

*The odds were against Keeper when a sudden illness landed him in the emergency room.*

**Researchers are seeking a happier ending for dogs facing the ogre of veterinary cancers—hemangiosarcoma.**

By Mara Bovsun

# Rewriting the Script



Last April, Elizabeth Fletcher, of Cashiers, North Carolina, was on the road to a Pennsylvania dog show when she got a panicked call from her pet sitter.

“Keeper’s acting weird,” the sitter said.

The usually confident Bernese Mountain Dog was very clingy and panting heavily. The sitter put Keeper on FaceTime so Fletcher could see for herself. She told the sitter to get her

beloved show dog to a vet ASAP.

Given the symptoms, Fletcher’s first thought was bloat, a common and potentially deadly condition in dogs of Keeper’s size, about 124 pounds.

It wasn’t bloat. It was much worse.

The vets found two large tumors on his spleen. One had ruptured, filling his abdomen with blood, a condition called “hemoabdomen”—blood in the belly.

“This is cancer,” the vet said with

certainty. “Probably hemangio.”

Few words are more terrifying to dog owners than hemangio, short for hemangiosarcoma. Experts call it the “ogre of veterinary cancers.” Tumors arise from cells that line blood vessels, so they can pop up anywhere—skin, muscle, heart—and metastasize quickly. The spleen is among the most common sites.

There may be no symptoms until a tumor ruptures, then things careen

BAROGRAPHY BY KIM HOLLIS

downhill. A dog may seem fine at breakfast and be gone by suppertime.

The vets told Fletcher there was virtually no chance the tumor was benign. Euthanasia, they suggested, was the kindest, most sensible course of action.

Only in Keeper's case, it would have been dead wrong.

## FACT FINDING

"Almost a coin toss" are the words veterinary oncologist Chand Khanna, DVM, Ph.D., DACVIM (Onc), uses when discussing the odds that a splenic tumor is malignant or benign.

Khanna, president of Ethos Discovery, a nonprofit incubator of scientific innovation, says the tragic script most vets follow is based on studies that have been around for years. "The script is based on low-evidence retrospective studies," he says. That data said a splenic tumor was most likely malignant and that treatment would buy, at most, a few months.

With such a grim prognosis, vets often advise owners that it would be kindest to put the dog down.

"Misinformed euthanasia" is how Khanna characterizes it.

Ethos is conducting a 5-year study of 400 dogs who have come to a vet or emergency room with a bleeding splenic tumor.

The trial is called Ethos-PUSH, which stands for Precision Medicine Umbrella Study for Hemangiosarcoma. It is partly supported through a \$348,000 grant from the AKC Canine Health Foundation.

Ethos-PUSH is about halfway through patient enrollment—with about 200 dogs—but early findings are already challenging two assumptions:

- The widely accepted notion is that splenic tumors are almost always malignant in large, older dogs. But the Ethos study has found that the chance that a splenic tumor in this population is benign is approximately 40 percent.

- Another belief is that a dog,



*Dr. Chand Khanna and his canine companion, Odin, 13. Khanna, a veterinary oncologist with a Ph.D. in cancer biology, chose hemangiosarcoma as a target because veterinarians across disciplines have labeled it the worst cancer dogs face.*

especially an older one like Keeper, 8, will probably die during surgery. But data from the Ethos study suggests that over 95 percent of dogs walk out of the hospital within 40 hours of surgery.

The worst possible scenario was presented to Fletcher on the phone when she had to choose between gambling on an emergency splenectomy, which could cost up to \$10,000, or gently ending her dog's life.

Fletcher was on the road, in a panic, and struggling to make this life-or-death decision on the fly. She called a friend, Georgeann Reeve, president of the Bernese Mountain Dog Club of America. Among Berner people, Keeper is a fluffy, four-legged celebrity. He has an impressive list of accomplishments, including co-starring in the movies with Mark Wahlberg.

"Elizabeth," Reeve told her, "you owe it to Keeper to give him that chance."

In a snap, Fletcher made up her mind.

"Go for it," she told the vets.

"You do realize he may not make it through the surgery," she recalls one vet saying. Another said, "It's probably

cancerous. We just want to tell you this."

"Yes, I realize that," she said. "Let's just go for it."

Then she drove nonstop through the night to be by the side of her once-in-a-lifetime companion.

## SURFING FOR SURVIVAL

Consistent with the new Ethos Discovery data, Keeper defied the first grim prediction by sailing through the operation. The surgeons removed the organ and whisked tumor tissue samples to a testing lab.

It would be an agonizing 11-day wait before Fletcher would know the results.

"Just enjoy your dog. Spend all your time with him," her regular vet advised. She did that. But she also remembered advice from a dog show friend she called during her frantic drive home.

"Why don't you look for a clinical trial?"

She hit the internet, Googling "hemangiosarcoma clinical trials." The PUSH study was among the first to come up. She contacted Ethos.



# Cure *is the Word*

Ethos Discovery is an independent nonprofit incubator of scientific innovation aimed at finding new solutions for some of the worst veterinary health issues, says Chand Khanna, the organization's president. Its goal, he told FD, is to bring high-level scientific research to veterinary medicine.

"High-level means prospective research," he says.

In prospective studies, information about individuals with a confirmed condition—such as dogs with spleen tumors—is collected over time, monitoring reactions to treatment, disease progression, and other variables.

Much veterinary research is based on retrospective studies, in which subjects, such as dogs who die from hemangiosarcoma, are chosen as a sample. Then scientists work backward—through interviews and written records—to fill in information about past events that may have contributed to the outcome. Khanna believes that this model leaves too much room for bias and error.

Ethos-PUSH is an example of a prospective study. The starting point is when a dog with a bleeding spleen tumor is brought to a vet. Over five years, the treatment section of the trial will test eight different drugs and combinations of them against the disease.

Khanna has a 30-year history of research innovation. Two decades ago, he spearheaded an initiative to study naturally occurring cancer in dogs and apply the findings to fighting human cancer. It blossomed into the National Cancer Institute's Comparative Oncology Program.

When discussing PUSH, Khanna uses a word seldom uttered in relation to hemangiosarcoma: cure. "I'm not afraid of saying the word 'cure' for hemangiosarcoma," he says.



"Without saying it, you can't achieve it."

He points to the history of childhood leukemia as his inspiration. About 60 years ago, there was little hope to cure a child with certain forms of this blood cancer; about 70 percent succumbed to it.

"Today, the majority of children with leukemia have a curative outcome," he says. In designing PUSH, he followed the roadmap established by pediatric cancer researchers. Among the elements he borrowed from the Children's Oncology Group were:

- Welcoming ideas from diverse sources, such as academic institutions and biopharmaceutical firms;
- Working with an extensive network of hospital groups, which will give more patients access to the trial; and
- Exploring several drugs and combinations instead of a single treatment.

"Our goal, without equivocation, is to deliver curative outcomes to dogs with hemangiosarcoma in the same way that it's been done in children with leukemia," he says.

Khanna quickly responded.

"Your vet gave you a small chance of him living, I'm sure. But we have found in our studies that these dogs, the older large dogs, have a 40 percent chance that it's not cancerous," he wrote in an email. He asked her to send him all medical records, including the surgeon's report.

"Then, we wait," he told her. If the diagnosis was cancer, Keeper could enroll in the treatment part of the PUSH study.

Eleven days later, the biopsy report came back.

"I cried. I just cried," Fletcher recalls. Both tumors were benign.

Khanna had his specialists run additional tests, looking for evidence of cancer. All came up clean.

Keeper is a living example of two findings from the Ethos study so far. Even in large, older patients, more than 95 percent of the dogs in a state-of-the-art emergency hospital will survive and be ready to go home in less than 40 hours.

"Surgery is not the problem it once was. That's not surprising, given the advances in care that have occurred in my lifetime in the profession," says Khanna.

Second, this study did not support

the idea that the tumor is likely cancerous. Previous research has led to the standard often-quoted estimate—much less than a 20 percent chance that the tumor is benign. But the PUSH study was finding there was double the chance of a benign result. For these dogs, removing the spleen is curative.

"Although euthanasia is always an important question to consider in the management of any complicated problem," Khanna says, "it doesn't *have* to be the answer for dogs with this medical problem."

Keeper and owner Elizabeth Fletcher had to wait 11 days to learn if his tumors were cancerous. The results of tests for several cancers were a big surprise that had them both jumping for joy.



Keeper's booming voice could be heard as Fletcher talked to FD on the phone in July. She is grateful he is still with her. Still, she can't stop thinking about another incident years earlier with another Berner.

That time, she heard the word "hemangio" and chose euthanasia, figuring, as the vets told her, that the tumor was most likely cancer. She will never know for sure—there was no necropsy—and it haunts her.

Khanna has a similar regret. "I believe that I misinformed people in my career based on this incorrect data," he told FD in a Zoom interview. "It's really important to change the discussion presented by the primary care veterinarian so that the dog isn't euthanized inappropriately."

What has Fletcher learned?

She told FD that she will never base major decisions on a single veterinary opinion. "I will definitely do my own research and be my own advocate for my dog—and for myself, too." **FD**

## Where to Look

There are many ways to find a clinical trial—including the internet, word of mouth, and breed clubs that help to fund these studies.

The Canine Health Foundation lists major research organizations with clinical trial databases, including the American Veterinary Medical Association and the National Veterinary Cancer Registry. To learn more, visit [akcchf.org/research/participate-in-research/clinical-trials.html](https://akcchf.org/research/participate-in-research/clinical-trials.html).



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