

MEDICAL UPDATE

# The challenge of the blood-brain barrier in chemotherapy

HE BLOOD-BRAIN BARRIER (BBB) is a naturally occurring protective mechanism that was first discovered in the 19th century by a German researcher, Paul Ehrlich. He injected dye into the bloodstream of an animal and found that the dye leaked into the blood vessels of all body parts except the brain. Ehrlich's student, Edwin Goldmann, extended this discovery by injecting the dye directly into the cerebrospinal fluid surrounding the brain and spinal cord. This time, the dye stayed in the brain, but didn't leak into any blood vessels anywhere outside the brain. These researchers knew there must be something that acted as a wall or membrane between the brain and the rest of the body.

In fact, the BBB is a selective, or semipermeable membrane which restricts the movement of some substances into the brain while allowing others. It is composed of very tightly joined endothelial cells, the very thin cells that line blood vessels. These cells are surrounded by "feet," or projections of brain cells called astrocytes, which further restrict penetration of many substances into the brain. In general, the BBB very effectively protects the brain from harmful substances like bacteria, but permits the passage of essential substances like oxygen. Specialized proteins assist the transport of certain critically important molecules, such as glucose, across this membrane. Other proteins such as the MDR (multidrug resistant protein) actively pump out drugs that cross into the brain. In this way, the BBB helps to maintain a stable and safe environment for normal brain function.

Unfortunately, the BBB can also prevent the effectiveness of treatments for diseases of the brain, including brain tumours. Malignant brain tumours are nourished by an extensive network of abnormal blood vessels, and these disrupt the BBB to some extent, allowing some drugs to penetrate into the brain to varying degrees. Researchers are actively engaged in efforts to improve delivery of treatments into the brain. These efforts include the direct administration of drug treatments into the brain at the time of surgery.

Chemotherapy wafers (Gliadel®) can be placed in the tumour bed at the

time of surgery. These wafers contain carmustine, a variation of a commonly used drug called lomustine, which is an oral form of chemotherapy (that is, a pill taken by mouth). The chemo wafers have not been shown to be more effective than taking the same drug as an oral capsule or intravenous infusion, and the wafers can be irritating to the brain tissue, resulting in swelling and other side effects. As a result, in British Columbia the wafers are usually reserved for those individuals who cannot tolerate oral chemotherapy because their blood cells (white blood cells, red blood cells and platelets) have been lowered by treatment. Placement of carmustine wafers directly within the brain does not lead to effects on the blood cells.

The infiltrating nature of malignant brain tumours means that there are tumour cells scattered widely throughout the brain, and it's difficult for treatments to reach all these cells. Some research has focused on attempts to increase treatment penetration into the brain by means of convection-enhanced drug delivery, which uses constant pressure of a drug *continued on page 4* 

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## **Resources for Families** with Children

**Family Grief Support Program – Vancouver Hospice Society** This program is designed to meet the needs of children and surviving parents. The groups meet in separate rooms and are facilitated by qualified counsellors and trained volunteers.

The parents' group will include discussion of coping strategies, parenting issues and helpful resources. The children will have an opportunity for age-appropriate exploration of feelings and experiences and benefit from valuable peer support.

Pre-registration is required. Intake is ongoing.

**Dates**: September 23rd to December 16th, 2010 every other Thursday, 4:30 – 6:00 pm

**Location**: Vancouver Unitarian Community Building 949 West 49th Avenue (at Oak Street)

**Contact**: Noele Bird, Registered Clinical Counsellor Phone: 778 232 8272 or email: birdnoele@yahoo.ca

### The BCCA's Children's Club

This club is a support group for children, aged 6-12, who have a family member living with cancer. It meets from 1:00-4:30 on a Saturday afternoon, during which time the children make art, make friends, learn about cancer, and find support and answers to their questions. Parents are a part of the children's group at the beginning and end of the afternoon. In the middle of the afternoon, parents have their own support group.

If your family is interested in attending, there will be groups held at:

Dates and Locations: BCCA Vancouver Centre, October 16, 2010,

call to reserve at 604 877 6000, ext. 2194

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BCCA Abbotsford Centre, October 23, 2010, call to reserve at 604 851 4733 or 604 930 4000

**Empower** 

Empower is a new program designed to help family members and support persons of cancer survivors make the transition from active treatment to post-treatment life. The Program will provide support, information and tools to help participants with their own coping and self-care along with being better able to understand and help their loved one in dealing with post-treatment life.

Start Date: October 21st

Location: YMCA-YWCA, 851 Broughton Street, Victoria BC For more information or to register call 250 519 5525

## **Support Groups**

"The group is a place of healing for me." – patient

### Kelowna

3rd Monday of each month – 11:00 am to 12:30 pm Facilitator: Brigitte Wagner 250 712 3929 or 250 712 3963

Fraser Valley Contact Maureen Parkinson for more information 604 877 6000 x 2194

#### Vancouver

1st Wednesday of each month – 9:30 am to 11:00 pm Facilitators: Douglas Ozier and Rosemary Cashman 604 877 6000 x 2813, or 604 877 6072 Every other session is a split support group: one for patients, one for caregivers.

### Victoria

2nd Thursday of each month – 11:00 am to 12:30 pm Facilitator: Catherine Traer-Martinez 250 519 5528

## Did you know?

- It is estimated that 55,000 Canadians are surviving with a brain tumour, and each year a further 10,000 are newly diagnosed with a brain tumour.
- Brain tumours are the leading cause of solid cancer death in children under the age of 20, now surpassing acute lymphoblastic leukemia. They are the third leading cause of solid cancer death in young adults ages 20-39.
- There are over 120 different types of brain tumours, making effective treatment very complicated.
- Brain tumours in children are different from those in adults and are often treated differently. Although as many as 60% of children with brain tumours survive, they are often left with long-term side effects.



## **BCCA Community Forum –** Annual Cancer Conference

## A free public forum for all members of the community

When a loved one has cancer, family and friends become partners on a journey through care and treatment. Cancer patients, supporters, and caregivers are invited to learn how to better navigate this journey at the BC Cancer Agency's Community Care Forum, sponsored by the Provincial Health Services Authority. Learn about the latest in new cancer treatments, integrative cancer care, nutrition, lifestyle, cancer survivorship, and pain and fatigue management, and visit displays from the BC Cancer Agency and its community partners.



### **Community Cancer Forum – tentative schedule**

Time	Session A – Salon 1	Session B – Salon 2
10:00 am	What is cancer "Brain-Fog" anyway?	Nutrition to feed the soul and nourish the spirit
12:00 noon	Moving forward after cancer treatment	Empowering the mind, body and spirit
2:00 pm	Complementary Therapies	A personal journey: Bif Naked

### Date: Saturday, November 27, 2010

Time: 9:30 am to 4:00 pm

Location: Westin Bayshore Resort & Marina, 1601 Bayshore Drive, Vancouver B.C.

Registration is not required. More information: 604 707 5900 extension: 4626 or conference@bccancer.bc.ca

## **Cancer Transitions**

Cancer Transitions is a free, 2½-hour, six-week research program designed to help cancer survivors (for patients 2 weeks – 2 years post treatment) make the transition from active treatment to post-treatment life. Facilitators and guest speakers – including a nutritionist, oncology nurse and fitness specialists – will lead you in exercise, as well as helping with strategies for managing stress, eating nutritiously and managing your health concerns. Cancer Transitions will answer many of your questions about cancer survivorship after treatment. This course covers the following topics:

- Get Back to Wellness: Take Control of Your Survivorship
- Nutrition Beyond Cancer
- Exercise for Wellness: Customized Exercise
- Emotional Health & Well-Being: From Patient to Survivor
- Medical Management Beyond Cancer: What You Need to Know
- Life Beyond Cancer

### Vancouver

Dates: November 1st – December 13th, 2010 Follow-up ("Booster") session – January 10th, 2011

Time: Monday Afternoons 1-3:30 p.m.

**Location**: BC Cancer Agency, Vancouver Centre 600 West 10th Avenue

**Contact:** For more information and registration (pre-screening required):

Patient & Family Counselling Services 604 877 6000 ext 672196 1 800 663 3333 ext 672196

### Victoria

Start Date: October 21st

**Location**: YMCA-YWCA, 851 Broughton Street, Victoria BC For more information or to register call 250 519 5525

## Question + answer



I finished my radiation combined with chemotherapy 3 months ago and still feel very tired. How long should I expect to feel this way? Why am I so tried? Is it because I'm taking chemo again? Also, someone told me that the radiation will keep working and fighting the tumour for a long time. Is this true? If so, how long?

Cancer-related fatigue is a common side effect of cancer and its treatments. Fatigue due to radiotherapy tends to be cumulative (increases over time) over the course of treatment and can continue for weeks to months after treatment has finished. The degree of fatigue experienced varies between individuals. In general, the degree of fatigue tends to correspond to longer duration of radiation treatment, so more prolonged radiotherapy courses tend to make patients more fatigued. The part of the body receiving radiation can also have an effect, and it is recognized that radiation to the brain tends to cause greater levels of fatigue. Moreover, most chemotherapy also causes some degree of fatigue as a side effect. The severity of the fatigue depends on the type of chemotherapy and the dosage received, which varies among patients. It is known that patients having chemotherapy and radiation at the same time or one closely after another may experience more fatique.

There may also be other factors that are a source of, or contribute to fatigue, such as side effects from medications, anemia (low hemoglobin), dehydration, poor nutrition, pain, stress, or depression. A thorough evaluation by your physician may help to identify any of these contributing factors. Your health care team may recommend some steps that can be taken to reduce or even eliminate some of these causes of fatigue.

Fatigue tends to improve gradually after the end of radiation, although it is difficult to predict when it will completely resolve. There are several strategies that can help alleviate fatigue and reduce its impact on daily living. The BC Cancer Agency recommends drinking 8-10 glasses of non–caffeinated fluids a day when you are on treatment. Drinking fluids helps flush out the effects of radiation that lead to cellular fatigue. To maintain energy, balance your activities. Walking for 20-30 minutes a day increases the brain chemicals called endorphins that contribute to positive mood and energy. Modify, but try to continue your normal physical activities. A short nap during the day may also be helpful.

It is true that the effect of radiation on the destruction of tumour cells can continue for several months after the end of radiation. This is because of the way radiotherapy works. In simplified terms, radiation works primarily by causing damage to the DNA of cancer cells, which occurs almost immediately after exposure to the radiation. However, it is not until these damaged cells try to divide (as cancer cells do), that the presence of defective DNA results in errors, which become lethal for the cancer cells. Depending on the cancer type, some cancer cells may not divide for many months. Therefore, tumour cell destruction can keep occurring for months after the end of radiation treatment.

*By Dr. Arthur Cheung, Radiation Oncologist Abbotsford and Fraser Valley Centres* 

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through catheters to infiltrate the target area. Unfortunately, drug distribution to all tumour cells continues to be challenging. Promising new techniques include the use of improved catheter designs, as well as nanotechnology, whereby particles on a molecular scale are engineered to overcome the chemical and physical properties of the BBB and permit effective doses of drug delivery.

It should be noted that although further

research into improved drug delivery is important, the main reason for the failure of our current treatments for brain tumours is that tumour cells are, or become, resistant to these therapies, and as a result they will ultimately continue to divide and grow unchecked.

Editions of *Headlines* are also available as a pdf download at: www.bccancer.bc.ca/PPI/copingwithcancer/specificresources/Neurooncology.htm If you would like to submit an article, ask a question, or serve on our patient and family advisory board, please contact Rosemary Cashman at rcashman@bccancer.bc.ca or 604 877 6072 (phone) 604 877 6215 (fax).

All content by Rosemary Cashman unless otherwise specified.