposes of waste products. Chemotherapy drugs may cause liver damage because they are toxins and they place added stress on the liver's filtering function. The liver removes toxins and chemicals from the blood stream and changes them into products that can be readily removed through the bile or urine. If toxins accumulate in the body faster than the liver can process them, then liver damage will result. **Liver damage can be a serious condition and you should notify your doctor immediately if you experience any of the following symptoms:**

- Jaundice: yellowing of the skin, whites of the eyes, mucous membranes (moist areas around eyes and mouth) due to high levels of bilirubin in the extracellular fluid
- Severe fatigue
- Fever
- Abdominal pain, severe nausea and vomiting
- Bleeding that does not stop after a few minutes
- Any unusual swelling in your feet and legs, or weight gain of greater than 3 to 5 pounds in 1 week

Cause: Problems relating to the liver or gallbladder can sometimes be attributed to TPN, total parenteral nutrition but subside once the catheter is removed. And HAI can cause scarring of the liver. Colorectal cancer therapies may also damage the liver. These are: 5FU, xeloda, oxaliplatin, irinotecan, methotrexate, and mitomycin c.

Treatment: There is no treatment for liver damage once it occurs. The primary approach is to discontinue any medications that are processed through the liver. Your doctor may also prescribe medications that help reduce the symptoms of liver damage. For example, you may be prescribed a diuretic to reduce fluid accumulation or swelling by making you urinate out extra fluid. A commonly used diuretic is Lasix.

Prevention: There are a number of substances that you should avoid if your liver is not functioning properly and should also avoid in the prevention of further liver damage/dysfunction. The following are processed in the liver and may cause further stress or

damage.

- Alcohol
- Acetaminophen
- Medications that have caused liver dysfunction in the past
- Medications to treat high blood cholesterol levels, such as atorvastatin or simvastatin

Talk to your doctor before changing any medications.

## Low Blood Counts

Description/Symptoms: A blood count is a measurement of the number of blood cells an individual has in circulation based on laboratory evaluation of a blood sample. Blood is composed of three basic blood cell types: **red blood cells, white blood cells, and platelets**. There should be billions of these blood cells circulating throughout the body. However, certain circumstances may cause there to be fewer cells than is considered normal, a condition which is called “low blood counts”. The laboratory test that is conducted to measure the number of blood cells is called a complete blood count, or CBC. Symptoms will depend on which types of blood cells are low. Common symptoms of the different types of low blood cell counts are listed in the following table:

Symptoms of Low Red Blood Cells	Symptoms of Low White Blood Cells	Symptoms of Low Platelets
• Fatigue or tiredness	• Infection	• Excessive bruising
• Trouble breathing	• Fever	• Excessive bleeding
• Rapid heart rate		• Nosebleeds
• Difficulty staying warm		
• Pale skin		
• Dizziness or lightheadedness		

**Cause:** Low blood counts can be brought on by colorectal cancer therapies such as: oxaliplatin, irinotecan, 5FU, methotrexate, xeloda, mitomycin c, avastin, erbitux, and vectibix. Radiation therapy will also reduce certain elements of the blood following treatment. Diminished blood counts (specifically lymphocyte and platelet count) result from radiation exposure of bone marrow and sometimes direct damage to lymphocytes in the blood stream and lymph nodes.

**Treatment/Remedy:** The best treatment for low blood counts is to prevent them before they occur. This can be accomplished with the administration of blood cell growth factors. Blood cell growth factors are substances produced by the body that stimulate the cells in the bone marrow to produce more red blood cells, white blood cells, or platelets. These factors have also been produced in a laboratory and are approved by the Food and Drug Administration (FDA) and Health Canada for the treatment of cancer patients with low blood counts. Erythropoietin, used to elevate red blood cell counts, is a blood cell growth factor that selectively increases production of red blood cells but has shown to promote cancer progression and is therefore not recommended for use in colorectal cancer patients. The blood cell growth factors approved by the FDA for the prevention of chemotherapy-induced neutropenia (decreased white blood cell count) are Neupogen (filgrastim) and Neulasta (pegfilgrastim). The drawback of Neupogen, however, is that it must be administered daily. **A single dose of Neulasta, however, has been proven to be as effective as an average of 11 daily injections of Neupogen** for the management of neutropenia. The blood cell growth factor approved by the FDA for the prevention of low platelet count is called Neumega. If low blood counts (ie lymphocytes and platelets) are a result of radiation therapy, an interruption in treatment for a few days is usually sufficient to allow recovery.

The following table represents the reporting of a male patient’s complete blood count. The CBC is typically reported in the format shown below. If your blood counts fall outside of the normal range, which is shown in the “Reference interval” column, their values will be reported in the “Flag” column with an ‘L’ for low or an ‘H’ for high.

<u>Test</u>	<u>Result</u>	<u>Flag</u>	<u>Reference Interval</u>
White Blood Count	7.1		4.0-11
Red Blood Count		3.50 L	4.00-6.00
Hemoglobin		101 L	130-180
Hematocrit		0.314 L	0.390-0.540
Platelets	302		150-400
Neutrophils	4.4		2.0-7.5
Lymphocytes		68 H	1.0-4.0
Monocytes	0.6		0-1.0
Eosinophils	0.1		0-0.7
Basophils	0		0-0.3

MCV		104 H	78-96
RDW	13.5		10-14.5
MCH		33.4 H	28.0-32.0
Mean Platelet Volume	8.3		5.0-15.0
MCHC	0.322		0.310-0.360

The above counts can be explained through the following:

**Flag column:** The flag column shows counts that are lower ("L") or higher ("H") than the normal range.

**Reference interval (or reference range) column:** The reference interval shows the normal range for each measurement for the lab performing the test. Different labs may use different reference intervals.

**White blood cells:** White blood cells help protect individuals from infections. The above CBC report shows that the patient's total white cell count is 7.1, and falls within the normal range of 4.0-10.5.

**Absolute neutrophil count:** Neutrophils are the main white blood cell for fighting or preventing bacterial or fungal infections. In the CBC report, neutrophils may be referred to as polymorphonuclear cells (polys or PMNs) **or neutrophils**. The absolute neutrophil count (ANC) is a measure of the total number of neutrophils present in the blood. When the ANC is less than 2.0, the risk of infection increases.

**Red blood cells:** Red blood cells carry oxygen from the lungs to the rest of the body. The above CBC report indicates that the patient has a red cell count of 3.5, which is lower than the normal range of 4.00-6.00, and therefore, shown in the flag column.

**Hemoglobin (Hb):** Hemoglobin is a protein in the red blood cell that carries oxygen. The above CBC report indicates that the patient's Hb count is 101, which is below the normal range of 130-180. The **hematocrit (HCT)**, another way of measuring the amount of Hb, is also low. This means that the patient has mild **anemia** and may be starting to notice symptoms.

These ranges will vary depending on age and gender. For women, they will be lower than those shown here. For example, the Hb reference interval for a woman is 120-160.

**Platelets:** Platelets are the cells that form blood clots that stop bleeding. The above CBC report indicates that the platelet count for this patient is normal.

**Prevention:** The best treatment for low blood counts is to prevent them before they occur. This can be accomplished with the administration of blood cell growth factors listed above. Blood

cell growth factors are substances produced by the body that stimulate the cells in the bone marrow to produce more red blood cells, white blood cells, or platelets. These factors have also been produced in a laboratory and are approved by the Food and Drug Administration (FDA) and Health Canada for the treatment of cancer patients with low blood counts.

## Low Platelet Count (Thrombocytopenia)

Description/Symptoms: Platelets are the cells that form blood clots that stop bleeding. Thrombocytopenia refers to the presence of abnormally low levels of platelets in the circulating blood. Platelets, or thrombocytes, are a specific kind of blood cell that prevents bleeding. Platelets normally rush to the site of an injury and work with other blood factors to form a blood clot. Normally, there are billions of platelets in the blood; however certain chemotherapy drugs can lower the platelet count. The fewer platelets an individual has in his/her blood and the longer he/she remains without enough of them, the more susceptible he/she is to bleeding.

Cause: The most common reason that colorectal cancer patients experience thrombocytopenia is as a side effect of chemotherapy. When chemotherapy affects bone marrow, the body's ability to produce platelets, the body's chief defense against bleeding, is diminished. Chemotherapy-induced thrombocytopenia typically occurs 6-10 days following administration of the chemotherapy drugs and continues for several days before platelets recover to an appropriate level. Examples of colorectal cancer therapies producing thrombocytopenia are: 5FU, erbitux, vectibix, xeloda, oxaliplatin, irinotecan, mitomycin C, methotrexate and avastin. Infrequently, colorectal cancer patients may also experience thrombocytopenia from other medications or as a consequence of their underlying cancer. When discussing the consequences and management of thrombocytopenia, it is important to distinguish between chemotherapy-induced thrombocytopenia and thrombocytopenia resulting from other causes. The type and dose of chemotherapy also has an effect on how low the platelet count drops and how long it will take to recover. While receiving chemotherapy, a patient's blood may be tested frequently to ensure he/she has enough platelets. Thrombocytopenia, or "low platelets", are terms used to describe a low platelet level in the blood. Fortunately, having a low level of platelets can be corrected for many patients.

Treatment/Remedy: The most common way to treat thrombocytopenia, assuming it is severe enough to warrant treatment, is with platelet transfusions and blood cell growth factors such as Neumega. Transfusions only temporarily correct thrombocytopenia and are associated with complications as well as disease progression and Neumega's efficacy has yet to be confirmed in Canada. Most physicians prefer to take a wait and see approach after discontinuing therapy. A break from chemotherapy usually restores platelet levels at which point the patient may then resume therapy.

The reduction in the frequency and severity of thrombocytopenia and its associated complications has resulted from scientists developing a better understanding of the basic biology of bone marrow blood cell production and from participation in clinical studies designed to evaluate strategies directed at reducing thrombocytopenia and its complications. Currently, there are several strategies aimed at improving the prevention and management of thrombocytopenia.

- **New blood cell growth factors:** Several new blood cell growth factors are being developed and evaluated in clinical studies for the purpose of improving chemotherapy-induced thrombocytopenia. AMG 531 is an investigative agent that stimulates the body to produce platelets and thus reduce or reverse thrombocytopenia and is continuing to undergo testing.
- **Peripheral blood stem cells:** Stem cells responsible for the production of platelets can be collected in large quantities from the peripheral blood. Delivery of peripheral blood stem cells following very high doses of chemotherapy has been demonstrated to result in more rapid platelet recovery than with stem cells collected from bone marrow. Many doctors have begun evaluating the use of peripheral blood stem cells to support multiple cycles of dose intensive chemotherapy alone or in combination with Neumega or other blood cell growth factors for the purpose of reducing the frequency and severity of thrombocytopenia and its complications.

Prevention: Chemotherapy-induced thrombocytopenia occurs because the chemotherapy drugs have destroyed many of the normal rapidly dividing cells in the bone marrow responsible for platelet production. Naturally occurring substances called cytokines exist in the body to regulate certain critical functions at the cellular level. One group of cytokines is commonly referred to as blood cell growth factors. Blood cell growth factors are responsible for stimulating the cells in the bone marrow to produce more blood cells. A blood cell growth factor that is approved by the U.S. Food and Drug Administration (FDA) for the prevention of chemotherapy-induced thrombocytopenia is Neumega (oprelvekin). Neumega helps the bone marrow create more platelets and has been demonstrated in clinical studies to prevent thrombocytopenia and decrease the need for platelet transfusions in patients at high risk for developing thrombocytopenia. The most common side effect observed with Neumega is fluid retention or edema. This symptom persists while Neumega is being used and is reversible within a few days of discontinuation of Neumega.

## Lymphedema

Description/Symptoms: Lymphedema is the buildup of lymph fluid in the tissues just under the skin. As the blood travels into smaller and smaller vessels, excess fluid, protein and other

substances are pushed out into the surrounding tissue. This substance is called lymph fluid. Under normal circumstances, lymph fluid is removed from the tissues by the lymph system, which is a series of vessels and organs that move the fluid back toward the heart and filter it through lymph nodes. Lymph nodes are specialized structures that are composed of white blood cells and serve to “clean” the lymph fluid of bacteria or other contaminants. If there is damage to or blockage in the lymph system, the lymph fluid cannot be removed and builds up in the tissues. Notify your doctor if you have any of the following symptoms indicative of lymphedema:

- Feelings of tightness in the arm or leg
- Decreased flexibility in a hand, elbow, wrist, fingers or leg
- Difficulty fitting into clothing
- Ring, wristwatch, bracelet, shoe that fits tighter than usual
- Pain, aching, heaviness, or weakness in the arm or leg
- Redness, swelling, or signs of infection
- Skin that feels stiff or taut
- Pitting (small indentations left on the skin after pressing on the swollen area)

Cause: Lymphedema is caused by blockage or damage to the lymph system. It may be caused by a colorectal cancer treatment or the cancer itself. Damage to the lymph system by **surgery or radiation** is the primary cause of lymphedema in colorectal cancer patients, especially when treatment is conducted in the groin, or pelvic regions. Swelling may occur immediately after treatment, or it may arise weeks, months or even years later. Lymphedema that is caused by the cancer itself is usually related to:

- Spread (metastasis) to the lymph nodes in the neck, chest, underarm, pelvis or abdomen
- Growth of tumors (cancer) in the pelvis or abdomen that block lymph drainage by involving or putting pressure on the lymphatic vessels and/or the large lymphatic duct in the chest

Treatment/Remedy: While there is no single treatment for lymphedema, steps can be taken to manage the symptoms with the following:

- **Compression garments:** Your doctor may recommend that a specially made “elastic sleeve” be worn on the affected limb. This sleeve provides compression and has been shown to significantly reduce swelling. Talk with your doctor about when and how to use compression garments. Some people need to use compression garments both day and night.
- **Manual lymphatic drainage:** This is a specialized form of very light massage that helps to move fluid from the end of the limb toward the trunk of the body. Manual lymphatic drainage is different from standard massage and should be performed by a

trained professional. This individual may be able to teach you ways that you can massage yourself to increase lymph flow.

- **Exercise:** Lymphatic drainage is improved during exercise. Your doctor or physical therapist will recommend specific exercises.

Prevention: Lymphedema occurs less frequently now than in the past because of improved surgical techniques. Preventing or reducing lymphedema may also be accomplished by the following:

- Keep the arm or leg raised above the level of the heart, when possible.
- Clean the skin of the arm or leg daily and moisten with lotion.
- Avoid injury and infection of the arm or leg.
- Avoid tight clothing.
- Do prescribed exercises regularly as instructed by your doctor or therapist.
- Avoid pressure on the arm or leg:
  - Do not cross legs while sitting.
  - Do not carry a handbag on the arm that is swollen
  - Wear loose jewelry; wear clothes without tight bands.
  - Do not use blood pressure cuffs on the affected arm.
  - Do not sit in one position for more than 30 minutes.

## **M/**

### **Mucositis (Mouth Sores)**

Description/Symptoms: Chemotherapy- or radiation-induced damage to the cells lining the mouth, throat and gastrointestinal (GI) tract is called mucositis. This side effect of cancer treatment can significantly affect patient quality of life and may cause delays in treatment. Symptoms of oral mucositis commonly occur three to ten days following your treatment with chemotherapy. You may experience a burning sensation followed by ulcers, and your mouth may appear red (inflammation) with sores (ulcerations). There may be associated discomfort and pain. Mouth sores can make chewing and swallowing difficult, thereby interfering with your nutrition and food intake, resulting in weight loss. Your speech may also be compromised because of the soreness. Furthermore, the lining of your mouth serves to protect you against infection, so mouth sores may make you more susceptible to bacterial, fungal, or viral infections in the mouth. Ultimately, mouth sores can become severe enough that it is necessary to reduce your dosage or delay your treatment in order to allow your mouth to heal. Symptoms resulting from the inflammation, irritation and dysfunction caused by the mucosal reaction to radiation depend on the site of the reaction. There may be discomfort and dysphagia (difficulty in swallowing) or cough, hoarseness and tracheitis (inflammation of the

trachea/windpipe), or dysuria (painful urination) and frequent diarrhea and abdominal cramps.

Causes: Mouth sores are a common side effect of radiation and certain chemotherapy drugs. Chemotherapy and radiation kill rapidly dividing cells, a hallmark characteristic of some cancers. The GI tract, including the mouth and the throat, is made up of cells that divide rapidly. For this reason, the GI tract is particularly susceptible to damage by chemotherapy and radiation treatment. Those colorectal cancer therapies that may cause mucositis are 5FU, xeloda, floxuridine, methotrexate, mitomycin c, irinotecan and oxaliplatin. A number of factors may contribute to the severity of mouth sores, including:

- Poor oral and dental health prior to treatment
- Kidney disease
- Younger or older adults
- Smoking and the use of chewing tobacco during episodes of mucositis
- Harsh foods and alcohol
- Concomitant disease such as diabetes or AIDS

Whenever mucous membranes are included in a radiation field similar reactions will be experienced whether in the mouth, pharynx (throat), esophagus, trachea, bowel, bladder or rectum. As with the skin, the mucosa is reddened at first but then may be covered with a plaque-like fibrin similar to crusting of the skin. The mucous membrane remains moist and the surface is covered by fibrin until the underlying mucosa is healed.

Treatment/Remedy: Until recently, the only approaches to managing oral mucositis (mouth sores) included good oral care (frequently rinsing the mouth with saline and brushing teeth 2-3 times per day); mouthwashes (salt and soda mouthwash has been shown to relieve mouth sores as well as medicated mouth washes); cryotherapy (sucking on ice chips) to minimize the damage from chemotherapy drugs (this technique works by decreasing blood flow to the cells in the mouth, reducing exposure to the drug and decreasing the risk of developing mouth sores. Apparently, this is the only measure proven to prevent mouth sores); Salagen, a drug that stimulates salivary flow; and other investigational treatments. A promising new approach to the prevention and treatment of mouth sores is the use of growth factors. Growth factors are natural substances produced by the body to stimulate cell growth. The new drug Kepivance (approved in the US) is a growth factor that is produced in a laboratory and designed to protect the cells in the mouth and GI tract from mucositis. Once mouth sores occur, treatments may also include the avoidance of very hot foods, carbonated beverages, eating soft foods till the sores heal, and using special medications such as viscous lidocaine and other mouthwashes designed to numb the mouth. There are several effective mouthwashes that can be prepared for mouth sores treatment by pharmacists; forward the request to your health care provider who will be able to assist. The treatment of radiation-induced mucositis, whether in the mouth, pharynx, esophagus, trachea, bowel, bladder or rectum include the following:

- Avoiding irritation by keeping food or stools soft and preventing trauma of any kind
- Local analgesic mixtures, antibiotics where indicated and steroids may help
- Maintaining hydration by encouragement and intravenous fluids if necessary
- Low fibre diet for those with bowel reaction
- Exercising patience until the healing begins

Prevention: It may be difficult to prevent chemo- or radiation-induced mucositis but adhering to the suggestions above may prevent severe mucositis. In some cases, mouth sores can be prevented by keeping the mouth very clean, using non-irritating toothpaste, and if time permits, having all dental problems resolved before beginning chemotherapy.

**N/**

## **Nausea/Vomiting**

Description/Symptoms: Nausea and vomiting are the result of some, but not all, of the drugs and radiation treatment used for colorectal cancer treatment. Nausea associated with radiation therapy usually occurs only if the area just above the navel is irradiated. Nausea is feeling queasy or sick to your stomach, like you're going to throw up. Vomiting is emptying your stomach by throwing up. Nausea and/or vomiting are frequent side effects of chemotherapy and radiation therapy. Chemotherapy-induced nausea and vomiting can be **acute** (within the first 24 hours), **delayed** (vomiting that occurs after 24 hours) and/or **anticipatory**. Anticipatory vomiting is a learned response, which means it happens in response to a stimulus, such as chemotherapy. With this type of nausea and vomiting, the symptoms usually occur after initial exposure to chemotherapy drugs and before subsequent treatments.

Cause: A specific location in the brain controls emesis (vomiting), called the vomiting center. Emesis occurs when the vomiting center receives a signal from the brain, the gastrointestinal tract, the heart and/or the inner ear, which detects motion. Chemotherapy causes the release of a substance called serotonin (5-HT), and of other chemicals in the small intestine, which through a series of signals stimulate the vomiting center in your brain to induce emesis. Colorectal cancer therapies that may cause nausea are: irinotecan, oxaliplatin, 5FU, methotrexate, leucovorin, xeloda and mitomycin c. Some patients who undergo radiation therapy also experience nausea and vomiting during the early part of the treatment and, in some instances, throughout the treatment. If it occurs, nausea is likely to be at its worst from two to several hours after treatment.

Treatment/Remedy: Fortunately, excellent drugs are available to control nausea and vomiting. **Zofran** (ondansetron) and **Kytril** (granisetron) are two such anti-emetics, and anti-anxiety

drugs such as Xanax, a drug similar to valium, may work for brief episodes of nausea. Some steroids such as decadron also work, for reasons that are unclear. Older, less effective drugs, such as compazine, are also still in use, sometimes in combination with newer drugs. If you are unable to keep food down in spite of nausea medication, feeding by IV line for a period of time will give your stomach a chance to recover. The **5HT-3 Inhibitors** are the most effective antiemetics and constitute the single greatest advance in the management of nausea and vomiting in patients with colorectal cancer. These drugs are designed to block one or more of the signals that cause nausea and vomiting. The most sensitive signal during the first 24 hours after chemotherapy appears to be 5-HT3. Blocking the 5-HT3 signal is one approach to preventing acute emesis, or emesis that is severe, but relatively short-lived. Antiemetics that block 5-HT3, called 5-HT3 inhibitors, are the most effective agents developed to date for preventing emesis and are available to be administered orally or intravenously. The newest 5-HT3 inhibitor, **palonosetron**, has a distinct advantage over the other 5-HT3 inhibitors because in addition to preventing acute nausea and vomiting, it also prevents delayed nausea and vomiting, which occurs during the 2-5 days after treatment. It is the only drug in its class that is approved by the FDA for the treatment of delayed nausea and vomiting. **Other drug therapy approaches** commonly used to prevent or treat nausea and vomiting, either alone or in combination with antiemetics, include:

- Corticosteroids (dexamethasone, methylprednisolone, Prednisone, and others)
- Dronabinol —stimulates appetite and controls nausea
- Benzodiazapines (Valium and others)—may help control anticipatory nausea
- Aprepitant - Aprepitant is part of a three-drug therapy that works to prevent delayed nausea and vomiting. Aprepitant is not used to treat nausea and vomiting that you already have; it must be taken before the symptoms occur to be effective. This is because it blocks the NK1 receptor in the brain which helps with nausea and vomiting that persists beyond 2 days after treatment.

In addition to the above, nausea resulting from radiation therapy can also be treated by ingesting salty foods or ice cold drinks, avoiding greasy foods, strong-smelling or overly sweet foods and by ingesting small, frequent meals eaten slowly.

Prevention: There are several things you can do to prevent nausea and vomiting. **First and foremost, make sure you receive and take your antiemetics as your doctor has ordered.** Also, call your doctor if you experience any of the following:

- You have vomiting and cannot take your medication
- Your antiemetics help reduce your nausea and vomiting, but not as much as you would like. The dose may have to be changed or the doctor may change you to a different antiemetic.

In addition to taking your medication, the following general suggestions may help you prevent

or control nausea and vomiting:

- Try eating foods and drinking beverages that have been easier for you to take or have made you feel better when you had the flu, morning sickness or were nauseated from stress consisting of bland foods such as dry crackers, ginger ale, flat soda or others. Eat small, frequent meals (5-6), instead of 3 large meals each day.
- Do not eat fatty or fried foods, very spicy foods or very sweet foods.
- If possible, have somebody else make the meals when you are nauseated.
- Do not eat your favorite foods when you are nauseated.
- If you have nausea and vomiting only for a few days after chemotherapy, cook and freeze several meals that you can reheat during times when you are nauseated.
- Eat foods that are at room temperature or cold. The smells from hot foods may make your nausea worse.
- Keep your mouth clean; brush at least twice a day.
- Consider shakes or liquid nutritional supplements to help maintain your nutrition.
- Ask your doctor or nurse about using acupressure (BioBands) on your wrists, which may help to decrease your nausea.
- Anticipatory nausea associated with chemotherapy is best controlled with relaxation techniques.
- Ask your doctor or nurse if they can help you learn a relaxation exercise. This might make you feel less anxious and more in control, and decrease your nausea.

## Neutropenia (Low White Blood Cell Count)

Description/Symptoms: Neutropenia is a condition characterized by abnormally low blood levels of infection-fighting neutrophils, a specific kind of white blood cell. Neutropenia increases your risk of bacterial and fungal infections. The most common reason that colorectal cancer patients experience neutropenia is as a side effect of chemotherapy. Chemotherapy works by destroying cells that grow rapidly, a characteristic of cancer cells. Unfortunately, chemotherapy also affects normal cells that grow rapidly, such as blood cells in the bone marrow, cells in the hair follicles, or cells in the mouth and intestines. **Chemotherapy-induced neutropenia typically occurs 3-7 days following administration of chemotherapy** and continues for several days before neutrophil levels return to normal. While receiving chemotherapy, you will frequently have your complete blood count (CBC) checked to determine whether you have enough neutrophils. Typically there are billions of neutrophils in the blood; however, certain chemotherapy drugs will lower the neutrophil count. When a doctor or nurse discusses CBC test results, they frequently refer to the “absolute neutrophil count” (ANC) or the number of neutrophils in the patient’s blood. A “low white blood count” is another common term used to describe a low neutrophil level in the blood. Fortunately, having a low level of neutrophils can be corrected. The CBC is used to determine whether a patient has neutropenia. The CBC measures the levels of the three basic blood cells: red, white, and

platelets. In Canada, the CBC is typically reported in the format shown below. If your blood counts fall outside of the normal range, which is shown in the “Reference interval” column, their values will be reported in the “Flag” column with an ‘L’ for low and an ‘H’ for high. The example CBC below shows that white blood cells (neutrophils) fall within the normal range:

<u>Test</u>	<u>Result</u>	<u>Flag</u>	<u>Reference Interval</u>
White Blood Count	7.1		4.0-11
Red Blood Count		3.50 L	4.00-6.00
Hemoglobin		101 L	130-180
Hematocrit		.314 L	0.390-0.540
Platelets	302		150-400
Neutrophils	4.4		2.0-7.5
Lymphocytes		68 H	1.0-4.0
Monocytes	0.6		0-1.0
Eosinophils	0.1		0-0.7
Basophils	0		0-0.3
MCV		104 H	78-96
RDW	13.5		10-14.5
MCH		33.4 H	28.0-32.0
Mean Platelet Volume	8.3		5.0-15.0
MCHC	0.322		0.310-0.360

**Cause:** The type and dose of chemotherapy affects how low the neutrophil count drops and how long it will take to recover. Agents such as irinotecan, oxaliplatin, 5FU, methotrexate, xeloda, mitomycin c, erbitux, vectibix, and avastin have been reported to cause neutropenia. Those at risk of developing neutropenia are as follows: patients receiving chemotherapy that decreases the number of white blood cells; patients who already have a low white blood cell count, or who have previously received chemotherapy or radiation treatment; patients age 70 and older who may be at risk of more severe infection and longer hospitalizations; patients with other conditions affecting their immune system

**Treatment/Remedy:** Infrequently, cancer patients may also experience neutropenia from other medications or as a consequence of their underlying cancer. When discussing the consequences and management of neutropenia, it is important to distinguish between chemotherapy-induced neutropenia and neutropenia resulting from other causes because they may be managed differently. The treatment of chemo-induced neutropenia involves the use of

white blood cell growth factors, which are naturally occurring substances called cytokines that regulate certain critical functions in the body. They are responsible for stimulating cells in the bone marrow to produce more blood cells. The white blood cell growth factors approved for the treatment and prevention of chemo-induced neutropenia are Neupogen and Neulasta which is approved for use in the US.

Prevention: Chemotherapy-induced neutropenia can be prevented in most patients with the use of white blood cell growth factors such as neupogen or neulasta.

## Neuropathy - Peripheral (Numbness and Tingling)

Description/Symptoms: Peripheral neuropathy is damage to the nerves that transmit signals between the extremities and the central nervous system (CNS). These nerves include those that transmit sensation from the extremities to the CNS or those that carry signals for muscle movement from the CNS to the extremities. In addition to numbness and tingling, other symptoms of peripheral neuropathy include weakness, pain in the arms, hands, legs and/or feet, and abnormal sensations such as burning, tickling, pricking or tingling, also known as paresthesia. The areas of the body most commonly affected by peripheral neuropathy are the fingers and toes. Symptoms usually start at the end of the extremity and gradually move upward. Bowel function may also be compromised, causing or worsening constipation and eventually causing blockage of the intestines. Depending on the type of nerve damage, the patient may fully recover without residual effects or may partially recover but have long-term deficits in their ability to feel or move. If severely affected, the patient may develop chronic muscular weakness and atrophy.

Causes: Peripheral neuropathy in colorectal cancer patients is oftentimes caused by the platinum-based therapy called oxaliplatin and it is temporary. Neuropathies of the pelvis may follow radiation for rectal cancer, including pain, loss of sensation or loss of bladder or anal control. These side effects are more pronounced when intraoperative radiotherapy is used. The other colorectal cancer therapy known to cause neuropathy in patients is xeloda. Both oxaliplatin and xeloda have been known to cause damage to the peripheral nerves, those in the fingers and toes, and in some cases, the damage can spread into the feet, legs and arms.

Treatment/Remedy: There are treatments to help address chemotherapy-induced neuropathy.

- **Gabapentin** (an anti-convulsant medication) is considered to be the treatment of choice.
- **Carbamazepine** (another anticonvulsant medication) may be beneficial but its hepatic and hematological side effects make it less desirable for cancer patients.
- **Lamotrigine** (another anti-convulsant) has shown promise indicating that a good

number of patients respond favorably. It also has the advantage of no hepatic side effects and the rash (if it occurs) is considered tolerable. Antidepressant medications like Elavil have been known to help some patients.

- **Capsaicin** (a colorless, pungent, crystalline compound that is derived from the capsicum pepper that gives hot peppers its hotness) can be used at any time.
- **Massage and stretching** help alleviate cramps and some benefit has been seen from quinine found either in tonic water or over-the-counter preparations. An effort should be made to keep the dose as low as possible due to potential hematological side effects (eg. Hemolysis, thrombocytopenia).
- Recovery from peripheral neuropathy is usually slow, but steps can be taken to encourage regeneration of the damaged nerves. Some approaches include **acupuncture** (a technique originating thousands of years ago in the Chinese culture wherein thin needles are inserted into the body at certain points controlling the energy, and sensation, such as pain or numbness), ongoing **massage** (increasing blood flow may provide pain relief associated with neuropathy), **physical therapy** (range of motion and stretching exercises may strengthen muscles that are weak and improve other symptoms of neuropathy), and **transcutaneous nerve stimulation** (TENS - special device that transmits electrical impulses through electrodes attached to the skin which may promote nerve regeneration)..

Prevention: In addition to the medications and therapies used for treatment of chemotherapy-induced neuropathy, researchers are investigating drugs that are able to prevent the nerve damage from occurring altogether. These drugs are called **neuroprotective agents** and they work by firstly, protecting the nerve cells from the toxic effects of chemotherapy; and secondly, by promoting regeneration of nerve cells without promoting tumor growth. These drugs include **thiols** containing sulfur, **lipoic acid** (an oral supplement used in Europe), and **amifostine** (a drug which might be particularly effective for the prevention of neuropathy caused by platinum-based drugs – approved in the US). Recent data show that **magnesium- and calcium-infusions** (mg/ca-) before and after oxaliplatin may reduce the acute neuropathy resulting from oxaliplatin therapy. According to the latest studies, among all of the agents, intravenous calcium and magnesium have shown the most promise in prophylaxis and treatment of oxaliplatin-induced neurotoxicity. **Neurotrophic agents** or nerve growth factors (NGF) work by ensuring the survival of neurons. Limited studies have shown that NGF decreases or disappears after administration of chemotherapy. **Pyrimidine isaconine** is a drug showing properties for enhancing regeneration of peripheral nerves but has side effects including hepatic toxicity which presently limits its clinical use.

**P/**

## **Pain**

Description/Symptoms: Pain can be caused by surgery, by drugs used for colorectal cancer,

or by radiation therapy. If not adequately managed, pain may have a tremendous effect on quality of life. Fortunately, there are many effective treatments for pain and most of your pain should be controlled with these treatments. **You should always notify your doctor if you have pain or if your existing pain increases** so that steps can be taken to find the medication or combination of medications and dose that will control it. Also, take your medication as prescribed.

Causes: Postsurgical pain may persist for months or years following surgical treatment of colorectal cancer. Although advanced surgical techniques are used to reduce pain, chiefly by avoiding nerve groups, the surgeon's primary concern is the curing of cancer by removing all diseased tissue. At times, healthy tissue must be sacrificed in order to achieve this goal. As a result, a variety of persistent painful phenomena might be experienced by colorectal cancer survivors, such as pelvic pain that spreads to other body parts, perineal pain, or phantom anus syndrome, a sensation of pain in nonexistent tissue after anal tissue has been removed. Severe back pain may be associated with degenerative changes to the spine following radiation therapy targeted near the spine. Surgery to fuse spinal discs may alleviate this pain. Painful radiation fibrosis, a reaction of the immune system after exposure to radiation, can develop in any tissue that has been irradiated. Burning perineum syndrome, a sensation of burning pain in or near the scrotum, vagina, or near the anus, is known to occur in some colorectal cancer survivors treated with radiotherapy. Pain in the hands and feet or abdominal cramps may arise during chemotherapy with 5FU, xeloda, and irinotecan. Pain during therapy that involves radiation implants may occur. Many other examples could be listed as pain is a symptom of many aberrant physical processes.

Treatment/Remedy: Medications are the cornerstone of cancer pain treatment, and their use is aimed at providing the greatest pain relief possible with the fewest number of side effects and the most ease of administration. Medications used for colorectal cancer pain are selected according to the needs of the patient. For some kinds of pain related to cancer, non-prescription medications may be sufficient. For other degrees and kinds of pain, prescription medications are used. The following medications may be used based on the severity of the cancer pain:

- **Mild Pain:** acetaminophen (such as tylenol) or nonsteroidal anti-inflammatory medications (NSAIDs), such as ibuprofen
- **Mild to Moderate Pain:** Opioid medications, usually in combination tablets with NSAIDs or acetaminophen. Also known as narcotics, these drugs are similar to natural substances produced by the body to control pain, called endorphins, and are the strongest pain relievers available. Examples of opioids used as combination products are hydrocodone, codeine, or oxycodone and tramadol. Adjuvant medications may also be used for pain that is difficult to manage. Adjuvants are medications that were originally designed to treat conditions other than pain, such as tricyclic antidepressants.
- **Moderate to Severe Pain:** Higher doses of opioid medications often not given as combination products. Adjuvant medications, NSAIDs, and acetaminophen may also be

used. Examples of stronger opioids are morphine, fentanyl, oxycodone, hydromorphone, methadone, and levophanol.

Pain medication may be given in many different ways, including:

- **oral** (meant to be swallowed),
- **oral transmucosal** (administered in the mouth but are meant to be absorbed through the oral mucosa in the mouth),
- by **injection** (intravenous, intramuscular and subcutaneous – under the skin),
- **transdermal** (through the skin using a medicated patch),
- **rectal** (morphine, oxymorphone and hydromorphone, are sometimes administered through the rectum in patients who are unable to take pain meds orally), and
- **infusion pump** (through a catheter near the spine connected to a pump with pain medication that is programmed to deliver medication over a period of time).

*Non-medication treatment* of pain may consist of:

- **surgery** to alleviate pressure on nerves,
- **draining fluids** related to cancer growth may stabilize bones treated by radiation or chemotherapy intended to reduce metastases;
- **nerve blocks** involve the injection of anesthetic medication into specific areas of the body where pain is experienced, notably the nerves;
- **Radiofrequency ablation** using a special needle to deliver radiofrequency current into a painful tumor; radiation can alleviate cancer pain.

There are many **alternative therapies** for controlling pain that you may wish to try to see if they work for you. Some of these consist of:

- **Cognitive/behavioral techniques** such as relaxation, distraction, meditation and visualization;
- **Physiatric techniques** include electrical stimulation (such as Percutaneous electrical nerve-stimulation or PENS and transcutaneous electrical nerve stimulation or TENS),
- **skin stimulation,**
- **therapeutic exercise,**
- and the use of **orthoses** and assistive devices;
- **Massage** which increases blood circulation and relieves tension;
- **Biofeedback** techniques using special machines to help patients learn how to control certain body functions;
- **Hypnosis** can change how pain is perceived and therefore reduce anxiety;
- **Heat** can relax muscles and ease spasms;
- **Cold** in the form of a cold pack wrapped in one or more layers of cloth reduces

- inflammation and can help ease nerve pain;
- **Positioning** using orthotic devices to immobilize and support painful or weakened areas of the body;
- **Acupuncture** wherein thin needles are inserted into the body at certain points and at various depths and angles;
- **Emotional support** and counseling received from a professional, family member, or clergy;
- **Menthol preparations** containing menthol which increases blood circulation to the affected area thereby producing a warm or cool soothing feeling that lasts for several hours; and
- **Regular exercise** can help you combat your pain by prompting your body to release special chemicals, called endorphins that actually block pain signals from reaching the brain.

A discussion group for those suffering from cancer pain exists at [www.acor.org](http://www.acor.org) and enrollment is easily accomplished.

Prevention: It may be difficult to prevent the onset of pain but with proper management, it can be well controlled.

## ***R/***

### **Radiation enteritis and Proctitis (RASBI)**

Description/Symptoms: Radiotherapy targeted to the abdomen or pelvis can cause abdominal or rectal pain, diarrhea, bloody stools, or mucus in stools, also called radiation-associated small bowel injury (RASBI). It may be a short-term effect that fades in four to eight weeks after treatment ends, or, in 5-15% of patients, it may become a long-term chronic problem.

Cause: The cause of enteritis or proctitis is radiation therapy delivered to the abdomen or pelvis. Interference with the absorption of nutrients is one of the chief concerns.

Treatment/Remedy: Enteritis is treated by controlling diarrhea with kaopectate, lomotil, immodium, or narcotics. Steroid foam may be prescribed if the rectum is quite sore. For some, a change in diet might alleviate symptoms. Avoidance of lactose, fats, wheat gluten and high carbohydrates reportedly help some colorectal cancer survivors with RASBI.

Prevention: Prevention of RASBI may be difficult to avoid depending upon the area radiated in the abdomen or pelvis but remedies are available to help treat the symptoms.

### **Reproduction/Sexuality**

Description/Symptoms: It is perfectly natural for people who have been diagnosed with colorectal cancer to be concerned about the effect of their illness on their sexuality. Especially right after the diagnosis, you may temporarily lose interest in sex as you focus on understanding your cancer and the treatments available. During or after treatment, you may have difficulty accepting the way your body looks or functions and may have fears about your partner's acceptance of the changes. Changes in your reproductive abilities or sexuality due to colorectal cancer treatment may include:

- Impotence (inability to achieve or sustain an erection)
- Infertility
- Irregular menstrual cycles
- Menopause, and related symptoms
- Reduced sexual desire
- Sterility
- Vaginal dryness

Some of these side effects will resolve after treatment is completed, while others may be more long term.

Cause: A variety of problems with sexual performance and enjoyment, such as those listed above, can arise after surgery, chemotherapy or radiotherapy for colorectal cancer. Chemotherapies such as methotrexate and oxaliplatin have been reported to cause reproductive problems in 10% or more of patients. Other chemotherapies such as irinotecan, 5FU and mitomycin c can cause the early onset of menopause as well as diminished sexual drive.

Treatment/Remedy: Coping with sexual dysfunction may be very difficult. Maintaining open communication with your doctor and your partner, as well as taking steps to improve your self-esteem may help. In recent years, several drugs have been developed for men with erectile dysfunction. These drugs help men maintain an erection by inhibiting an enzyme. Examples include Viagra, Cialis, and Levitra. There are also medications available to help women deal with the symptoms of menopause. Ensure your doctor is informed of the symptoms you are experiencing so that proper steps can be taken to provide some relief. If you think you may want to have children after treatment and the cancer treatment is likely to cause sterility, you may wish to bank eggs or sperm. However, you must do this before you receive your treatment. Talk to your doctor about your wish to have children, so that steps can be taken to assure that you have this choice available to you later. And finally, to support a positive self-image, follow these suggestions that have helped many people with colorectal cancer:

- It sounds simple, but looking better may actually help you feel better. Try to maintain the same grooming habits—fashion, hairstyle, and so on—as you did before your diagnosis.

- Plan special activities for both the days when you're feeling well and those when you aren't. Acknowledge that cancer and treatment can cause shifts in mood.
- Enjoy the days when you're feeling well. On those days that are difficult, keep a positive outlook—plan all you'd like to do as soon as you feel better.
- If you need help with clothes and hair and other aspects of your appearance, don't hesitate to ask for it.

A discussion group for those dealing with issues of sexuality following cancer treatment can be found at [www.acor.org](http://www.acor.org).

Prevention: The symptoms associated with sexual and reproductive dysfunction may be difficult to prevent but remedies are available to help patients cope and deal with the onset of the treatment-related symptoms.

## S/

### Skin Problems/Changes

Description/Symptoms: A variety of skin problems may result from colorectal cancer therapies. They range from pain, burning, discoloration, scaling, wrinkling, dryness, rash, hives, redness, peeling, to sun sensitivity. Dermatology problems can be complex and difficult to diagnose, and certain skin symptoms, such as itching, may be a sign of an allergic response, or of serious changes such as relapse in the liver. Informing your health care provider is imperative upon noticing the symptoms.

Cause: Radiation therapy can cause burns to the area of the skin being treated.

**Radiodermatitis** is a common side effect of radiation therapy. Radiodermatitis is characterized by red, inflamed and possibly peeling skin at the location where the radiation beam was focused. This condition is likely to be worse in fair-skinned people receiving high dose treatments. The skin may also act as an indicator of adverse reactions to treatment. 5FU and irinotecan can cause skin problems. A rash is usually caused by some foreign substance that irritates the skin and is commonly associated with an allergic reaction. An allergic reaction is sensitivity to a foreign substance, such as a drug. All colorectal cancer drugs have the potential to cause this allergic reaction in patients. A rash can also be a non-allergic reaction to a drug. And anti-egfr therapies such as vectibix and erbitux have been reported to cause mild-to-severe side effects to the skin consisting of a rash, redness and burning.

Treatment/Remedy: Common remedies may consist of **lotions** that do not contain alcohol to cool the skin. If your rash is a result of an allergic reaction to a drug, the first thing your doctor will do is stop the drug. For minor, non-allergic skin reactions, your doctor may recommend one of the following: **Corticosteroid cream** which works by reducing inflammation;

**Antihistamine** such as benadryl to reduce symptoms of an allergic reaction, such as rash, hives and shortness of breath; **Analgesics** are over-the-counter medications that can relieve pain associated with a rash. Examples are acetaminophen and aspirin. Some tips to help manage a rash include:

- Wear loose, non-binding clothing.
- Use mild soap without perfumes.
- Dry your skin carefully after bathing.
- Avoid harsh chemicals.
- Protect your skin from the sun with sunscreens or long, loose clothing.
- Try not to scratch.

Prevention: Radiation-induced rashes may be difficult to prevent but prophylactic treatment of anti-egfr therapies consist of moisturizers, sunscreens, topical corticosteroid (hydrocortisone cream 1%), and oral doxycycline (100 mg twice daily) commenced before and during the therapy which have been proven to reduce the onset of severe skin problems brought on by erbitux and vectibix.

**T/**

## **Thrombocytopenia (Low Platelet Count)**

Description/Symptoms: Platelets are the cells that form blood clots that stop bleeding. Thrombocytopenia refers to the presence of abnormally low levels of platelets in the circulating blood. Platelets, or thrombocytes, are a specific kind of blood cell that prevents bleeding. Platelets normally rush to the site of an injury and work with other blood factors to form a blood clot. Normally, there are billions of platelets in the blood; however certain chemotherapy drugs can lower the platelet count. The fewer platelets an individual has in his/her blood and the longer he/she remains without enough of them, the more susceptible he/she is to bleeding.

Cause: The most common reason that colorectal cancer patients experience thrombocytopenia is as a side effect of chemotherapy. When chemotherapy affects bone marrow, the body's ability to produce platelets, the body's chief defense against bleeding, is diminished. Chemotherapy-induced thrombocytopenia typically occurs 6-10 days following administration of the chemotherapy drugs and continues for several days before platelets recover to an appropriate level. Examples of colorectal cancer therapies producing thrombocytopenia are: 5FU, erbitux, vectibix, xeloda, oxaliplatin, irinotecan, mitomycin C, methotrexate and avastin. Infrequently, colorectal cancer patients may also experience

thrombocytopenia from other medications or as a consequence of their underlying cancer. When discussing the consequences and management of thrombocytopenia, it is important to distinguish between chemotherapy-induced thrombocytopenia and thrombocytopenia resulting from other causes. The type and dose of chemotherapy also has an effect on how low the platelet count drops and how long it will take to recover. While receiving chemotherapy, a patient's blood may be tested frequently to ensure he/she has enough platelets.

Thrombocytopenia, or "low platelets", are terms used to describe a low platelet level in the blood. Fortunately, having a low level of platelets can be corrected for many patients.

Treatment/Remedy: The most common way to treat thrombocytopenia, assuming it is severe enough to warrant treatment, is with platelet transfusions and blood cell growth factors such as Neumega. Transfusions only temporarily correct thrombocytopenia and are associated with complications as well as disease progression and Neumega's efficacy has yet to be confirmed in Canada. Most physicians prefer to take a wait and see approach after discontinuing therapy. A break from chemotherapy usually restores platelet levels at which point the patient may then resume therapy.

The reduction in the frequency and severity of thrombocytopenia and its associated complications has resulted from scientists developing a better understanding of the basic biology of bone marrow blood cell production and from participation in clinical studies designed to evaluate strategies directed at reducing thrombocytopenia and its complications. Currently, there are several strategies aimed at improving the prevention and management of thrombocytopenia.

- **New blood cell growth factors:** Several new blood cell growth factors are being developed and evaluated in clinical studies for the purpose of improving chemotherapy-induced thrombocytopenia. AMG 531 is an investigative agent that stimulates the body to produce platelets and thus reduce or reverse thrombocytopenia and is continuing to undergo testing.
- **Peripheral blood stem cells:** Stem cells responsible for the production of platelets can be collected in large quantities from the peripheral blood. Delivery of peripheral blood stem cells following very high doses of chemotherapy has been demonstrated to result in more rapid platelet recovery than with stem cells collected from bone marrow. Many doctors have begun evaluating the use of peripheral blood stem cells to support multiple cycles of dose intensive chemotherapy alone or in combination with Neumega or other blood cell growth factors for the purpose of reducing the frequency and severity of thrombocytopenia and its complications.

Prevention: Chemotherapy-induced thrombocytopenia occurs because the chemotherapy drugs have destroyed many of the normal rapidly dividing cells in the bone marrow responsible for platelet production. Naturally occurring substances called cytokines exist in the body to

regulate certain critical functions at the cellular level. One group of cytokines is commonly referred to as blood cell growth factors. Blood cell growth factors are responsible for stimulating the cells in the bone marrow to produce more blood cells. A blood cell growth factor that is approved by the U.S. Food and Drug Administration (FDA) for the prevention of chemotherapy-induced thrombocytopenia is Neumega (oprelvekin). Neumega helps the bone marrow create more platelets and has been demonstrated in clinical studies to prevent thrombocytopenia and decrease the need for platelet transfusions in patients at high risk for developing thrombocytopenia. The most common side effect observed with Neumega is fluid retention or edema. This symptom persists while Neumega is being used and is reversible within a few days of discontinuation of Neumega.

## Tiredness (Fatigue)

Description/Symptoms: Fatigue is a general tiredness or an overwhelming lack of energy. It may be associated with an increasing need for rest, an inability to regain energy with rest, difficulty concentrating, or a disinterest in activities or events. 95% of those being treated for colorectal cancer report fatigue as a major side effect of therapy. Compared with symptoms such as nausea or pain, fatigue can be very difficult to identify and discuss. Sensations such as weakness, dizziness, difficulty thinking, being worn out, drained, and tiredness may be part of the feeling. Other symptoms associated with fatigue are leg pain, difficulty climbing stairs or walking short distances, and shortness of breath after light activity. People sometimes think they are just being lazy or depressed. They may tell themselves, “I can snap out of this if I really try.” Sudden changes in feelings of fatigue may mean there is a serious problem. Slower, gradual development of fatigue may lead to a decreased ability to perform everyday activities. There are no medical tests to measure fatigue; however, fatigue can be treated in many circumstances. Patients experiencing fatigue should report this feeling to their nurse or physician in order to determine whether a treatable cause of fatigue exists and to develop a strategy to reduce the amount of fatigue. Symptoms usually start out mild and become progressively worse such that you are unable to perform everyday activities.

Cause: The reasons that colorectal cancer patients experience fatigue are many and complex. In fact, fatigue often results from more than one cause and may require the use of many strategies for effective treatment. Generally, however, patients treated by surgery, radiation or chemotherapies experience such side effects as fatigue as a consequence of the therapy itself. All of the following can contribute to fatigue by decreasing the body’s ability to produce energy or by consuming the limited energy produced. **Anemia** is an inadequate supply of red blood cells, resulting in a decrease in the oxygen-carrying capacity of the blood. A common reason that colorectal cancer patients experience anemia is as a side effect of systemic therapies (**irinotecan, oxaliplatin, methotrexate, 5FU, xeloda, mitomycin c, avastin, erbitux, and vectibix**). Anemia is important because it may cause unwanted symptoms, such

as fatigue, tiredness or shortness of breath, and may exacerbate or cause other medical problems, such as a heart condition. The presence of **infections** in the body utilizes extra energy to fight the infection which can contribute to fatigue. Many drugs, including those used for the treatment of nausea (**antiemetics**), pain (**analgesics**), anxiety (**anti-depressants**), and other conditions, can cause fatigue as a side effect. Cancer or cancer treatments may also cause you to lose your appetite, or feel full early (early satiety). **Insufficient intake of calories** and vitamins reduces the body's ability to produce energy and may cause anemia. **Bed rest** or even restriction of activity for 1 or 2 days can decrease the body's ability to produce energy. Researchers have not identified how much rest is required for recovery versus how much rest contributes to low energy production. However, it appears that extended rest may contribute to fatigue and modest amounts of activity and movement can improve fatigue. Pain, anxiety, or depression can cause **stress** or result in sleep deprivation, causing increased fatigue.

Treatment/Remedy: Because fatigue can have so many causes, - nutritional deficit, colorectal cancer drugs, drug interactions, tumor activity, tumor death, inability to exercise, depression, changed sleep patterns – it is difficult to treat fatigue with other than trial-and-error methods. Fatigue has so many different causes and patterns that it may require the use of many strategies for effective treatment. For these reasons, it is important that you discuss your symptoms with your nurse or physician in order to devise an individual plan that will work. While there are no standard medical treatments for fatigue, new tools exist for evaluating and coping with fatigue. The following suggestions may also help you to cope with fatigue and have more energy:

- **Anemia** is the most common cause of fatigue in cancer patients. It is also very treatable. Treatment of anemia may involve the use of red blood cell boosters such as Procrit or Aranesp, a longer-acting form of erythropoietin that allows patients to receive fewer injections but these agents have been reported to promote cancer progression. Patients should discuss the risks and benefits of treatment with a red blood cell booster or blood transfusion with their doctor.
- Maintaining good **nutritional intake** with vitamin/mineral supplementation during treatment is especially important because cancer treatments increase the nutritional demands of the body. However, treatments may also cause you to lose your appetite, or feel full early (early satiety). Work with a dietician or nutritional specialist to ensure that you are getting proper nutrition. Conserve your energy by being realistic about how much energy you have and what you can and can't do. Only do the things that are most important and ask friends or family for help. It is important to recognize which activities create the most fatigue and also note the frequency, degree, and duration of fatigue so that you can report these to your doctor. If you're having difficulty managing fatigue, you may wish to ask your nurse or doctor to help family members understand how they can help.
- Maintaining normal **rest and sleep patterns** is important for ensuring quality rest. Plan your daily activities carefully, and schedule rest times between activities throughout

your day. Try to rest when you feel the worst and do your activities when you feel better.

- Review your **medications** with your doctor, pharmacist, or nurse to ensure that the medications are not causing or contributing to your symptoms. While conserving energy is important, it is equally important to understand that too much rest or inactivity can actually decrease the body's ability to produce energy and can worsen fatigue.
- Moderate **daily exercise**, such as walking, may help to increase your energy level.
- Counseling, support services, and medications can all play a role in **reducing stress** and thereby alleviating fatigue. The literature shows that even psychological counseling can help to alleviate fatigue.

A web site staffed by oncology nurses for cancer survivors suffering from post-treatment fatigue can be found at [www.cancerfatigue.org](http://www.cancerfatigue.org) . A discussion group for those suffering from cancer fatigue exists on the internet. Visit [www.acor.org](http://www.acor.org) to enroll in the cancer-fatigue discussion group. Support Groups affiliated with Colorectal Cancer Canada may be accessed at [www.colorectal-cancer.ca/en/find-support/colorectal-groups/#](http://www.colorectal-cancer.ca/en/find-support/colorectal-groups/#)

Prevention: It may be difficult to prevent the onset of fatigue brought on by colorectal cancer therapies, but the management may be more easily achievable than patients believe by adhering to the recommendations above.

## Tumor Lysis Syndrome

Description/Symptoms: The waste products of a tumor as it dies may disrupt natural levels of body substances such as electrolytes or antidiuretic hormone. Tumor lysis syndrome, arising from the death of large tumors, may arise shortly after chemotherapy is started. Tumor lysis syndrome may occur spontaneously, although the occurrence of this is rare. Some patients feel no symptoms of TLS in its early stages, but have abnormal laboratory results indicative of its progression. Laboratory results will show high potassium, uric acid and phosphorous levels and low calcium levels in the blood. Some patients with TLS may have initial symptoms including nausea and vomiting, shortness of breath, an irregular heartbeat, clouding of urine, lethargy and/or joint discomfort. If TLS is untreated, its progression may cause acute kidney failure, cardiac arrhythmias, seizures, loss of muscle control and death. Fortunately, TLS is a preventable and treatable condition, particularly in its early stages. Symptoms of kidney failure (such as excessive thirst, unusually high or low levels of urination, swollen limbs, yellowing skin, decreased sweat, abdominal pain) or heart or circulatory symptoms owing to excessive amounts of calcium, phosphate and potassium being released by dying tumors are noteworthy, and can be offset with oral or IV hydration, careful monitoring of electrolytes and use of diuretics.

Cause: Tumor lysis syndrome is caused by the sudden, rapid death of cells, particularly

cancer cells in patients with leukemia or lymphoma but can occur in colorectal cancer as well, in response to cancer therapies. Tumor lysis syndrome may occur spontaneously, without the introduction of therapies, although the occurrence of this is rare. When cancer cells are killed by therapy, they may spill their inner (intracellular) contents, which accumulate in the body faster than can be eliminated. These intracellular contents cause the metabolic and electrolyte disturbances that result in TLS. All colorectal cancer therapies have the potential to bring on TLS.

Treatment/Remedy: Intravenous hydration, medications including allopurinol or Elitek (rasburicase); and alkalization of the urine with sodium bicarbonate are typically employed. Once TLS has actually developed, a patient is also treated for the specific medical abnormality that is present, which typically includes one of the following:

- **Hyperuricemia** refers to excess uric acid in the blood. Uric acid is the end product of the digestion of certain proteins and is normally eliminated through the urine. When excess uric acid is present, it is converted to crystals formed of sodium urate. These crystals may deposit in the tiny tubes that are part of the kidney and cause acute kidney damage, which can ultimately lead to kidney failure. Treatment for hyperuricemia may include intravenous administration of fluids, diuretics to promote excretion of uric acid in the urine, an agent such as Elitek to reduce the formation of uric acid and the alkalization of urine;
- **Hyperkalemia** refers to excess potassium in the blood. Elevated levels of potassium can cause irregular cardiac (heart) rhythms and neuromuscular dysfunction. Treatment for hyperkalemia may include calcium administered intravenously to counterbalance the effects of elevated levels of potassium on the heart; dextrose (sugar) and insulin so that potassium is taken into cells, which reduces levels in the blood; agents to bind to potassium and promote elimination through the bowel; diuretics to promote potassium excretion in the urine; and sodium bicarbonate or an alkalizing agent to help neutralize the effects of hyperkalemia;
- **Hyperphosphatemia** refers to the presence of excess phosphates in the blood. Elevated levels of phosphates can cause low levels of calcium in the blood, or hypocalcemia. Complexes of phosphates and calcium can form and deposit in tiny tubes of the kidneys, which can ultimately lead to kidney failure. Treatment for hyperphosphatemia may include agents that bind to phosphates and promote elimination through the bowel so that they do not have an effect on the body. Diuretics may also be used to promote excretion of phosphates through the urine. In addition, dietary intake of phosphates should be restricted or eliminated; Hypocalcemia is the presence of low levels of calcium in the blood and may result in severe cardiovascular effects and neurological dysfunction (i.e. seizures, hallucinations, and numbness). Treatment for hypocalcemia may include the intravenous administration of some form of calcium and a diuretic to promote excretion of phosphates in the urine.

**Prevention:** Prior to starting treatment for colorectal cancer, patients should discuss their risk of developing TLS with their physician, as well as early warning signs that may indicate the onset of TLS. Careful monitoring of blood electrolytes can identify the early warning signs of TLS and therefore be remedied with and prevented by adhering to the above-noted treatments.

**W/**

## **Weight Loss**

**Description/Symptoms:** Weight loss is a common complication of cancer and cancer treatments that can result in a poor prognosis for patients. Cancer or cancer treatments first cause a loss of appetite or aversion to food, also known as anorexia, which then may lead to drastic weight loss. It is characterized by a significant loss in body mass.

**Cause:** Most colorectal cancer therapies can cause rapidly dividing cells to die more frequently than other cells. As the cells lining the gastrointestinal tract are rapidly dividing cells, when these are exposed to anticancer drugs, they die sooner than their natural cycle would dictate. As a result, it may become difficult to absorb nutrients during treatment for colorectal cancer. Clearly, the effect is made worse if nausea and diarrhea are present. Anorexia, which is a loss of appetite or aversion to food, can lead to drastic weight loss and compromise a patient's ability to get adequate nutrition through food sources. When you do not take in adequate calories and nutrients, your body is forced to "burn" fat and muscle stores, which is precisely why the patient loses weight. While not all colorectal cancer patients will develop anorexia and subsequent weight loss, anorexia and weight loss are very common. Anorexia may result from the cancer, chemotherapy, radiation or a variety of other causes, including physical and psychological causes. Anorexia that is a direct result of the cancer occurs in the majority of patients with advanced-stage cancers. For these patients, the cancer has changed the way their metabolism works, dramatically impacting their weight. In addition, cancer can have psychological and social impacts that cause stress and changes in eating patterns which can, therefore, lead to anorexia and weight loss. In many cases, cancer treatment, rather than the cancer itself, will cause anorexia. Both chemotherapies designed for the treatment of colorectal cancer (such as oxaliplatin, irinotecan, 5FU, xeloda, methotrexate and mitomycin C) and radiation therapy cause a variety of side effects that can lead to anorexia and weight loss, such as nausea and vomiting, fatigue, changes in how things taste and a dry mouth. In addition, cells in the body release tumor necrosis factor (TNF) and interleukin-1 in an attempt to fight the cancer, both of which cause anorexia. Destruction of cancer cells by radiation therapy increases levels of TNF and interleukin-1, resulting in anorexia and weight loss.

Treatment/Remedy: Treatment of anorexia and weight loss may include one or more of the following:

- **Total Parenteral Nutrition (TPN):** the intravenous delivery of a nutritionally adequate solution. It is used for patients who cannot eat and may be beneficial in the perioperative setting for cancer patients with severe malnutrition.
- **Enteral Nutrition:** the delivery of nutrients directly into the GI tract and is used when a patient cannot ingest, chew, or swallow food, but can digest and absorb nutrients.
- The use of **appetite stimulants** to aid in weight gain: These stimulants consist of **marinol** (part of the cannabinoids family produced in the lab and is a version of a naturally occurring substance in marijuana), megestrol acetate or **megace** (a progesterone, or steroid hormone, that improves appetite in patients with advanced cancer. Approved in the US), **dexamethasone** (a corticosteroid that is often prescribed for cancer-associated anorexia. Corticosteroids are substances produced by the adrenal gland which serve important functions in the body, including regulating metabolism and reducing inflammation).

Prevention: Some approaches that may help prevent anorexia and weight loss may include:

- **Control of nausea and vomiting** (through the use of anti-vomiting drugs administered 24 hours before and after therapy)
- **Maintaining adequate nutrition** (Receive adequate nutrition through food sources, as well as receiving it in addition to your diet in the form of **parenteral nutrition** (administered into the veins), or directly into the intestines with **enteral nutrition**).
- **Stimulating appetite** (through appetite stimulants which can help you to maintain adequate calorie and nutrient intake from food sources. These include **Marinol, megestrol acetate or Megace and dexamethasone**).

Try seeking out the advice of a nutritionist before and during therapy who may recommend that you focus on eating higher calorie foods, such as protein-rich foods. For example, you may try including more of the following in your diet:

- Protein drinks (powdered protein supplement mixed with fruit, milk and/or yogurt)
- Milk
- Dairy products
- Eggs
- Meat
- Sauces or gravies
- Oil

## Drug Monographs – Side Effects

The following links provide side effect monographs for each drug administered in the treatment of colorectal cancer.

**Avastin (Bevacizumab):** <http://www.drugs.com/sfx/avastin-side-effects.html>

**Decadron (Dexamethasone):** <http://www.drugs.com/sfx/decadron-side-effects.html>

**Erbix (Cetuximab):** <http://www.drugs.com/sfx/erbitux-side-effects.html>

**5FU (Fluorouracil):** <http://www.drugs.com/sfx/fluorouracil-side-effects.html>

**Irinotecan (Camptosar):** <http://www.drugs.com/sfx/irinotecan-side-effects.html>

**Leucovorin (Folinic Acid):** <http://www.drugs.com/sfx/leucovorin-side-effects.html>

**Methotrexate (Trexall):** <http://www.drugs.com/sfx/methotrexate-side-effects.html>

**Mitomycin C (Mutamycin):** <http://www.drugs.com/sfx/mitomycin-side-effects.html>

**Oxaliplatin (Eloxatin):** <http://www.drugs.com/sfx/oxaliplatin-side-effects.html>

**Regorafenib (Stivarga):** <https://www.drugs.com/sfx/regorafenib-side-effects.html>

**Vectibix (Panitumumab):** <http://www.drugs.com/sfx/vectibix-side-effects.html>

**Xeloda (Capecitabine):** <http://www.drugs.com/sfx/xeloda-side-effects.html>

## Sources

**The following links have aided in the compilation of treatment- and cancer-induced side effects as they relate to colorectal cancer:**

<http://www.about.com>

<http://www.drugs.com/>

<http://www.cancer.gov/cancertopics/chemo-side-effects>

[http://www.cancer.ca/Canada-wide/About%20cancer/Treatment.aspx?sc\\_lang=en](http://www.cancer.ca/Canada-wide/About%20cancer/Treatment.aspx?sc_lang=en)

[http://www.cancer.org/docroot/ESN/content/ESN\\_3\\_2x\\_Managing\\_the\\_Effects\\_of\\_Illness\\_and\\_Treatment.asp?sitearea=ESN&from=search](http://www.cancer.org/docroot/ESN/content/ESN_3_2x_Managing_the_Effects_of_Illness_and_Treatment.asp?sitearea=ESN&from=search)

<http://www.cancerhelp.co.uk>

<http://www.cancersymptoms.org>



<http://www.cancerbackup.org.uk/>

<http://www.cancerconsultants.com>

<http://www.cancer-pain.org/treatments/>

[http://www.healthcastle.com/se\\_radiation.shtml](http://www.healthcastle.com/se_radiation.shtml)

<http://www.mayoclinic.com/health/symptoms/SymptomIndex>

<http://www.mayoclinic.com/health/cancer-survivor/CA00073>

<http://www.medicinenet.com/script/main/art.asp?articlekey=21716>

<http://www.medifocus.com>

<http://www.merck.com>

<http://www.oncolink.org/coping/coping.cfm?c=5>

<http://www.patientcenters.com>

[http://hcd2.bupa.co.uk/fact\\_sheets/html/chemotherapy.html](http://hcd2.bupa.co.uk/fact_sheets/html/chemotherapy.html)