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VICTOR CHANDLER TWITTY

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A Biographical Memoir by

NORMAN K. WESSELLS

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V. C. Twitty

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Control of growth of the eye, reasons for the appearance of stripes of pigment cells along the sides of a tadpole, homing to a stretch of stream by a salamander climbing over a dry, thousand-foot-high ridge, searching for the sensory basis of homing in salamanders—two records of distinguished research in the seemingly disparate fields of vertebrate embryology and animal behavior.

Victor Chandler Twitty was a master experimentalist in both venues—the laboratory bench and the mountain terrain and streams of the American West. The unpredictable path of scientific discovery, curiosity about nature, and chance led to this unusual personal history. As Twitty wrote in an autobiographical sketch in 1966, "The role of chance in research and discovery is greater than is generally recognized, and this will be exemplified as the narrative moves from New Haven to Berlin to Stanford, from microsurgery to natural history and back again, and from the study of cell populations in tissue culture to the study of animal populations in the streams and hills of northern California." Telling this story reveals much about the rich intellectual and personal life of one of the mid-century America's leading embryologists.

Victor Chandler Twitty was born near Loogootee in Martin County, Indiana, on November 5, 1901. He was the youngest of five children of John McMahon Twitty and Emma Chandler Twitty. After a boyhood in southern Indiana, he graduated from high school and spent a year in the service of industry and finance. His meteoric rise during that period from factory flunky to filling-station attendant to bank teller transformed Twitty into a painfully earnest young man, and reawakened his father's hopes that there might be some scholarly possibilities in him after all. So, Twitty enrolled in Butler College (now a university) in Indianapolis, where he did exceptionally well from the very start. It was good fortune for him and for science that he took that year off prior to entering Butler, for if he had gone directly to the state university with his high school friends he would have been immersed in basketball, fraternities, and a very different life. Twitty received an A.B. degree in chemistry from Butler in 1925, and then went on to graduate school.

Twitty described his choice of Yale University's Department of Zoology for graduate training as "fortuitous and fortunate." The faculty of the Osborn Zoological Laboratory, headed by Ross Granville Harrison, included several outstanding scientists at the peak of their careers and a group of graduate students who would go on to make significant contributions. Of his choice of embryonic development for graduate training and specialization, he says, "I arrived at Yale with little preparation or bias that would predispose me in choosing among areas of modern research and specialization in the department." Years later Twitty regarded his chance wandering into the Harrison orbit as the single greatest piece of good luck in his life. His choice of Harrison and field of study was surely apt, for it resulted in a career of distinction and honor.

The 1920s were exciting years in embryology. The definitive paper on the discovery of the embryonic organizer was

published in 1924. Harrison, who invented cell and tissue culture in 1910 as a means to investigate growth of the nerve fiber, and Hans Spemann in Germany were the two world leaders in embryology. Harrison and his students used microsurgery, transplantation of tissues between amphibian embryos, and tissue and cell culture to investigate problems of growth accommodations and conflicts and the means by which the sizes and the orientations of body parts (eyes, limbs) are regulated as an embryo develops. Experiments using vital dyes (that stained cells and allowed them to be followed in living embryos), among other things, had made mapping the embryo a possibility. Embryonic induction, cell migration, and cell and tissue interactions were being discovered and analyzed for the first time. A new Yukon was opening to which eager miners, in the words of Harrison, were now rushing to dig for gold.

Victor Twitty received his Ph.D. degree from Yale in 1929. His thesis research involved salamander embryos and indeed those sorts of animals would keep his attention for the ensuing forty years in both laboratory and field. The processes by which sets of hair-like cilia on embryos establish regularized patterns of beating, and the relative growth of eyes transplanted between large and small or slow and fast growing species were investigated in the graduate years. Twitty stayed on in New Haven for two years as an instructor and, besides continuing to develop into a superb teacher and investigator, truly struck gold in meeting a talented art student, Florence Eveleth, who was to become his wife on August 3, 1934. But, before then, in 1931, Twitty himself went as a National Research Council fellow to Otto Mangold's laboratory at the Kaiser Wilhelm Institute in Berlin.

Harrison urged the great European metropolitan center of Berlin, perhaps as a means of cultural salvation for his young Indiana Hoosier protege. Mangold, one of Spemann's students, had in fact just completed the line of experiments

Twitty proposed for the fellowship year, namely, to investigate whether the absence of an organ in a species of salamander is due to a hereditary inability to form the organ or whether the inductive stimulus for the organ is absent. So Twitty started another imaginative project on the determination of the initial size of organ rudiments. Though his experiments were fully successful, the results were never immortalized in print, because Twitty learned too late that a student of Spemann (Rotmann) had finished similar investigations. These were "maturing" but not discouraging incidents in Twitty's early scientific life, for they reflected that he was aiming at central questions of interest to the best laboratories in Europe. The Berlin year was not a waste; besides learning new techniques, Twitty met Spemann, Richard Goldschmidt, Johannes Holtfreter, Viktor Hamburger, and Dietrich Bodenstein, who would become lifelong friends or visiting scientists in Twitty's laboratory.

Twitty was well aware in 1932 of the tightening of the job market because of the Great Depression, so he declined a second year in Berlin and became an assistant professor in the Department of Biological Sciences at Stanford University in Palo Alto. The first decade of Twitty's career at Stanford was an exceptional time in the university's history. George Beadle and Edward Tatum began their Nobel Prize-winning work on genes and metabolism. C. B. van Niel at Stanford's Hopkins Marine Station was solving the fundamental chemistry of photosynthesis. And the physics and electrical engineering that was to give birth to the Stanford Industrial Park—and later Silicon Valley—was underway. Twitty's experimental program was diverse and path breaking, his experimental designs elegant, and his science rigorous and self-critical. He investigated the factors that control the proportional size of organs—for example, why an eye with all its complex parts grows to just the right size in its normal

host embryo, although that same eye might grow to be much larger if placed in a host embryo of another large-bodied species or smaller if into a smaller-species embryo. He was fascinated by the phenomenon of cell migration, how and why certain pigment cells migrate long distances in embryos and take up residence at just those appropriate sites that yield recognizable color patterns. Such patterns include the stripes along the sides of salamander tadpoles and adults or the striping of zebras and tigers, and of course such patterning has survival value or behavioral roles in various species. Among other discoveries was the effect of a restricted volume, in the form of tissue culture fluid inside narrow capillary tubes, on the ability of primitive migrating cells to mature into blackened mature pigment cells. Such observations led years later to the identification of conditioned medium effects and growth factors on cells. Twitty also had that valuable capacity to recognize the unexpected observation as scientifically significant; he and a student noticed, for example, that embryos of eastern salamanders remained motionless as if anesthetized after they received grafts of tissue from western salamanders. That led to discovery and chemical identification by colleagues in chemistry and medicine of a unique and powerful neurotoxin produced by both embryonic and adult western salamanders.

Perhaps Twitty's greatest strength as an investigator lay in an exceptional ability to cut through the complications of a problem or observation and to frame scientific questions in simple terms, which led to straightforward experiments with a minimum of variables and a maximum of interpretable results.

Twitty's productivity and fine teaching were recognized quickly, and he advanced to the rank of professor in just four years. Soon numerous capable graduate students came to study with Twitty. The result was a stream of scientific

papers that brought respect and admiration to Twitty and excellent careers for many budding scientists, who later worked and taught at leading American colleges and universities.

Between the 1930s and the 1950s a number of established experimental embryologists, including Bodenstein (a leading student of insect development from Germany), went to Palo Alto to work with Twitty and his students, thereby enriching the intellectual breadth and experimental approaches of the laboratory. To students and senior visitors alike Twitty gave generously of himself, both as a scientist and as a friendly and compassionate man. He was able to instill his own instinct for and understanding of the experimental approach, his ability to analyze problems into their simpler components, and his appreciation of the role of chance in research and discovery, as well as his unusual talent for accepting scientific or personal disappointment philosophically. His quiet, soft-spoken demeanor put undergraduates, graduates, and professional peers at ease; yet, always present was a sharpness of intellect and penetrating understanding, which taught, served as model, and goaded others to think more precisely and prudently.

Twitty was one of the few twentieth-century American biologists who made very significant contributions in different disciplines of biology. After doing so much in experimental embryology, Twitty was led inadvertently by his experimental material to a new career in animal behavior. While collecting embryos from streams in different parts of California, Twitty and his students noticed differences in egg laying and in pigment patterns of embryos. A long story cut short, this led to identification of different species of the renamed genus *Taricha*. Twitty's analyses of migrating pigment cells in embryos of different *Taricha* species involved at one point creation of hybrid embryos between

two species. Difficulty in rearing the hybrids to sexual maturity in the laboratory made it impossible to tell whether the hybrids would have any evolutionary potentiality or consequence. That led fortuitously to a 14,000-acre mountain ranch in northern California, where hybrids were freed in the ideal habitats of the Pepperwood Creek system. Soon new questions about the juveniles and adults arose; would individual hybrids, or members of the separate parental species for that matter, return for breeding to the site on streams where they were embryos or tadpoles or juveniles? Not being willing to wait the four to six years it takes for California newts to reach sexual maturity, Twitty and his "field crew" of associates and students began immediately to mark and release breeding adults. Oscar Anderson, Herbert Little, and David Grant were the core of that talented and observant team.

The results were spectacular. A very high percentage of individuals returned the following year to their breeding sites; indeed the same individuals came back again, year after year, to their particular spots on the creek. In fact, over 20,000 individuals marked over a number of years have yielded only *one* animal that entered one of the other creeks in the drainage! Could animals return home to specific stream sites if moved many yards or a mile upstream or down, or even over thousand-foot-high ridges? The answer was a resounding yes; even in the case of release five miles away over two mountain ridges and with an inviting intervening creek, animals returned with a remarkably high frequency to their original stream sites. In fact, Twitty's traps set along the way revealed that the small amphibians took a beeline route to home. Random wandering or searching down one stream and up another was not the way of homing.

Naturally, questions followed. What senses were used in the extraordinary homing process that Twitty and his stu-

dents discovered? Vision? Olfaction? What? Understand that no such work had been done on salamanders in the 1950s when this work began, and Hasler's discoveries of the olfactory basis of salmon homing in streams were just being revealed. Twitty's simple and elegant experimental design, used so long in the laboratory, was applied with equal rigor to these field studies.

Twitty's humanity and respect for nature showed through, too. Investigations on the sensory basis of homing involved at one point removing the eyes from embryos, releasing the operated animals various distances downstream and then waiting until the following year. Amazingly, the operated newts began appearing at the original stream site where they had been reared prior to capture and operation. They came overland, not eating normally as they traversed the dry, rocky hillsides. Twitty's reaction (1966) to one animal tells much about him:

> Of the countless displaced newts that I have handled, I think none has made such an impact on me as the first one of these blinded animals to be recaptured. As I examined its empty eye sockets and emaciated body (many blinded newts do not feed at all!), and then looked downstream toward the heavy forest and rugged terrain it had traversed in coming home, my respect for its accomplishment came as near awe and reverence as can be inspired by lowly organisms or possibly even by their highly evolved descendants.

The release and recaptures told Twitty new things about newt life spans; that released hybrids survived and reproduced very well; and that olfaction was likely to be one of the senses involved in homing. (We know today, but did not then, that many vertebrates use magnetic clues to orient during migration or homing.) Unfortunately, Twitty's untimely death ended this fruitful line of observation and experimentation, although there is solace perhaps that even now in the late 1990s some of his marked newts and hybrid populations march each rainy season to remembered breed-

ing sites on Pepperwood Creek. He may be there in spirit to observe in admiration their journey home.

During this field phase of his career, Twitty was not just a field naturalist who goes and watches nature. He was in heart and mind an experimentalist; whether during the early decades at the laboratory bench or during the last two decades in the field in Sonoma County, he could think only in terms of experimental questions and manipulations. Looking and wondering, which he did with such pleasure, was just not enough; his science demanded more than that to reach satisfying answers.

Victor Twitty's distinction as a scientist was recognized in his election to membership in the National Academy of Sciences and the American Academy of Arts and Sciences. He was also a member of numerous other scientific societies in the United States and abroad, and he was a frequent referee of papers submitted to the *Journal of Experimental Zoology*, *Growth*, and other journals that held the mid-century literature of his science. His string of papers on newt homing and behavior that appeared in the *Proceedings of the National Academy of Sciences* was widely read and quoted as this field of animal behavior unfolded. He was honored in 1964 by being named the Herzstein Professor of Biology at Stanford, that university's oldest, most honorific endowed chair.

Twitty's special ways with people included the ability to lead productively. He was executive head of biological sciences at Stanford from 1948 until 1963. That was a momentous time in biology worldwide, and those departments that hesitated in moving toward new paradigms of research were long in recovering. Twitty's foresight led to the appointment of Charles Yanofsky, Donald Kennedy, Paul Ehrlich, Peter Raven, Clifford Grobstein, Winslow Briggs, the author of this memoir, and many others, just as the move of

Arthur Kornberg and much of the Washington University microbiology department to Stanford Medical School transformed basic medical sciences just a few hundred yards from the Biological Sciences Department. Twitty brought to the chairmanship a sense of direction and purpose, good judgement, tact, an ability to delegate responsibility, and a capacity to compromise the desirable with the possible. He recognized what was coming in biochemistry, the neurosciences, and his own embryology before it metamorphosed into "developmental biology." Although he had no interest in leaving his beloved studies of newt homing, he helped assure that those sorts of evolving disciplines would thrive in Palo Alto.

I met Victor a few days after arriving in Palo Alto as a postdoctoral fellow (with Clifford Grobstein) in August 1960, after a painfully slow drive across the country from New Haven in an old Plymouth. A new Ph.D. in embryology from Yale was a sign to him that I was okay, so off we drove to Rossotti's Alpine Inn in Portola Valley for beer in the warm, dry afternoon of flickering sunlight under the sweet smell of eucalyptus trees. Talk of "the chief," as Harrison was known, and Yale and eastern embryologists was the only agenda, but welcome was the message. Soon Victor couldn't resist describing his Pepperwood newts and his new love in science. That same sort of personal warm welcome went to new Assistant Professor Donald Kennedy, future president of Stanford University, who arrived from Harvard by way of Syracuse that same hot August. This was in a way a benign facet of what has come to be called an old-boy network; institution of graduate training, major professor, and such went with the more objective credentials of quality of scientific work itself. From that first meeting through times of pleasure and trial for the department as geneticists and biochemists from the medical school tried to chart its fu-

ture until Victor's death in 1967, warmth and friendship are the two dominant memories that Kennedy and I, as well as others, have of Twitty.

Victor Twitty's other personal life was full. Florence and he had five children: John, Eveleth, Sarah Ellen, Edith Ann, and an adopted son Kalevi Holsti (whose brother Ole Holsti is a distinguished political scientist at Duke University). The Twitty home was warm and open, an oasis of friendship for students and visiting scientists, a place for informality and the sharing of a beer or bourbon whiskey and talk about embryos or newt homing or art and water colors. Victor was from boyhood an ardent, successful fly-rod fisherman, especially when it came to rainbow and steelhead trout. He and Florence loved the outdoors, so the many weeks of hard science work at the newt ranch in northern California was a cherished time each year. At home on Alvarado Row on the Stanford campus their annual summer vegetable garden supplied family, friends, and biology department colleagues with sweet corn, zucchini, and the produce of shared, enjoyed labor under the warm California sun. Their homes were also the sites of biology department "high teas," receptions for faculty, graduate students, retirees, and their families, and where laughter, conversation, and a feeling of belonging were generated by vivacious Florence and relaxed Victor. The "high," in fact, was both literal because of Victor's notoriously heavy hand in pouring libations and figurative in the good way we all felt in being part of the extended Twitty family.

It is rare for a person to do really distinguished work in two fields of science so widely different. It is rarer still when that person can write about both of them with the felicity, charm, humor, and wit that characterizes the book *Of Scientists and Salamanders*, which Twitty completed shortly before his death in 1967. He notes how some scientists seem hard

put to accept that his change of scientific field "just happened that way"—all the new things followed once the hybrid newts were released. He wrote, "Discriminatory judgements about the importance of different fields or levels of biology are in my opinion intellectually naive." Tolerance for different fields of biology—not arrogance that the study of molecules or cells or genes in developing embryos or ecology is inherently most important—was a Twitty plea. And of him: self-imposed standards of excellence and scientific rigor, clarity in framing scientific questions and experiments, fundamental love and respect for nature, newts, and embryos, and sincere caring for colleagues, students, and family all permeate Twitty's book and make it happy reading. The unusual trail from Harrison and Yale, through Germany and Stanford to newts in Pepperwood Creek is not at all a typical successful science career in the twentieth century. Twitty's history illustrates how unanticipated events, chance, good fortune, and a talented nose for scientific discovery led to his odyssey and to a life of accomplishment, contribution, and satisfaction.

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