



Photo by Lincoln Ritter

I Wondered as I Wandered

By Sue Ritter

According to my Mother, my first scientific observation was that the lady bug “hads two eyeds on its nodse.” Although that observation was made at a very young age, it took many years for me to discover the scientist within me. There were no scientists in my family or among any of my acquaintances. We had no television. Until I went to college, I had little or no concept that science was still going on somewhere or that real people did it. But the seed of that reality was planted in my mind one night as my Dad and I sat on the hill in front of our house watching the stars in the Oregon sky. I was probably pestering him with questions — although I don’t remember that part of the story, I had been told more than once that when God passed out the questions, he gave me more than my share.

What I do remember was that my Dad said to me, “Someday you could be an astronomer and study the universe. Maybe you could find the answers to some of the questions you’re asking me.” That statement, which may well have reflected my Dad’s exasperation, turned out to be my inspiration. Someday maybe I could find the answers.... That thought captivated me the moment it was spoken and has scintillated in my memory since that night.

I didn’t become an astronomer. I spent most of my childhood – well into my high school years – kicking stones, so to speak. Climbing through the dark bowels of the giant cedar trees in the middle of the pear orchard where the owls roosted during the day. Riding my horse “like the Indians did,” with no saddle or bridle. Poking around the pack rats nests on the mountainside behind our house. That sort of thing. And when I married Bob – on the day after his college graduation – the stone kicking didn’t stop.

The thing about Bob was that he had a driving interest in biology. As newly weds, we spent endless hours in the woods looking for salamanders, toads, snakes, butterflies. It seems that no stone in Pennsylvania, where Bob had entered vet school, was left unturned. No log went unlifted, no puddle unnoticed in the search for nature’s treasures. But Bob’s interest in biology had a scholarly bent and that gave stone kicking a new dimension for me. The process of learning about nature that Bob was already obsessed with quickly drew me in. As opposed to idle curiosity, which had previously been my specialty, Bob pursued what I think of as vectored curiosity. Always observing, digging

Without precise routines, detailed searching and meticulous recording, human ideas could never be validated nor replicated; but it is the human spirit of curiosity, the very human “need to know” that drives scientific progress. That element—the *human* conduit—provides the connection. It is to this humanness we owe all modern progress, and it is for those among us who believe that the creative human impulse basic to discovery is worth exploring that we dedicate this forum: *The Human Side of Science*.

Thanks to Ken Campbell for giving creative birth to this series and to Sue Ritter for this third contribution. Volunteers are needed to continue this most entertaining and enlightening journey. Please let Ken or Jeanne Jensen know if you would willingly share your own human story.

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deeper, reading, trying out new thoughts. There were ways to find answers! I caught the excitement. In discovering Bob, I discovered myself. But the big idea of making science my career was still a synapse away.

I came upon the field of neuroscience by walking around the corner of my last semester of undergraduate

school and bumping into it. After wandering through undergraduate school for seven

semesters, changing paths 3 or 4 times, it was a startling experience.

Out of necessity, I had delayed my last semester to work and had ended up time-slipping in the lab of a neurologist, Dr. Richard Harner, who was studying sleep cycles in cats. My work ranged from cleaning cages to analyzing EEG records and assisting in surgeries. In his lab, I discovered that there were so many more questions needing answers than I had previously imagined! Dr. Harner insisted that I read journal articles on the physiology of sleep, and he talked to me about them. He invited me to come with him to neurology rounds at Children's Hospital. He introduced me to other scientists, including graduate students, at the University of Pennsylvania. He gave me a virtual reality

experience of being a scientist. He gave me Marie Curie's biography to read. Dr. Harner changed my life. Now I could see the path ahead and I could see myself already on that path. A Velcro path – like in *2001, A Space Odyssey* – and me in Velcro shoes. I was bonded to the idea of becoming a neuroscientist.

There were a few obstacles ahead.

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Most of them were products of the time and sound trite now

in the retelling. Like having the chairman of the department where I first applied to graduate school tell me that they didn't accept women because it was a waste of time training them (they always had babies and left the field). Like discovering that the male graduate student in the program where I was accepted received a graduate assistantship that was three times more than mine (mine was roughly \$1,500 per semester) because he would probably, since he was male, be better at maintaining the equipment in the laboratories we both taught. Like trying year after year to get summer salary at WSU and having the chair tell me that I should be at home during the summer with my children and like having the dean scold me as if I were a child myself for finally going over my chairman's head to try to make it happen. Like having

the vet students file a formal complaint because they found it hard to take a pregnant professor seriously. But I was stuck on that Velcro path and I still am.

Curiosity has been the vector in my scientific career. I believe my career has been driven at every step more by curiosity than by insight. I think of curiosity as God's invitation into the hemispheres of His mind. It is a compelling invitation. One thing that is amazing to me is that the focus of my curiosity has remained so constant for so long a time. The rest of my adult life has changed in the normal dramatic ways, going from children at home again to no children at home, but I am still pursuing the same core questions that I inherited from my own Ph.D. mentor, Dr. Larry Stein, and my adoptive mentor, Dr. Alan Epstein. There has always been one more step to take and each step has launched another. Like stones at the creek crossing, I hope each footing will be true and that together they will provide a route to solid ground.

I have always been fascinated by the controlling grasp of biological need on brain function. I've studied this through the narrower question of how an animal's need for glucose is detected and translated into neural signals that orchestrate the multiple levels of response required to reduce that

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need. Because the brain has an absolute requirement for glucose as a metabolic substrate, glucose deficit is acutely life threatening. Detection of glucose deficit activates systems that seemingly or maybe actually commandeer the animal's entire response network. The animal's life is instantly reorganized, priorities are dramatically altered, sensation

is re-directed, physiology is changed from cells to systems, reproductive capacity is

put on hold. The animal is driven behaviorally to find and to consume food, while its physiology is shifted to meter out the remaining metabolic fuels in a way that will ensure that the food-seeking behaviors can be carried out. This is amazing. How does it happen?

After many years of work, the determination and unfailing expertise of my long-time co-investigator, Thu Dinh, the energies and insights of several stellar graduate students, and the always pivotal input from Bob, we now know that receptor cells that detect glucose deficit are located in the hindbrain and that these glucoreceptors control multiple brain systems through catecholamine (norepinephrine and epinephrine) neurons. The cell bodies of these catecholamine neurons are

located in the hindbrain glucoreceptive zones. Their processes distribute to all parts of the central nervous system, thus enabling their executive role in arousal of multiple glucoregulatory responses. Thus far, we have shown specifically that projections of catecholamine neurons to the forebrain arouse feeding behavior

and projections to the spinal cord increase adrenal medullary secretion (which in turn

elevates blood glucose). Through their innervation of hypothalamic cells containing the peptide, CRH, these catecholamine neurons also control secretion of glucocorticoids, which have powerful modulatory effects on the responsiveness of multiple glucoregulatory systems.

The brain has other mechanisms that operate at the cellular level to adjust local glucose flux to accommodate local changes in neural activity, but the hindbrain glucoreceptors operate at the systems level to ensure the delivery of glucose to the brain as a whole. It has become clear from the recent work of my student, Nicole Sanders, that disruption of the hindbrain mechanisms we have identified is the cause of the glucoregulatory failure known as Hypoglycemia Associated Autonomic Failure (or HAAF), a

potentially lethal side effect of insulin therapy in diabetic patients. We now also know that there is a peripheral system(s) for monitoring the availability of metabolic fuels utilized by tissues outside the brain that is separate from the hindbrain glucoreceptive system. This system is especially sensitive to fat, a major energy source for most peripheral tissues, but one that does not enter the brain. The receptors that activate this system are located outside of the brain, possibly in the abdominal viscera or fat pads. Like the central glucoreceptors, these peripheral receptors also drive food intake, but their full range of action on physiological function is not yet known.

This process of curiosity-driven discovery has presented me daily with challenges and rewards. It is an exciting way to live. And if my students continue to keep me in line, I think I can be fairly optimistic that that some of our more recent hypotheses will turn out to be closer to the truth than my debut "eyes on its nose" hypothesis of ladybug sensation.

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From ladybugs to neuroscience, the path of human discovery can yield many turns. Please share the story of your unique path with your VCAPP colleagues!

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