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Life-saving surgery gets prof back to work UA researcher has part of his skull removed, then reattached, after stroke

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April 20, 2002, is the line of demarcation in John Pepper's life.

Before that day, he was strong and confident. After, he was passive and helpless.

Before, he was decisive, clearheaded and witty, attributes prized in his life as a researcher and father. After, he left faucets running all over his house, didn't know his daughter's birthday and was cranky a lot.

Before, his name appeared on the programs of symposiums and seminars, highlighting his expertise in biology. After, for nearly three years, it is absent from the scientific roll call, as though Pepper had disappeared.

In a way, he had.

Vibrant man changed

Pepper, an associate professor of ecology and evolutionary biology at the University of Arizona, does ground-breaking research with cancer cell computer modeling that could change the way doctors treat the disease. He supervises graduate students' lab research and teaches undergraduates the joys of science.

And he does it with nearly one-quarter of his brain tissue dead from of a blood clot that shook itself loose in 2002.

Pepper, 49, ticks off the effects of his stroke dispassionately, as a scientist: "Initially, I was very dulled down. I can't touch-type as well. I still work hard at enunciating. My speech is clumsy."

His wife, Gillian Pepper, 53, and daughter, Delia Pepper, 14, are more specific about the effects of the event that shattered their lives: Pepper lost the concept of time, slept 23 out of 24 hours, was unpredictably irritable and unsafe at certain times.

"The John I knew before the stroke was very funny, goofy, sensitive and full of energy," Gillian Pepper said. "After the stroke, it was like an old man woke up in my bed. He was basically sleeping away most of his life. He was no longer my partner inspiring me on, but somebody I looked after in addition to Delia."

Pepper was a postdoctoral fellow at New Mexico's Santa Fe Institute in early 2002 and had sent out applications for a tenure-track position at various universities.

UA offered him a job and, in April, he and his family flew to Tucson to look for a house. Pepper was 43, a

daily exerciser and in seemingly perfect health.

"I got out of bed one morning and just fell to the ground," he recalled.

Annoyed that his wife and aunt were hovering over him, he tried to tell them to move so he could stand up. In his mind, he heard the words, but what came out of his mouth was gibberish.

He was taken to Northwest Medical Center and was given a clot-busting drug. Testing revealed he had high blood pressure and a hole in his heart, neither of which he knew about. In less than 24 hours, his brain tissue was so swollen doctors performed a hemicraniectomy, a controversial procedure in which a portion of the skull is removed to relieve pressure.

"He was dying," his wife recalled. "They removed the right half of his skull and kept it in the freezer. Then they induced a coma to reduce his metabolism to give his brain a chance to stop swelling."

Pepper was brought out of the coma after about 10 days.

His medical team recommended long-term rehabilitation at Craig Hospital near Denver and advised Pepper - who had regained the ability to speak - to be realistic about his future.

"I kept talking about how I was going to be a professor when I got out and they basically said, 'Good luck with that,' " he recalled.

"Nobody . . . really believed it would ever be possible for him to go back to work," his wife said. "At the time we thought he was being pigheaded and we were despairing because he would never accept his deficits."

John Pepper described his determination matter-of-factly.

"I don't give up on what I want until I have no choice," he said. "I decided to keep trying to return to biology until I was forced to give up, or it became clear that it was impossible. Being a scientist is not just a way to make a living for me. It feels like my calling - my way of expressing my creativity and contributing to the world. No other work I've done feels like that to me."

Plenty of support

Pepper's family advised Richard E. Michod, head of UA's ecology and evolutionary biology department, of his stroke and asked Michod for a deferral of Pepper starting work at UA. Michod agreed.

The Santa Fe Institute volunteered to extend Pepper's contract so he would have medical coverage, and faculty and staff donated sick time and vacation hours so his salary could continue.

Pepper spent about four months in Colorado, returning to Tucson once to have his skull - which was still in a freezer at Northwest Medical Center - reattached. During that time, he went from wheelchair to walker to walking with a cane.

In Santa Fe, Pepper worked with therapists on his balance, speech and strength. He worked at the institute as much as he could, trying to build up endurance so he could work at UA.

"Immediately following the stroke, I was much slower and I made a lot more mistakes," Pepper said. "I had less mental energy. I'd have a conversation and have to sleep for one or two hours to recover."

But he never gave up.

Gillian Pepper said her husband was completely unaware of - and unwilling to accept - his deficits. She thinks that internal blindness, the necessity of the brain to see itself as whole in spite of its injury, might account for his determination.

"No one thought we should pursue coming to Tucson, but John was so passionate about it, I felt I had to support him," she said. "By the time he came to Tucson to take up work, his seizures were under control and he had a whole army of external memory aids. He was as ready as we could make him."

After consulting with College of Science Dean Joaquin Ruiz and his department's faculty, Michod allowed Pepper to buy a recliner for his office so he could take a nap in the afternoons if needed.

"It was tragic this happened to John and we all wanted him to recover," Michod said. "We wanted to give him the best chance for the life we knew he could have had before the stroke."

There were no promises, Michod said, in that when Pepper comes up for tenure review next year, he will have to meet the same standards everyone else meets.

"I suppose we didn't have to keep him," Michod said. "John was chosen from a search and there were runners-up, so we could have just checked him off and gone to the second-place person and, in the short term, maybe it would have been beneficial to our program."

"But when you hire someone you view them as part of your family. Even if he hadn't come back and produced independent research, we still would have done it. He's a clever guy, he's got good ideas, but that's normal stuff you expect from scientists."

"The human situation, though, that helped all of us grow as people."

John Pepper said conventional wisdom holds that brain cells destroyed equal a part of the brain lost forever.

"But new research shows that the brain can retask," he said. "A part of the brain assigned to one task can learn to take over the tasks normally assigned to another part of the brain."

He points to his life as proof it works.

"It set me back a couple of years professionally," he said of the stroke. "I'm productive now, but my first couple of years as a professor here, I didn't publish at all. All my yearly reviews were, 'You've got to do better,' and I would say 'I will do better.' At your three-year review, they can fire you, and I barely squeaked by by getting published right before that."

He considers himself "close to 90 percent back" to normal. Which is about where his wife and daughter think their family life is nowadays.

Reconnecting with daughter

As a scientist, Pepper knows human bodies are not meant to survive a brain injury, so when they do, there are side effects. For him, those were the grand-mal seizures, extraordinary fatigue and family relationships that were "turned upside down."

Delia was 8 when he had his stroke and remembers being angry and afraid in its wake.

UA researcher has part of his skull removed, then reattached, afterstroke

"For awhile, he would literally sleep all through the night and day and wake up only for dinner," the 14-year-old University High School freshman said. "A lot of it was the (anti-seizure) medicine, but it was really hard for me because I never got to see him or talk to him or anything."

Gillian Pepper attributed her husband's behavior to "medication fog."

"He'd leave the gas stove on, faucets gushing, left the doors open and the puppy would escape," she said. "Delia ended up kind of scolding him and something changed in their relationship that was very sad to see."

His daughter said therapy helped her understand why she was scolding her father.

"He would forget all sorts of things and it was pretty unsettling to see an adult not acting like he should," she said. "I was pretty confused by that. Adults are the ones who are supposed to take care of you and make the rules, and I was trying to let him know that wasn't what I wanted him to do as a father."

Because John Pepper had always been a devoted parent, his wife said he recognized the trauma his daughter was experiencing and "tended that relationship with her."

"He was gracious about her trying to teach him how to play chess again, and he spent a lot of his little time (awake) with her, so they survived," said.

So did their marriage, which some might say was a miracle equal to his return to science. They've been married 16 years, six of those under the uncertainty that marks a life after stroke.

"I missed the John who used to be, but at the same time, I was forgetting who that John was with the passage of time," his wife said. "It was a loss with no name. It seems now like I'm getting John back, the essential John. He was always there, and when he was rested, I could connect with that John and that was a very important part of my staying."

"He might have lost the outer things I fell in love with, but the deep, sensitive person was always there. . . In recent times, as he gains more vitality, I find I'm being charmed by him again. We've had a bad thing happen to us in the very best way."

Delia Pepper said that her relationship with her dad "probably isn't the usual father-daughter relationship" but she brims over with emotion when speaking of how far he's come.

"I'm so proud of my dad when I see he does this incredible stuff and he's becoming more and more well-known in his field, and this is from a man they didn't think would ever walk again," she said.

"He does stuff with part of his brain gone that most normal people can't do with a whole brain."

Professor pursues new therapies to help conquer cancer

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Undeterred by the debilitating stroke he suffered in 2002, John Pepper has pursued his research on the evolution of cancer cells as a way to curb the often deadly disease that is adept at developing resistances to drugs.

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Natural selection is an important - and fast moving - part of the evolution of cancers, Pepper said.

"Normally when someone thinks about natural selection they think about the history of the Earth, from slime to fish to dinosaurs to mammals," said Pepper, assistant professor of ecology and evolutionary biology at the University of Arizona.

"We're doing a pretty dramatic frame shift here in how we speak of natural selection. Instead of millions of years on the planet Earth, we're talking about a handful of years inside a human body."

Human cells can reproduce numerous times a day, he said.

"When cells die, they pass on the traits that make them better or worse at surviving and reproducing," he said.

"Over many generations of cells, on the order of a day or so, the cells get better and better at surviving and reproducing, and reproducing more quickly.

"Cells get better and better at freeing themselves from anything that would limit reproduction. Finally they remove all limitations and are able to just divide constantly, and that is cancer."

Doctors have long used poisonous drugs called cytotoxins to kill off individual cancer cells.

While that method can kill many of the cancer cells present, Pepper said, some are resistant to the cytotoxin poisons and evolve through natural selection to return stronger - and more deadly.

He likened the scenario to a crop infested with insect pests.

When farmers use herbicides to try to wipe out pests, offspring from bugs resistant to the poison will come back stronger the following year. They'll be better able to reproduce and grow because of less insect competition for eating the crops, and the herbicide will not harm them.

By looking at the evolutionary traits of cancer, with the rapid changes as the cells reproduce and become stronger through evolution, Pepper has determined that other therapeutic methods may better fight diseases like cancer.

Cancer tumors are solid and have no natural blood supply of their own, Pepper said. They must instead tap into other sources of nourishment to flourish and spread.

"If you apply a drug that blocks the formation of blood vessels, then the tumors can't grow," he said. "They suffocate and die."

Such drugs have been available for years, but have not been widely seen as a primary method of battling cancer, he said.

"There are ways to fight cancer that are more sophisticated than just trying to kill the cancer cells," he said. "The drugs that block the birth of blood vessels are not poisons that poison cancer cells, and they don't trigger the evolution of resistance."

New therapies could control the growth and spreading of cancers without the threat of the cancer cells developing a resistance to the drugs, he said.

Pepper said he looks to medical research specialists to move such alternative cancer therapies from lab theory to the pharmacy shelf.

Facts about stroke

Stroke happens when a blood vessel carrying oxygen and nutrients to the brain is blocked by a clot or bursts.

The first stroke type is called ischemic and the second is hemorrhagic. John Pepper's stroke was ischemic.

Both types result in the brain being starved of oxygen. When that happens, the brain starts to die. Depending on how major the stroke is and how long before a person receives treatment, a whole section of the brain may die.

The part of the body controlled by the section of the brain affected by the stroke displays the symptoms. Paralysis, diminished language and vision can result.

Stroke can cause problems with thinking, awareness, attention, learning, judgment and memory. Survivors often have problems understanding or forming speech, and may have difficulty controlling their emotions.

Recurrent stroke is frequent; about 25 percent of people who recover from their first stroke will have another stroke within five years.

SOURCE: National Institute of Neurological Disorders and Stroke

Warning signs of stroke

The National Institute of Neurological Disorders and Stroke lists the following as symptoms of a stroke:

- * Sudden numbness or weakness, especially on one side of the body
- * Sudden confusion or trouble speaking or understanding speech
- * Sudden trouble seeing in one or both eyes
- * Sudden trouble with walking, dizziness or loss of balance or coordination
- * Sudden severe headache with no known cause.

Caption: John Pepper (left), an assistant professor at the University of Arizona, had a stroke in 2002. He and his daughter, Delia, 14, and wife, Gillian, shown at dinner last week, worked to put it behind them. Doctors at Northwest Medical Center removed a large portion of John Pepper's skull to relieve pressure from his brain's swelling after his stroke. The piece of his skull was kept in a freezer and later reattached. John Pepper and his daughter, Delia, had to work hard on their relationship after his stroke. 'I decided to keep trying to return to biology until I was forced to give up, or it became clear that it was impossible. Being a scientist is not just a way to make a living for me. It feels like my calling - my way of expressing my creativity and contributing to the world.' john pepper John Pepper and Gillian Pepper have been married for 16 years, six of those after his stroke. Their daughter, Delia, right, attends University High School. Gillian Pepper with husband John Pepper after he awoke from a medically induced coma after surgery to remove a large part of his skull. John Pepper, assistant professor of

ecology and evolutionary biology, works in a University of Arizona lab with graduate student Will Driscoll.

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