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# Cancer chemotherapy is shown to impair the brain

**Findings that it can kill cells and cause areas to shrink lend support to patients' reports of feeling mental effects.**

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Cancer chemotherapy can impair the brain, killing crucial neural cells and causing key parts of the organ to shrink, according to two studies released this week.

The new findings add to a growing body of evidence suggesting that "chemo brain" — the mental fuzziness, memory loss and cognitive impairment often reported by cancer patients but often dismissed by oncologists — is a serious problem.

"Those of us on the front lines have known this for a long time, but now we have some neuropathological evidence that what we are seeing involves an anatomic change," said Dr. Stewart Fleishman, director of cancer supportive services at Beth Israel Medical Center and St. Luke's-Roosevelt Hospital Center in New York.

He said the most common question he encountered from patients during his public lectures was: "My doctor doesn't believe me. How can I convince him this is real?"

The new studies should help convince physicians who are skeptical about the issue, said Fleishman, who was not involved in the research.

Because chemotherapy is a crucial cancer treatment and cannot be abandoned, scientists are calling for increased research on shielding the brain from its toxic effects and developing more-selective cancer drugs.

"There are no easy answers," said Dr. Patricia K. Duffner of the State University of New York at Buffalo medical school. "We must balance the need for survival with quality of life."

Several studies have suggested that 40% to 80% of cancer patients receiving chemotherapy suffer from chemo brain. The problem is particularly severe for breast cancer patients, Fleishman said, because the treatment induces hormonal changes typical of menopause, and these changes can also produce memory problems.

The condition has also become more common as chemotherapy has increasingly been used at an early stage of treatment rather than as a last resort.

Dr. Masatoshi Inagaki of the National Cancer Center Hospital East in Chiba, Japan, led a team that used high-resolution magnetic resonance imaging to compare the brains of 51 women who received chemotherapy for breast cancer with those of 54 breast cancer patients who had only surgery.

Inagaki and his colleagues reported Monday in the current issue of the journal Cancer that, one year after treatment, key areas of the brain involved in cognitive processes — including the prefrontal, parahippocampus and cingulate gyri — were significantly smaller in the women who had chemotherapy.

The greater the volume loss in those areas, the team found, the greater the difficulty shown by the women in tests of concentration and memory.

When the researchers studied the same women three years after therapy, however, the volumes were about the same in both groups of women, suggesting that the brain has unsuspected recuperative powers.

In the second study, biomedical geneticist Mark D. Noble and his colleagues at the University of Rochester Medical Center in New York exposed human brain cells and brain tumor cells grown in a laboratory dish to three of the most commonly used cancer drugs: carmustine, cisplatin and cytarabine.

They reported Thursday in the Journal of Biology that low doses of the drugs caused a 60% to 90% reduction in the viability of the brain cells but had little effect on tumor cells. To kill 40% to 80% of the tumor cells required doses that killed 70% to 100% of the brain cells tested.

Even though the cancer drugs target replicating cancer cells, the researchers found that replicating and nonreplicating brain cells were killed.

The researchers then administered the drugs to mice and autopsied their brains. They found that the drugs killed cells in several regions of the brain and that cells continued dying, in some cases for several weeks after the cessation of treatment.

"This is the first study that puts chemo brain on a sound scientific footing," Noble said.

In a third study, reported last month in the journal Breast Cancer Research and Treatment, Dr. Daniel Silverman and his colleagues at UCLA's David Geffen School of Medicine used positron emission tomography to study brain metabolism in 16 women who underwent chemotherapy and surgery for breast cancer and five who had only surgery. They also studied 13 women who did not have cancer and received no treatment.

They imaged the brains while the women were at rest and while they were performing exercises in short-term memory. They found that the women who received chemotherapy had lower metabolism rates while they were resting than did the women in the other two groups. The lower the resting rate, the more difficulty the women had on the memory tests.

During the memory tests, the metabolism of the women who received chemotherapy rose sharply.

"In effect, these women's brains were working harder than the control subjects' brains to recall the same information," Silverman said.

They also found that the effects persisted in some of the women for at least 10 years. Silverman

said they were able to detect abnormalities for a longer period than the Japanese group could because PET is a more sensitive assay.

Some research has also shown that stimulant drugs such as dexmethylphenidate — trade-named Focalin and used in treating attention deficit disorder — help combat fatigue and cognitive impairment associated with chemo brain, Fleishman said.

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