Rumored effect is still a puzzle

There's never an ideal time to be hospitalized. But some anecdotal evidence has hinted that midsummer might be the worst time of all to find yourself admitted to a teaching hospital. In July, interns and residents begin their new positions. The idea that these inexperienced physicians could negatively affect patient outcomes is known as the "July effect."

Studies of the July effect are few, however, and their conclusions have been mixed. To take a fresh look at this rumored phenomenon, DMS researchers compared mortality and complication rates at teaching hospitals to rates at nonteaching hospitals for hip-fracture patients aged 65 and older.

Fragile: "Hip-fracture patients are frail and pretty fragile, and they actually have relatively high morbidity and mortality," says Kenneth Koval, M.D., a coauthor of the paper, which was published in the *American Journal of Orthopedics*. "We thought if there was a July effect, we might see it on these patients who are most vulnerable."

With Kane Anderson, M.D., then a resident at DHMC, and research associate Kevin Spratt, Ph.D., Koval gathered data from the National Inpatient Sample on nearly 325,000 patients treated for hip fractures between 1998 and 2003. They divided the years into two-month blocks and compared patient outcomes during each block at the two hospital types. They found that patients aged 65 and older who were treated for a hip fracture during the July-August block had a slightly higher risk of death in teaching hospitals (3.92%) than in nonteaching hospitals (3.50%). But the relationship was just the reverse in September-October.

The hip-fracture mortality rate was *lower* in July-August.

And that wasn't the whole story. They did *not* find an increased risk of complications at teaching hospitals in July-August, though they'd be expected to go hand-in-hand with mortality. Even more perplexing, the mortality rate for hip-fracture patients was actually *lower* in July-August at both hospital types than in most other two-month periods. In other words, though the aggregate risk of death was slightly higher in teaching hospitals, July-August was one of the least risky times to be treated for hip fracture. "We don't know why that is, but it seems to be a consistent finding," Spratt says, noting that it was observed in each of the years examined.

Despite this unexplained dip, Spratt adds, the July effect appears to be a real phenomenon that holds true year after year among hip-fracture patients. But, he cautions, "I would be reticent to assume that a July effect is pervasive across all kinds of patients."

Puzzling: Koval agrees that the findings are puzzling—but he sees no evidence that patients should be worried about being hospitalized in the summer. "What it all means is unclear, and more research is necessary," he says. So it seems that for the time being, the existence of the July effect remains an open question. KIRSTEN WEIR

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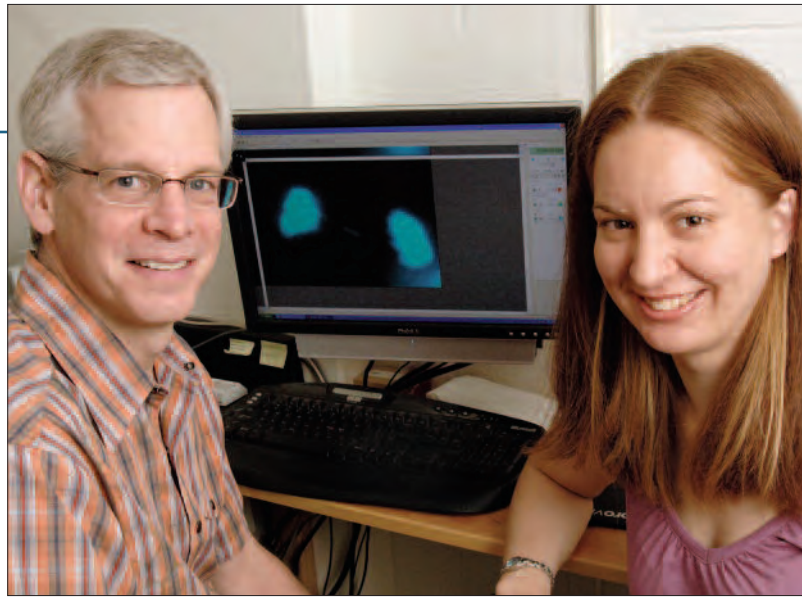

Compton, left, and Thompson study chromosome missegregation in tumor cells.

When good cells go bad

Two DMS biochemists have identified a link between a tumor suppressor gene and a crucial step in cell division. During cell division, cells copy their chromosomes and then split them evenly between two "daughter" cells. This process—chromosome segregation—usually goes smoothly. But about one in every hundred divisions, a chromosome missegregates; it ends up in the wrong daughter cell, leaving one daughter cell with too many chromosomes and one with too few, a condition called aneuploidy. One in a hundred sounds like a successful rate, says Duane Compton, Ph.D. "But when you consider that in our bodies there are tens of millions of cells that divide every minute, one in a hundred is pretty bad actually."

Potent: Aneuploidy is common in tumors and can indicate a poor prognosis. But as Compton and graduate student Sarah Thompson already knew, something often prevents aneuploid cells from proliferating. "We wanted to understand what was happening to those aneuploid cells," Thompson says. They hypothesized that a tumor-suppressor gene, p53, might play a role. Compton says p53 is "very potent. . . . When it gets activated, it just shuts down the cell cycle."

To test that hypothesis, Compton and Thompson induced cells from human tissues to missegregate chromosomes and measured p53 levels in the resulting cells. They found higher levels of p53 in aneuploid cells than in normal cells. And as expected, the aneuploid cells did not continue to grow and divide. But when they knocked out the p53 gene, preventing cells from producing the p53 protein, they found that even aneuploid cells were able to continue to divide.

Next, they combined a loss of p53 with elevated rates of chromosome missegregation and found that this combination produced cells that resemble tumor cells. "In essence, we can convert a normal cell into what looks like an aneuploid tumor cell," Compton says. Eventually, this knowledge may help the researchers find a way to prevent aneuploid tumor cells from growing and dividing. AMOS ESTY