



## Research Update

### Bacterial toxin kills most common form of brain cancer

A toxin produced by certain strains of *Escherichia coli*, such as the one that causes “hamburger disease,” induces programmed cell death in astrocytoma, the most common and most deadly primary brain tumour in humans. In the first animal model of the human tumour, researchers from Toronto’s Hospital for Sick Children and the University of Toronto achieved complete regression of human tumours growing in mice with just one injection of verotoxin (*Oncol Res* 1999;11:33-9).

Astrocytomas are “particularly resistant to treatment,” explains Dr. Clifford Lingwood. Patients with the most malignant form of astrocytoma, glioblastoma multiforme, survive an average of 12 months. Current treatment consists of surgical debulking of the tumour and radiation therapy.

Now that verotoxin has shown its worth in mice, Lingwood is hoping to test it in humans, pending approval of the research. “The plan is to have a few adult patients staggered with older children. We would be looking at its safety in adults before trying it in children.”

During cranial surgery, the neurosurgeon would debulk the tumour and inject verotoxin directly into any residual tumour. The main concern about using verotoxin is that verotoxin-producing *E. coli* can cause hemolytic uremic syndrome.

“It’s an obstacle, but I don’t think it’s insurmountable,” Lingwood says. He points out that the syndrome occurs mainly in young children. “It’s quite likely that adults and children older than 3 years are resistant to the

toxin.” There is also evidence that the bacterial infection itself, not just the toxin it produces, is implicated in hemolytic uremic syndrome. “Verotoxin given alone may be less pathogenic.”

There has been a flurry of research into the cancer-killing properties of verotoxin in astrocytoma, Burkitt’s lymphoma, ovarian cancer and some other cell lines. The receptor for verotoxin is found in elevated levels in many samples from these forms of cancer, and particularly from drug-resistant tumours.

Verotoxin induces cell death in both the tumour cells (antineoplastic) and the vascular cells around the tumour (anti-angiogenic). Thanks to this 2-pronged approach, it appears ideally suited to use as a cancer treatment, the authors conclude. — *C.J. Brown, CMAJ*

#### Research news

##### ***New view of tumours and blood vessels***

The traditional view that tumours lack blood vessels (avascularity) at first and then develop them as they grow (angiogenesis) is challenged by a new study of tumour growth in rats (*Science* 1999;284:1994-8). Researchers found that tumours initially grow by “co-opting” blood vessels in the host. The co-opted vasculature then regresses, causing the tumour to shrink and lose cells. The remaining tumour is then “rescued” by angiogenesis, which leads it to grow again. Two growth factors appear to regulate the balance between vascular regression and growth, determining whether the tumour will become established.

##### ***Tracking down the enzyme that causes metastasis***

Two research teams in Israel and Australia have cloned the enzyme that leads to cancer metastasis (*Nat Med* 1999;5:793-802,803-9). The enzyme, heparanase, is expressed in samples from human breast, colon and liver carcinomas. In experiments in mice, heparanase causes T-lymphoma and melanoma cells to become highly metastatic. The enzyme appears to degrade the extracellular matrix of healthy cells, allowing invading cancer cells to colonize. Researchers are hopeful that cloning the enzyme will allow them to develop molecular probes for early detection and treatment of cancer metastasis.

### A taxing situation

Quebec physicians with gross incomes of \$150 000 will pay over \$10 000 more in provincial and federal tax than their counterparts in Alberta in 1999, *Strategy* magazine reports. The magazine, published by MD Management Ltd., reported in July that a Quebec doctor would pay \$68 500 in taxes, compared with \$58 200 for doctors in Alberta. The magazine’s calculations assume that the taxpayer claims only the basic personal exemption tax credit.

The roughly 40 doctors in the Northwest Territories/Nunavut pay the least territorial and federal tax in Canada — \$56 800 on gross incomes of \$150 000. In comparison, Ontario physicians can expect to pay \$60 700 for earning the same income, and British Columbia doctors will pay \$64 500.

