

# Headlines

Fall 08

A newsletter for brain tumour patients and their families

## MEDICAL UPDATE

### How does chemotherapy kill brain tumours?

**C**HEMOTHERAPY (meaning therapy using chemicals) has been used to treat cancer for decades, but brain tumours pose special treatment challenges. The brain is protected by a "blood brain barrier," composed of projections from brain cells and small blood vessels, which keeps toxins from entering the brain. Unfortunately, this barrier also keeps out some helpful drugs, including chemotherapy. In the last few decades, a number of drugs have been identified that successfully penetrate this barrier, including temozolomide and lomustine.

Radiation therapy and surgery are also important treatments for brain tumours. Their effects are confined to the area that receives the radiation beam or is under the surgeon's knife. We sometimes call these "local therapies." By contrast, chemotherapy is a "systemic therapy," meaning that it has the potential to affect all vulnerable cells throughout the body. This is an important distinction, and helps to explain some of the side effects of chemotherapy, as well as reasons why your doctors may choose to use chemotherapy.

**Cytotoxic chemotherapies:** Our bodies are composed of cells that must grow and reproduce in order to replace

cells that die or are injured. All of the cells of your body, whether normal or cancerous, go through a series of steps which result in the reproduction of one cell into two cells, each identical to the first. Some cells, like heart muscle cells or nerve cells, do not require constant replenishment and therefore do not constantly replicate, but others, including blood cells, do. Cancer cells are very active cells that must also keep up a steady rate of cell replication in order to grow.

Many cancer chemotherapies selectively target those cells that undergo continual cell reproduction, such as cancer cells. Commonly, this is done through damage to deoxyribonucleic acid, or DNA, which contains the blueprint, or recipe, for each cell, and must be faithfully copied in any new cell. When the damage occurs, the cell is unable to reproduce normally and dies. Because the goal of cytotoxic (meaning "toxic to cells") chemotherapy is to kill tumour cells by damaging tumour DNA, substances with the potential to repair DNA damage should be avoided during chemotherapy. Antioxidants, including vitamins C and E taken in large doses, may allow tumours to escape destruction by promoting the tumour cell's DNA repair.

Unfortunately, most chemotherapy cannot distinguish between cancer cells and normal cells, so any body cell that is actively reproducing may be affected by chemotherapy. Usually the damage to normal cells is not as severe as to cancer cells, but cancer doctors must plan chemotherapy doses at intervals that will allow time for normal cells to recover from damage. This is why we ask you to have a blood test before each chemotherapy dose, to ensure that the vulnerable blood cells have recovered to a safe level before you start a new round of treatment.

Not all tumour cells are actively dividing at one time. Less active cells are also less malignant, and these are not as vulnerable to the effects of chemotherapy. They may become more malignant over time, but we still cannot see them on a CT or MRI scan until they reach a sufficient number. Since chemotherapy is a systemic therapy with effects on all actively dividing cells, it is capable of killing even those malignant cells which are not numerous enough for us to see on scans, and which we therefore cannot identify to treat with radiation or remove surgically.

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## Managing the side effects of chemotherapy

**C**HEMOTHERAPY FOR BRAIN TUMOURS has advanced considerably in the past decade, both in terms of effectiveness and in terms of tolerability for patients. However, there is still a potential for side effects. Here are some of the most common ones, and suggestions for how you can prevent or treat them.

### Fatigue

This is the most commonly reported problem in any cancer centre, no matter what sort of cancer you have. The reasons for cancer-related fatigue are numerous, including anemia; the body's efforts to fight the cancer and adjust to treatments; anxiety; poor sleep; inadequate nutrition; and the effect of other medications such as seizure medicines. Try to remain active, but allow for short periods of rest during the day. Long naps in the daytime may prevent you from sleeping at night. Try to organize your day so that you are most active at the times when you feel most energetic. Mental fatigue may coexist with physical fatigue, resulting in or worsening memory problems. Use a notebook to write down the things you need to remember; keep pills in an organizer so that you don't forget to take them; write appointments down on a calendar kept in plain view; and rely on family and friends to help you get organized and accomplish the tasks you need to do each day.

### Infection

As noted in the Medical Update of this issue, blood cells are actively reproducing cells, and therefore vulnerable to the effects of chemotherapy. The white blood cells, including neutrophils, are responsible for fighting infections. Rarely the white blood cells may drop so low that an infection could be lethal. Blood tests are routinely done throughout chemotherapy to ensure that the blood cells remain at a safe level. If you are

taking chemotherapy, wash your hands frequently and avoid people who are sick. Check your temperature daily – a fever greater than 38 degrees Centigrade should be investigated and may require treatment with antibiotics, so call your doctor or nurse, or go the nearest emergency room. Dexamethasone, a steroid medication, may also affect the body's ability to fight infections. Your doctor may recommend that you take an antibiotic as a precaution if you are taking chemo as well as the steroid medication. White blood cells usually recover to safe levels if chemotherapy is stopped, delayed and/or reduced. These cells cannot be transfused.

### Bleeding

Another type of blood cell is the platelet, which helps the blood to clot when you cut yourself. If platelets are reduced by chemotherapy, you may be at risk for bleeding. Report signs of bleeding, for example from the gums when you brush your teeth, or with bowel movements or urination. Sudden onset of severe headache may indicate bleeding in the brain, a very rare complication of chemotherapy for brain tumour patients. The appearance of bruises or small red spots ("petechiae") on the arms, legs or trunk of the body may represent tiny hemorrhages under the skin. In severe cases of thrombocytopenia (meaning reduction in platelets), platelets may be replaced by a transfusion.

### Anemia

Hemoglobin is contained in red blood cells and carries oxygen to the body's tissues. Anemia occurs when hemoglobin is low and leads to fatigue, dizziness, pale skin and headache. If you are anemic, you are at a greater risk for falls because of lightheadedness and weakness. A transfusion of red blood cells may be ordered by your doctor.

### Nutrition

Eating well will help you feel your best. Nausea can usually be controlled by medications and diet, so let your health care team know if you are feeling ill on treatment. Follow the Canada Food Guide to ensure a nutritious diet.

[www.hc-sc.gc.ca/fn-an/food-guide-aliment/index\\_e.html](http://www.hc-sc.gc.ca/fn-an/food-guide-aliment/index_e.html)

See also Headlines Spring 2007 for information about diet and cancer.

[www.bccancer.bc.ca/NR/rdonlyres/41981E57-778D-4E85-82E2-58D8EE5C16D8/21890/HeadlinesSpring07.pdf](http://www.bccancer.bc.ca/NR/rdonlyres/41981E57-778D-4E85-82E2-58D8EE5C16D8/21890/HeadlinesSpring07.pdf)

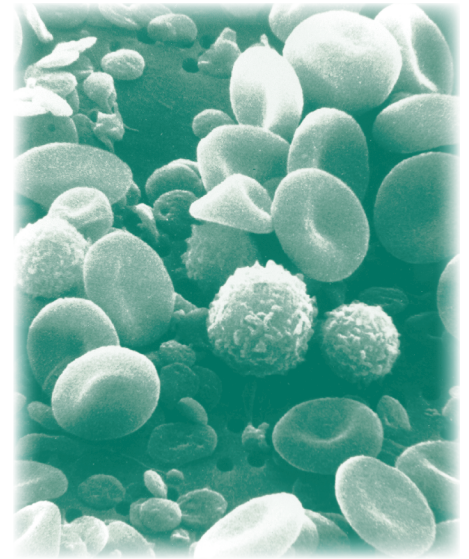


# Understanding your blood test results

## – The complete blood count (CBC)

**T**HE CBC IS A COMMON TEST that gives a very general picture of a person’s health. It is also an indication of a person’s ability to tolerate chemotherapy, which can cause a drop in the blood cells. If you are taking chemotherapy, this test is done at every clinic visit, and at outside labs between visits. Some terms you may hear:

- Cytopenia = Reduced blood cells
- Leukopenia = Reduced white blood cells
- Neutropenia = Reduced neutrophils
- Thrombocytopenia = Reduced platelets
- Anemia = Reduced red blood cells or hemoglobin
- Pancytopenia = All blood cells are reduced



Type of cell	Function	Normal range	If very low
White blood cells or “leukocytes”	Fight infection	4.0 – 11.0	Wait for recovery; avoid sick people; wash hands frequently; take temperature once a day and report fever greater than 38.
Neutrophils	Most common type of white blood cell; Fight bacterial and fungal infections	2.0 – 8.0	See above – low white blood cells
Hemoglobin	Carries oxygen to the body’s tissue	135 – 170 g/L men 115 – 155 g/L women	Transfusion of red blood cells
Platelets or “thrombocytes”	Clot blood	150 – 400	Transfusion of platelets

**How does chemotherapy kill brain tumours?** *continued from page 1*

**Therapies affecting blood supply of tumour cells:** Aggressive brain tumours are composed of rapidly reproducing cells. These very active tumours require nutrition and a means of removal of the waste products of metabolism. These processes occur through the blood, and in fact, aggressive brain tumours activate the growth of their own blood vessels. Some treatments target these blood vessels as a way of starving tumours. Such treatments are called antiangiogenic, meaning

“against the development of blood vessels.” Bevacizumab, also known as Avastin®, is a drug that blocks a protein called VEGF (vascular endothelial growth factor), which normally promotes the development of blood vessels. Interestingly, when temozolomide is given in a low dose, its mechanism of action against tumours is altered. Rather than killing tumour cells through DNA damage, it is believed that low doses of temozolomide have an antiangiogenic effect on tumour cells, too. In addition, the low daily dose combined with radiation sensitizes tumour cells to the harmful effects of

radiation, resulting in the destruction of more cancer cells. A third mechanism of the daily “dose intensive” therapy is the effect on a DNA repair gene, called MGMT (for methylguanine methyltransferase). When this DNA repair gene is inactivated, damage to brain tumour DNA by temozolomide goes unchecked, resulting in a more effective treatment against the tumour.

There are active research efforts underway to identify ways to increase the damaging effects of treatment on tumour cells, while minimizing harm to normal cells.

**Q** I finished my chemotherapy and radiation treatment in April and was taking chemo alone. After two months of chemo I had an MRI which showed that the tumour was bigger. My oncologist said I should continue with the same chemo, because the new growth might not really be tumour growth at all. He called it "pseudoprogession."

**A** Pseudoprogession is something that can happen in the first three to six months after radiotherapy or chemo-radiotherapy for high grade brain tumours such as glioblastomas and anaplastic astrocytomas, oligodendrogliomas and mixed tumours. In patients who have radiotherapy together with daily Temozolomide chemotherapy, it occurs about 20% of the time. Pseudoprogession can cause worsening symptoms in one third of patients. In the other two-thirds of patients that experience pseudoprogession, it is detected only on CT or MRI scans. What makes it "pseudoprogession", as opposed to "real progession" is that the cancer is actually not growing,

even though the patient may have more symptoms and their scan may look worse. Radiotherapy, especially when combined with chemotherapy, causes changes in the tumour's blood vessels, leading to swelling and tumour death that may mimic the appearance of tumour growth.

Patients often wonder why their oncologist recommends waiting for three months after the end of radiotherapy before booking a follow-up MRI. The reason is that pseudoprogession is most likely to be seen on a scan in the first three months. It can cause the scan to look worse, even though the patient feels fine and their cancer is in remission. A too-early MRI causes needless stress and anxiety for the patient (and their doctor) and can mistakenly lead to stopping an effective course of chemotherapy.

For patients who have worsening symptoms in the first three months after

radiotherapy, imaging is necessary and real progression of cancer is more likely than pseudoprogession, but pseudoprogession is still possible. If a patient is symptomatic, but otherwise in good health, it may be helpful to re-operate to relieve symptoms and remove the abnormal

areas on the scan. The pathologist can look at the abnormal tissue under the microscope to determine if it is real progression or pseudoprogession. Some studies have observed that patients with pseudoprogession actually do better in the long run than patients with steady improvement on their scans. The researchers surmised that pseudoprogession

represents a more rapid and complete response of the cancer to treatment.

*by Dr Alan Nichol, Radiation Oncologist  
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## Question + answer



## Nutrition for healthy blood

Chemotherapy and radiation may temporarily affect blood cells. A healthy diet will help your blood recover from these treatments and optimize your general health. The following nutrients are especially important:

### Protein

found in:

- Meat, poultry, fish
- Eggs
- Milk, yogurt, cheese
- Peanut butter, seeds, nuts
- Dried beans and peas
- Soy products, including tofu

### Iron

found in:

- Organ meats, like liver and kidneys
- Red meat, poultry
- Eggs
- Dried fruit, like figs, prunes, raisins
- Whole grain and enriched breads, cereal, pasta
- Soybeans, tofu
- Dried beans and peas
- Baked potato with skin
- Blackstrap molasses

To improve absorption of iron, have a vitamin C-rich food at the same meal with the iron-rich foods above

### Folate

found in:

- Organ meats,
- Dried beans and dried and fresh peas
- Green leafy vegetables, like spinach, romaine lettuce, broccoli and brussel sprouts
- Beets

### Vitamin B-12

found in:

- Organ meats and red meats
- Egg yolks
- Milk and milk products

Editions of *Headlines* are also available as a pdf download at:

[www.bccancer.bc.ca/HPI/CancerManagementGuidelines/NeuroOncology/PatientResources.htm](http://www.bccancer.bc.ca/HPI/CancerManagementGuidelines/NeuroOncology/PatientResources.htm)

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