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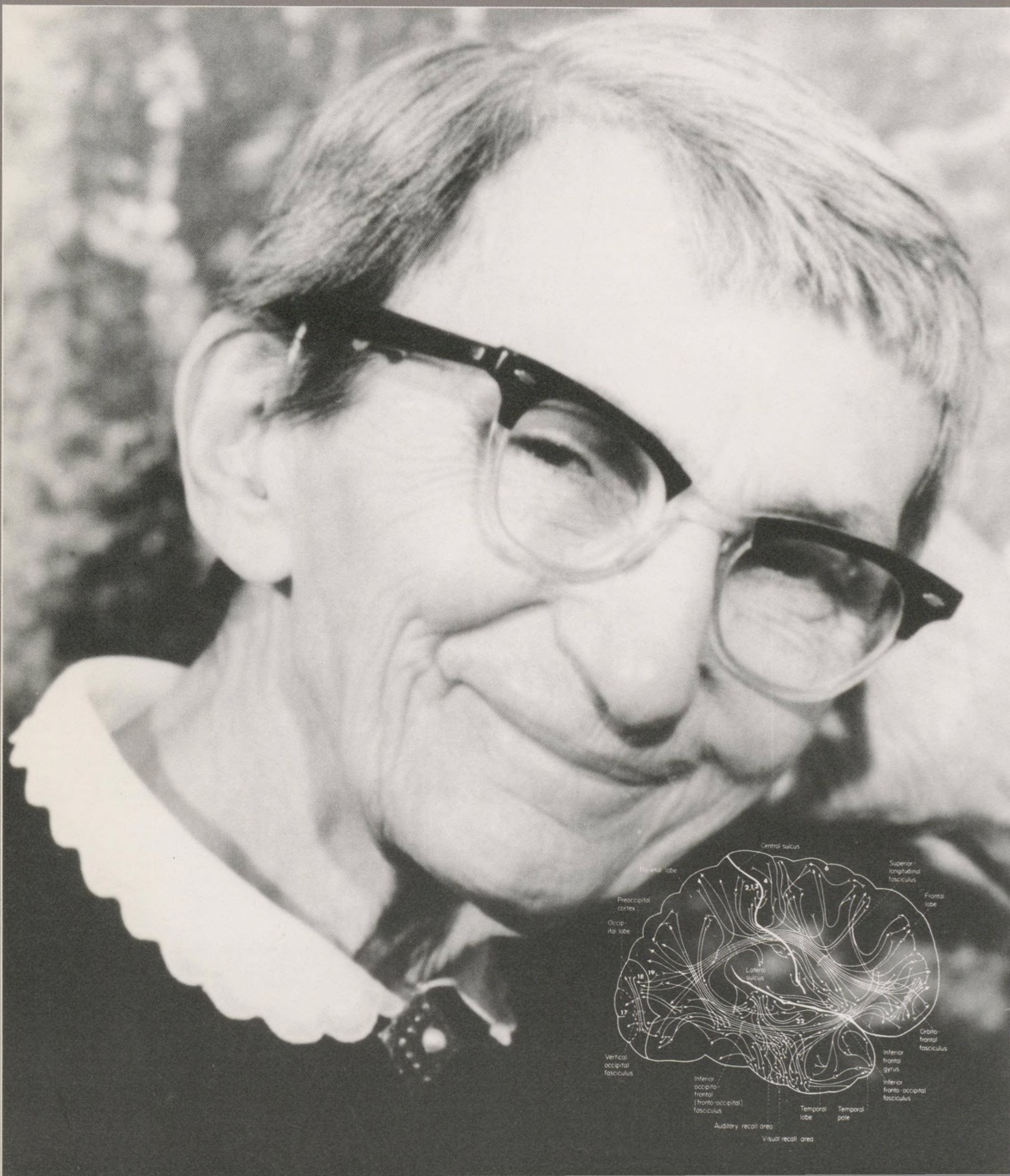
Elizabeth Crosby: Laying the Foundations of Neuroscience



THE RESEARCH NEWS

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Inset On the cover:

Crosby was especially proud of this complex diagram showing connections among distant parts of the human brain, *via* association bundles.

Donald Thackrey
Assistant Director for Program Development and Publications

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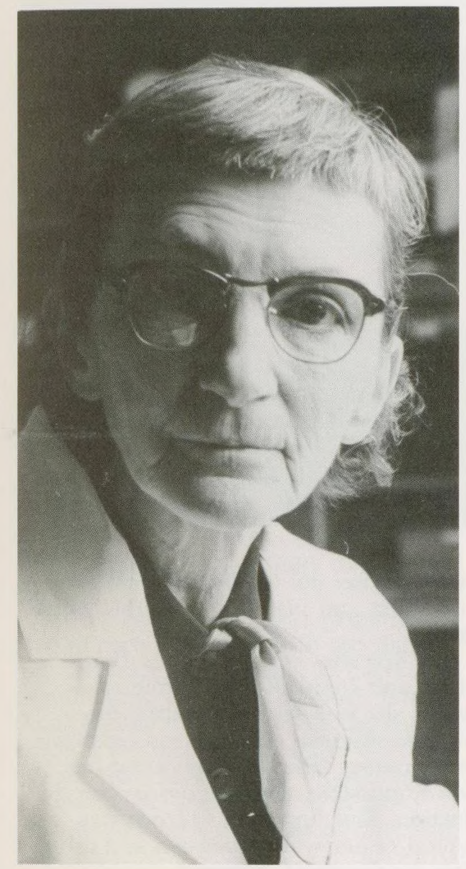
Elizabeth Crosby: Laying the Foundations of Neuroscience



Elizabeth Crosby died while we were preparing this issue devoted to her life's work as an anatomist of the brain. We bring you the article nonetheless, since it provides an opportunity to describe a remarkable University of Michigan scientist, and a remarkable woman. And since Crosby worked with some of U–M's greatest scientists and neurosurgeons, we will tell you about them too—Crosby was always a team worker, and her co–workers' contributions are very much a part of her work.

Crosby's contribution to science fell in three areas: by carefully describing reptile as well as other vertebrate brains, she helped outline the evolutionary history of the brain. In a "second career," she applied her comprehensive knowlege of the human brain to neurosurgery. Thirdly, her research advanced the interdisciplinary field known as neuroscience, and many of her students went on to become noted neuroscientists and surgeons in their own right. She taught 8500 students between 1920 and 1958.

While Crosby's major works are routinely cited in current neuroanatomy papers, her career is remarkable in several other respects. First, she made her mark as a woman in the male–dominated world of science and medicine. Often today she is seen as an anomaly, since only recently have women entered science in significant proportions. Crosby, however, did not describe herself as a feminist, at least in the way that many people use the word. Nonetheless, she has served as an inspiration to many young female scientists. It is surely no accident that many such women have received Ph.D.s from the Department of Neuroanatomy, and that five women serve on its current faculty. Sarah Winans chairs the department.

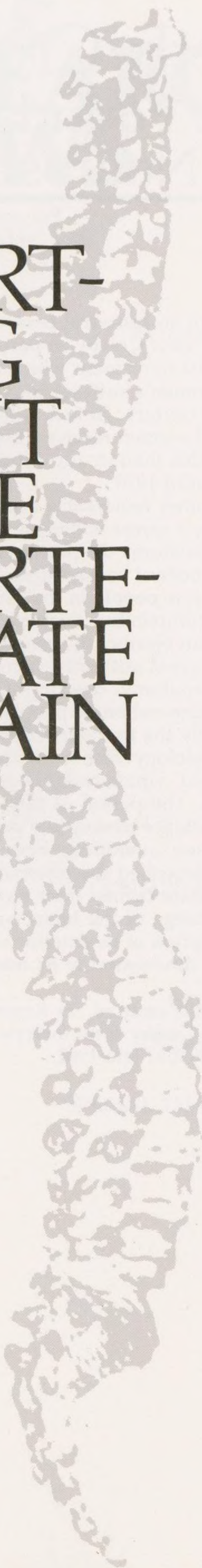
From an historical perspective, one might view Crosby as part of an earlier feminist movement which accompanied the women's suffrage movement early in the century. In fact, a higher proportion of women received Ph.D.'s during the 1920s than in any subsequent decade until 1970.

Another remarkable aspect of Crosby's career is her pre–eminence in neuroanatomy despite coming from a non–medical background. In those days, few people in the field arrived from comparative anatomy, as she did.

Glenn Northcutt, recognized as U–M's current authority in comparative neuroanatomy, describes Crosby as one of "a generation of people who were essentially the founders of comparative neurobiology. She knew the 'giants' in the field, which really began in the late 1800's. The period of 1880 to 1935 was a very intense descriptive period. For the first time, anatomists here and in Europe described the internal details of vertebrate brains. Prior to that, knowledge of the brain was limited to a description of its exterior shape, and a crude description of its interior contents."

In this issue of *The Research News*, we quote Crosby from interviews with her in 1980 and late 1982.

SORTING OUT THE VERTEBRATE BRAIN



"I have only one year, and I want to learn as much as I can," explained the young woman at Judson Herrick's door. Her father had promised to pay for three years of education, so she had squeezed her four–year undergraduate program into three, and pegged the fourth year's money for a year of graduate study. Herrick, a famous neuroanatomist at the University of Chicago was intrigued, but startled by her request. With only one course in biology, she was demanding a seat in his classes. True, she must be fairly clever, but she was from an obscure southeast Michigan college in Adrian. No, this would never do. He'd have to refer her to more basic courses.

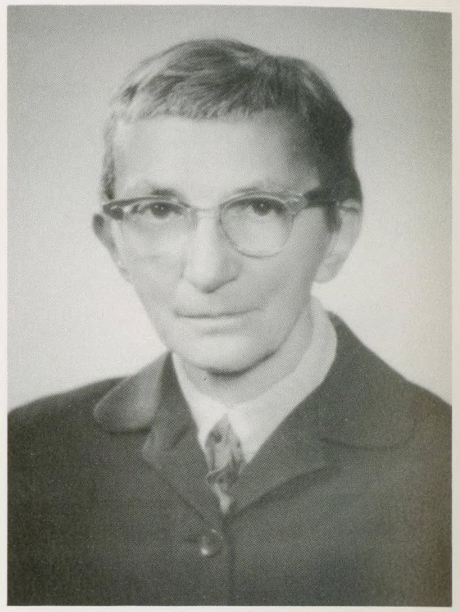
Little did Herrick know that he was arguing with Elizabeth Caroline Crosby, the woman who was to become his most famous student. She became America's foremost authority on the anatomy of the brain, and its evolution. But as far as Herrick could see at the time, he was facing an elfin woman who seemed intent on disappointing herself in classes far too advanced for her. Fortunately, Herrick lost his first argument with Crosby; her determination and sheer intelligence overcame anything she lacked in stature.

As a child growing up in a log house on a Michigan homestead, Elizabeth C. Crosby had loved puzzles. In school she fancied mathematics, although few problems stumped her for long. Not surprizingly for a puzzle–lover, she liked geometry best.

"I decided to take some science at college," she recalls of her undergraduate training. So, while earning Honors in Latin and mathematics at Adrian College, near her southeastern Michigan home, she took one term of elementary zoology from Professor Elmer M. Jones. The course intrigued her so that she decided to pursue graduate work in the field. Jones advised her to seek out Professor C. Judson Herrick, a well–known neuroanatomist at the University of Chicago; Jones had studied with Herrick a decade before.

Nonetheless, Herrick was taken aback by the young woman who stood at his door in 1910. Years later he wrote, "I questioned her and learned that upon graduation at Adrian...her only preparation in biology was one term of elementary zoology. I had to tell Miss Crosby that if she wanted to study zoology she should first devote about a year to making up her deficiencies in biology, chemistry, and physics."

But Miss Crosby had made up her mind. She insisted, "Let me try." Herrick, impressed by her competence and determination, finally gave way. "She had done a little dissection in comparative anatomy at Adrian, and this suggested to me a way to give her the opportunity she wanted. I asked if she would like to go into the dissecting room with our medical students. To my surprise, she said yes, that would suit her perfectly...I also allowed her to attend my medical course in neuroanatomy. For this she was quite unprepared and I warned that probably it would be



better for her not to take the final examination and plan to repeat the course later.

"At first she was, of course, disoriented and confused, but within a few weeks she was doing as well as the medical students and received credit for both courses. She did what I told her was impossible, and she did it with distinction. This first term's record was typical of her whole program as a candidate for the Ph.D. degree."

Unbeknownst to Herrick, he was introducing Miss Crosby to the most fascinating puzzle she had yet encountered. "Neuroanatomy represented a real challenge to work out. From that time on, it has been my greatest interest," she said seventy–three years later.

Crosby's intensity awed professors and fellow students. She worked so late into the night at the laboratory that they soon became concerned for her health. Herrick decided to take her lab key away from her. A few days later, he encountered his student as she trudged home. She was struggling to carry her texts, notebooks, a heavy microscope, and slides. The stubborn young woman was carrying her equipment home so that she could still work late! At last, Herrick realized that nothing could keep Elizabeth Crosby from pursuing her life's work. He returned the lab key.

A Landmark Dissertation

Within five years of arriving in Chicago, Crosby had earned a master of science degree and her Ph.D. in anatomy. Her dissertation described the forebrain (please see illustration) of the American alligator, *Alligator mississippiensis*. When she began this endeavor, little was known about reptilian brains. A few people had described the external convolutions of turtle and alligator brains, and one or two had identified large fiber tracts within.

At the time though, scientists were most curious about the origin of the brain's cortex, the "grey matter" forming the outer layer of much of the brain. In human beings, the cortex functions as the center of reasoning. How did this cortex evolve? One way of finding the answer was to examine the brains of vertebrate animals which had evolved *before* mammals. Advanced reptiles were a case in point.

"Those were the days when everybody was arguing what is, and what isn't cortex," recalled Crosby. She decided to provide the definitive answer by making careful dissection of the alligator brain, and drawing what she saw.

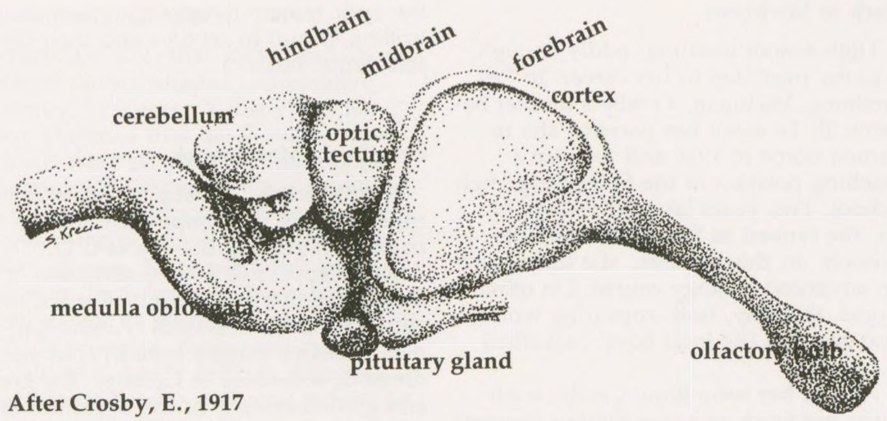
The result, her dissertation, remains a classic today. Years later, Herrick described the work as a "model of exact and concise presentation of intricate detail illustrated by beautifully clear drawings".

Crosby established that a primitive type of cortex did appear in the alligator, although it was generally devoted to processing the sense of smell, rather than "higher" functions. The last sentence of her dissertation states with confidence that this cortex is "undoubtedly the immediate precursor" of more sophisticated cortex materials of other animals.

Crosby's dissertation, published in the *Journal of Comparative Neurology* in 1917, was an immediate success. The story commonly told to illustrate this point describes Crosby a few years later in Europe. She knocked on the office door of Italy's most famous neuroanatomist. It was the first day of the semester; the professor was deluged by academic chores. His secretary informed Crosby it was unlikely that the Professor could speak to her that day. However, when the professor heard her name, he dropped everything and greeted her warmly. *This* was the Crosby of *Alligator mississippiensis*! He spent the next several hours discussing science with her.

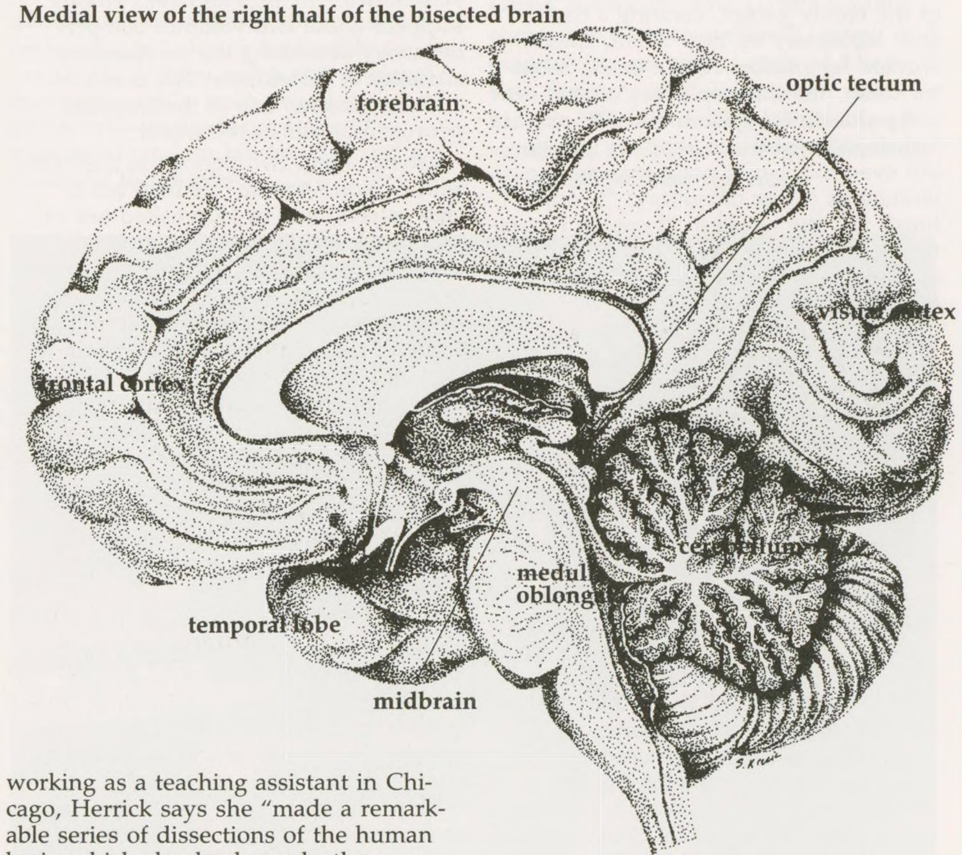
Comparative anatomy and the evolution of the brain captured Crosby's interest first. She was soon fascinated, however, by the human brain. While working as a teaching assistant in Chicago, Herrick says she "made a remarkable series of dissections of the human brain which clearly showed...the courses of many of the conduction pathways of major clinical significance. These were demonstrated to the students." In 1918, Crosby and Herrick jointly published *A Laboratory Outline of Neurology* in which Crosby gave medical students detailed instructions for brain dissection.

These two works—her dissertation on the alligator brain, and the human brain dissection manual—heralded the dual nature of Crosby's seven–decade career. She became a reigning expert on the evolution of the vertebrate brain in her day, and then applied this huge range of knowledge to medicine. As early as 1918, this combination of interests was clear, as was her great skill as a teacher.



After Crosby, E., 1917

Medial view of the right half of the bisected brain



The reptile brain (above) and the human brain (below) exhibit variations on a similar basic plan of forebrain, midbrain, and hindbrain.

Brain illustrations Sandy Krecic

Back to Michigan

High school teaching, oddly enough, was the next step in her career. In Petersburg, Michigan, Crosby's mother became ill. To assist her parents, she returned home in 1916 and took up a teaching position in the Petersburg High School. Two years later, at the age of 25, she ranked as Superintendent of Schools. In this position, she introduced an advanced zoology course. On other fronts, this tiny, frail–appearing woman also coached the local boys' basketball team!

And in her *spare* time, Crosby continued her work as a comparative neuroanatomist. Her father remodeled the attic of the family garage, creating a makeshift laboratory for her. There, Crosby worked on another region of the alligator brain, the diencephalon, a deep central portion of the forebrain. Her characteristic determination kept her going, but even that could not overcome the limitations of her laboratory. "I couldn't finish it," she recalled. "I couldn't make the slides because I didn't have the microtome to cut the material. There was no way I could do it."

With her father's consent, she decided to seek a position at the University of Michigan, thirty miles north of Petersburg. It is fortunate for U–M that the distance was only thirty miles, because her father asked her to find a position near enough for him to visit regularly.

Crosby sought out Dr. G. Carl Huber, a professor of Anatomy and Director of the Anatomical Laboratories. Crosby asked merely for "a corner to work in." Huber, however, offered her a student assistantship which Crosby accepted gladly. When one of Huber's staff unexpectedly left to head a department in Buffalo, Crosby was promoted to a junior instructorship—something like a teaching fellow these days. A year later, she became an Instructor. Sixteen years after she arrived at U–M, she became its first female full professor at the Medical School. Crosby's success paved the way for many women after her, but she described her career matter–of–factly, "I got promoted—the way people do."

Huber wasted no time in developing a close working partnership with Crosby. They picked up where Crosby had left off in Chicago, and examined the parts of the alligator brain just behind the forebrain. In reptiles, these areas (the diencephalon and mesencephalon) integrate sensory information and control bodily functions and movements. Huber and Crosby published six papers together, two concerning this dominant region of reptilian brains. Other papers compared the structure of the optic tectum (brain region controlling vision) in reptiles and their descendents, birds.

Creating a Masterwork

Intermittently, Crosby travelled to Europe to study with important neuroanatomists. Among these was C.U. Ariëns Kappers (a double surname), a Dutch scientist at Holland's Central Institute for Brain Research. Ariëns Kappers' research ranged broadly, but addressed, according to Crosby, "the great and glorious sweep of the evolution of the brain from the lowest to the highest vertebrates." In 1920 and 1921 Ariëns Kappers wrote two volumes comprehensively describing the comparative anatomy of vertebrates. The books established him as one of the foremost neuroanatomists in the world.

Crosby spent two periods in the 1920s with Ariëns Kappers. He held her in high esteem, and in 1926 asked her to translate his book from the original German into English. At first, the idea was to make a straightforward translation, incorporating more recent literature into the text.

Crosby returned home to Ann Arbor, and Huber became a third partner in the work. What began as a translation soon grew into an enormous project. Neuroanatomy moved so quickly during those years that they soon realized Ariëns Kappers' original book would have to be re–written entirely. The project took ten years.

In 1934, Huber died unexpectedly of leukemia. Even while mourning her mentor and close friend, Crosby persevered. She gathered information, analyzed it, and wrote chapter after chapter. Her former students, including Tryphena Humphrey and Russell Woodburne, did much of the indexing, an enormous chore for a book of over 1800 published pages. Humphrey later became a faculty member of the University of Alabama, and collaborated with Crosby on many research projects. Woodburne, who later turned his endeavors to gross anatomy, later chaired U–M's Department of Anatomy.

Woodburne wrote later, "Doctor Crosby's contribution to the revision of this text in its new enlarged format stands as a monument to her mastery of comparative neuroanatomy." The text "came to be regarded as the last word in reference material in this field. Doctor Crosby's tremendous capacity for work and her attention to detail is never more apparent than in her accurate reporting of other workers' findings as recorded in this textbook."

Impact of a Masterwork

So comprehensive, so accurate, and so detailed was *The Comparative Anatomy of the Nervous System of Vertebrates, Including Man* that it had an interesting double effect on neuroscience. The text's authority was unquestioned. But while providing the most complete and up–to–date look at the evolution of the nervous system, some say its acceptance tended to supress new ideas. Crosby's word, in effect, became dogma.

The publication marked the end of an era, says Glenn Northcutt, comparative neuroanatomist in U–M's Department of Zoology. "The descriptive phase of the field ended with that publication. Comparative neuroanatomy went into dormancy after that, superceded by neurophysiological studies."

> *"She set up a road map for large parts of the brain of reptiles."*
>
> —Glenn Northcutt, comparative anatomist

Crosby, meanwhile, became a somewhat controversial figure. Her interests turned to clinically–oriented experiments, working with Edgar Kahn and Richard Schneider, well–known U–M neurosurgeons. Others in comparative neuroanatomy turned to experimental methods using powerful new staining techniques. The first, a silver staining method developed by Walle J.H. Nauta at the Walter Reed Hospital, attracted a new generation of neuroanatomists back to comparative neuroanatomy. During the 1950s and 1960s, Nauta's energetic group worked at the forefront of comparative neuroanatomy.

Nauta, a Dutch physician who came to the United States after World War II, developed new staining techniques which enabled investigators to trace neuron pathways in the nervous system. Northcutt says that Nauta and three or four of his students stimulated the field so greatly that neuroanatomists have generated as much literature in the past twenty years as in the previous sixty or seventy.

Leaving comparative neuroanatomy behind for the time being, Crosby experimented with laboratory animals to determine the subtleties of facial control, eye movements, and muscle tone. This work had many clinical applications. She never did, however, employ the modern, extremely powerful biochemical "tricks" for tracing individual nerve fibers. Nor did she turn to the electron microscope, although she acknowleged its importance as a research tool. She preferred to explore the brain at the visual level a neurosurgeon experiences—structures seen by the naked eye, or through a binocular operating microscope. She concentrated on such clinical work until, as an emeritus professor at Alabama (a position held simultaneously with emeritus status at U–M) she returned to comparative studies with Humphrey and others. Her last comparative work was the book, *The Comparative Correlative Neuroanatomy of the Vertebrate Telencephalon*, co–edited with H.N. Schnitzlein, of Alabama.

Comparative Neuroanatomy Today

Glenn Northcutt, U–M's current authority on the evolution of vertebrate nervous systems, spent graduate school with Crosby's Ph.D. dissertation tucked under his arm in a folder. The folder contained all that was known about the reptilian brain—and three of the papers were by Crosby. Northcutt wrote his dissertation about the brain of another reptile, the western painted turtle. This year, 50 years after Crosby's dissertation, Northcutt edited a 300–page book on forebrain organization in reptiles and birds. The book was written by Northcutt's colleague Philip Ulinski of the University of Chicago. The two men have also published two books on reptile neurology, as part of a series on the biology of reptiles (edited by U–M's Carl Gans).

"Crosby's thesis on the telencephalon of the American alligator is the most detailed, elegant, and complete description of that part of the brain of any reptile. Her work was a benchmark. Generally, you can judge the merit of a paper by whether anyone reads it ten years later. Her paper was published in 1917, and it's probably as useful today as it was then. She set up a road map for large parts of the brain of reptiles.

"At the time of my doctoral dissertation in 1968," Northcutt adds. "I could carry all the papers on the reptile brain in one folder. Today, there are well over 200 papers. No one person can be competent in the whole field any more. There is even a 1000–page book on the brain of frogs alone!"

Northcutt and his colleagues explain that comparative neuroanatomy still serves as the foundation of neuroscience. "If you want to understand how human brains work and have evolved, you have to look at what they evolved *from*. We assume they evolved from reptiles. Understanding the brains of modern reptiles is a major clue to the stages that mammalian brains passed through historically. U–M anatomy professor Sarah Winans adds, "We now try to understand animals as *models* of neurological phenomenon. Comparative anatomy is still very important."

Fundamental Changes

Northcutt says that some fundamental changes have reshaped comparative anatomy, however. "Crosby and her peers assumed that the brains of other animals were simpler than the brains of mammals. Therefore, if we understood them, we would be able to see the *scala natura*—the notion of evolution as a linear process. Now, we don't see it that way. Each animal's brain is structured to suit its particular ecosystem and life activities. Even a so–called 'primitive' animal's brain is delicately attuned to its needs—and may indeed be quite complex."

Northcutt applauds the dissolving of disciplinary boundaries taking place in neuroscience today. Interdisciplinary research has yielded many sophisticated methods used to trace neural pathways—methods developed by turning to modern biochemical and microscopic techniques.

Glenn Northcutt, now U–M's leading comparative neuroanatomist, spent graduate school with a copy of Elizabeth Crosby's 1916 dissertation under his arm. He is puzzling out details of vertebrate evolution through examining the brains of many species.

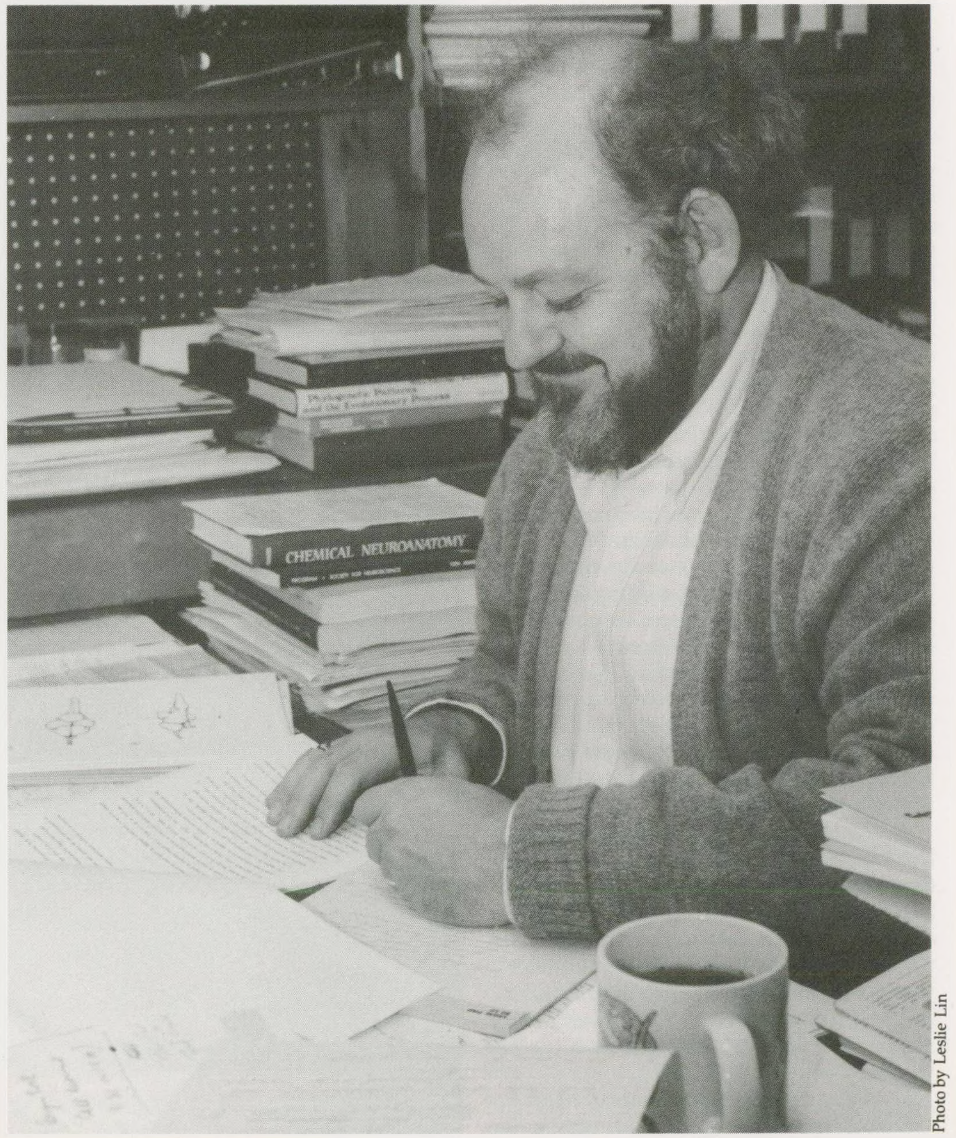


Photo by Leslie Lin

At the time Ariëns Kappers, Huber and Crosby published their masterwork, the vertebrate brain had been pretty much described, in a sense. Anatomists could tell you what kinds of nerve cell bodies, fibers (axons), and nerve endings were located in various parts of the brain for most major species. They could only guess, however, how some of these cell groups were connected.

Dissection, in the early days, served as the major method of tracing nerve pathways. Huber and Crosby were masters at dissection—Huber, for instance, was famous for dissecting out a single uriniferous tubule in the kidney, a process which took an entire 24-hour period to accomplish. Even for such skilled practicioners, however, tracing nerve pathways was bound by the physical limits of the eye, dexterity, and a few staining methods available. Says Northcutt, "Given the methods available at the time, it was only possible to follow gross nerve pathways in their routes from one location to another. Comparative neuroanatomy had to await new experimental methods before we could get beyond that stage."

New Ways to Trace Nerves

The big breakthrough came in 1954, when Walle Nauta and P. Gygax published a method of impregnating *degenerating* nerve fibres with silver. They destroyed one section of the brain and allowed a few days for the nerve axons to degenerate. Then they killed the animal and stained the brain . Only those nerves which were degenerating would pick up the silver, and thus show up on microscopic slides. (Previous silver stains adhered to *all* nerves.) This breakthrough helped spark the rennaissance of comparative neuroanatomy.

Although the silver impregnation was very powerful, it was difficult to pull off. Because there are literally thousands of variables in timing, staining concentrations, and other factors, it requires experience. Only Nauta-trained people have had much luck with it. An improved variation of the silver stain solved some of these problems. Northcutt's doctoral research was one of the first applications of this method to reptile neuroanatomy.

A weakness of the Nauta method was the "axon of passage" problem—if you destroy the cells in a certain brain area, two kinds of axons will begin to degenerate. The axons originating in the area will therefore pick up the silver, but so will axons passing through and not originating in the area. The silver stain methods cannot tell you which is which.

Anatomists needed a method in which a traceable chemical would be taken up by cell bodies but not by axons. U-M's Bernard Agranoff, a professor in the Mental Health Research Institute, and Maxwell Cowan, now at the Salk Insititute of California, solved this problem. This feat is considered by many as a major turning point in neuroanatomy. They found that radioactive amino acids would be taken up by living cell bodies and passed down the same cell's axon. Axons in the same area as these cell bodies would not pick up the proteins. This solved the problem of "axons of passage." It also solved another problem with the silver method—having to wait from 4 to 30 days while the nerves degenerated. With this method, one could trace pathways in a and prepare the material for microscopic examination almost immediately.

Naturally, neuroanatomists wanted an efficient method of checking where certain nerve endings *began*. This problem was solved by wife-and-husband team Jennifer and Mathew LeVail in l972. They found that a substance called *horseradish peroxidase* would be taken up by nerve terminals and sent back towards the originating cell bodies.

With these methods, neuroanatomists had efficient methods of looking at any area of the brain and detecting its nerves' origins and destinations. Even a few cells could be traced this way. Since that time, certain fluorescent dyes have been found to stain nerves in either direction.

Using all these methods, Northcutt claims that "We can now do in a month what it took me five years to do as a doctoral student. The brain is so complex though that chances are it will take us at least another 100 years to reach the point where we know what is connected to what, let alone how they work." . He has studied the neuroanatomy of a wide range of vertebrates ranging from lampreys to birds. Unlike most neuroanatomists though, Northcutt is a zoologist first, and an anatomist second. "That's rare," he says. "I can only think of two early neuroanatomists who were Ph.Ds instead of M.D.s—Crosby and J.B. Johnston, both founders of comparative neuroanatomy." (Johnston, trained at U-M in the late 1800s, conducted his later research at the University of West Virginia, and later became an authority on higher education at the University of Minnesota. He can, however, be claimed as the first U-M neuroanatomy "great" to be trained here. Johnston wrote the first classic vertebrate neuroanatomy textbook in English in 1906.) Today, many neuroanatomists are Ph.D.s, but most are trained in medical schools rather than in biology departments.

M I C H I G A N 'S F I R S T G R E A T A N A T O M I S T

Gotthelf Carl Huber, U-M class of '87, began his career as a lowly Assistant Demonstrator of anatomy in U-M's Medical School. His interests soon narrowed to the newly-emerging field of histology— anatomy at the microscopic scale. He quickly realized, though, that The University of Michigan was years behind in histology. Before he'd be able to teach and use histological methods effectively, he would have to journey to Europe. There he could study with Dr. Paul Ehrlich, the great bacteriologist who had invented the methylene blue staining technique, still used today in high school biology labs and the many advanced research institutions.

Huber took a leave of absence from U-M and travelled to Europe. Without warning, he simply arrived at Ehrlich's door and asked for a chance to study with him. Ehrlich sighed. Another acolyte from the provinces—and his lab was already overcrowded! Hoping to discourage the young man, Ehrlich said that he didn't even have a knife (a microtome) for cutting microcopic sections. "Not one?" asked Huber, pressing him. Ehrlich finally admitted to having one microtome, but that it was in such bad shape that no one could use it. The instrument had been dropped and huge gouges marred the blade. If Huber could fix it, perhaps there was a chance.

For three days, Huber sat in a corner working on the blade. It was the worst microtome he'd ever seen. But there he was in Europe; he had no job to return to for a year, and had already spent a good part of the grant supporting his year abroad. On the third day, as he honed the wretched knife, he sensed someone looking over his shoulder. It was Ehrlich, who asked how he was doing. Without a word, Huber pulled a hair from his own head and cut it on the knife. Ehrlich took the knife and examined its edge under a microscope. Quietly, he returned it to Huber with the announcement that this determined young man from America could stay.

Huber learned the methylene blue method from Ehrlich, as well as other methods. When he returned to Michigan, he was as up-to-date in histology as anyone else in the world. His reports of methylene blue stainings of nerve endings were the first North American accounts of the technique. His first research interests centered on degeneration of peripheral nerves. During World War I he served as an army surgeon and explored methods of their surgical repair.

Huber's second anatomical interest was the kidney, that mysterious organ which filters salts and wastes from the blood, and deposits them in urine. He published some of the first descriptions of the interconnections of kidney blood vessels and urine-concentrating tubules. Some of these reports described the development of the kidney in embryos and in vertebrates other than humans. This work made his name, putting Huber and The University of Michigan on the map, as far as anatomy was concerned.

When Elizabeth Crosby came to him, asking only for a bench in his laboratory, perhaps Huber remembered Ehrlich's kindness to him twenty years before. At any rate, he soon recognized her talents and embarked with her on his third anatomical career—the evolution of the vertebrate central nervous system. He worked with her on the monumental two-volume book *The Comparative Anatomy of the Nervous System of Vertebrates, Including Man.* Huber died before the work was completed, but its publication crowned his lifetime of careful observation and thoughtful analysis of vertebrate evolution.

Photo courtesy Michigan Historical Collection, Bentley Historical Library

G. Carl Huber worked with Crosby for over a decade. Before his work in neuroanatomy, he was already well-known for his description of the kidney.

A Pioneering Woman in Science

Nothing irritated Elizabeth Crosby more than to be pointed out as remarkable due to her gender. "It's not very popular to say this," she would say, "But I have never felt discriminated against." In recent years, she was almost apologetic for this view, since she acknowledged that some women she knew *had* suffered discrimination. But as for herself, she said, "I've had as much opportunity as a man—maybe not quite as much pay—but then I didn't do as much work. True, I did as much teaching."

Crosby's explanation of her success in a male–dominated world reflects both her excitement about her work and her explanation of the world as a Victorian woman. "I came in when there weren't very many women. There wasn't much competition."

If Crosby meant competition from women though, she was probably underestimating the field. In the 1920s, approximately 20 percent of anatomists were women—anatomy was the scientific field with the highest percentage of female practicioners. (Astronomy was a distant second, with 8 to 9 percent, according to Columbia University's Harriet Zuckerman.)

Glenn Northcutt recalls, "As a graduate student, I grew up knowing that three of the major scientists in my field as women. One was Crosby, of course. Tilly Edinger was another. She was a contemporary of Crosby's who was the world's authority on fossil brains. Edinger was at Harvard. At the University of Chicago there was Libby Hyman, who wrote the most popular comparative vertebrate anatomy textbook, as well as a book on the anatomy of invertebrates." Before Crosby, two women wrote important works in neuroanatomy. Mrs. Susanna P. Gage wrote on the brain of turtles, and Marion Hines researched the sphenodon, a rare New Zealand reptile. Thus, for Crosby, there were respected female role models in her field, and plenty of competition once she got there.

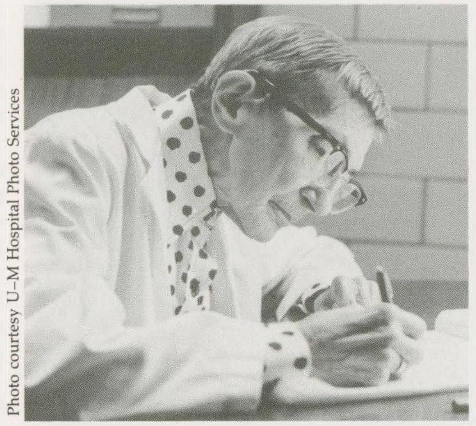


Photo courtesy U–M Hospital Photo Services

"I got promoted, the way people do."

—Elizabeth Crosby, on being the U-M Medical School's first female full professor.

But Crosby continued, "Because I liked it, people helped me. And I wasn't expecting anything—that makes a lot of difference. Nowadays, women are competing with men for positions and jobs. In my day, you never thought of it. If you had an instructorship as a woman, you thought you were pretty good."

Crosby's attitude seems typical of her generation's female scientists. They asked for so little that any recognition they did achieve was regarded as a "bonus," rather than their due.

Crosby's deliberately non–competitive stance extended to how she presented her findings in publications and at scholarly meetings. "I've belonged to the American Anatomical Association since about 1917 or 1918 and I've never yet given them a talk. Science wouldn't go on if everybody were like me, and maybe that's why I don't feel discriminated against. I just stayed home and did what I liked to do." Crosby's ingenuous explanation for this odd phenomenon was expanded upon by U–M anatomy professor Muriel Ross, a one–time student of Crosby's. Crosby confided in Ross that her mentor Dr. Huber co–authored many papers with Crosby, but he did not think it "quite proper" for a woman to speak before the group.

In most of her scholarly papers and books, Crosby accepted second or third authorship. She deferred to her peers or students, even when her ideas or actual writing dominated the work. Such was the case with the mammoth *The Comparative Anatomy of the Nervous System of Vertebrates, Including Man*. Although Crosby actually wrote most of the two–volume work, she listed herself as third author. Says U–M neurosurgeon Edgar Kahn, "She was like Cyrano de Burgerac, who wrote love letters for another guy."

Russel Woodburne, later to become Chair of the U–M Department of Anatomy, wrote of Crosby, "..Dr. Crosby felt no strong urge for publication herself. Her intellectual satisfactions came with the determination of the facts and fitting them into the total picture. It was primarily to further her graduate students' careers and make the data available to other workers that the material was prepared for publication. Once publication was decided upon, however, the care and thoroughness she insisted upon resulted in the preparation of model manuscripts in every particular—another aspect of the well–rounded training her graduate students received."

Crosby's willingness to share the publication limelight with her colleagues may have been an unwitting discovery of a survival technique for a woman in science. Her apparent disinterest in recognition undoubtedly helped her excel while minimizing antagonism or defensive reactions from male peers—reactions so typical in the annals of other women in science. Her penchant for overwork probably made it difficult for her peers to overlook her for promotions.

Crosby's years at U–M were not without their difficulties. She was often so burdened with teaching that she had little time for research. At least twice she was on the verge of moving to other universities. Colleagues such as Edgar Kahn, however, always found ways to ease her burden and persuade her to remain here.

After her U–M "retirement" in 1958, Neurosurgery chief Kahn employed her as a consultant to his staff. Says Kahn, "Getting Dr. Crosby to join our Service was the best thing I ever did for it." In 1963, Crosby also accepted a concurrent position at the University of Alabama, where her life–long friend (and early graduate student) Tryphena Humphrey worked. For years into her retirement, Crosby commuted by air twice a month between U–M and Alabama.

A Woman of Enterprise

The reader should not get the idea that Crosby's life was one of quiet labor in some remote laboratory. She led an adventurous career, travelling and working around the world with some of the greatest figures in neuroscience. "In those days, we went abroad to study. Now they come here," she noted.

"In those days we went abroad to study. Now they come here."

— Elizabeth Crosby

In a 1960 letter to a friend, she describes teaching recently in Montreal and Aberdeen, Scotland, and attending meetings in Holland and Germany. Obviously loving the pace, she wrote, "Isn't that pretty good for an old lady?" She frequently summed up her career with the assertion, "I've had a whale of a good time." Seeing her fascination with science, one is inclined to believe her.

Despite Crosby's modesty and her traditionally "feminine" low profile, she stood out as a figure of great intellectual power and independence. Her example, says Ross, "set standards of thoroughness and objectivity. The most valuable thing she taught her students was to *trust what it is you see*. She was never awed by authority, and she insisted that you should not try to bend what you saw to someone else's idea. One of her students chaired the Department of Anatomy in Alabama. He says that Crosby taught us to "look at our own stuff and *then* go look up what the authorities say. We students of hers find it odd that everyone else does it the other way around." Undoubtedly, Crosby would have disapproved of scientists treating her work as "gospel."

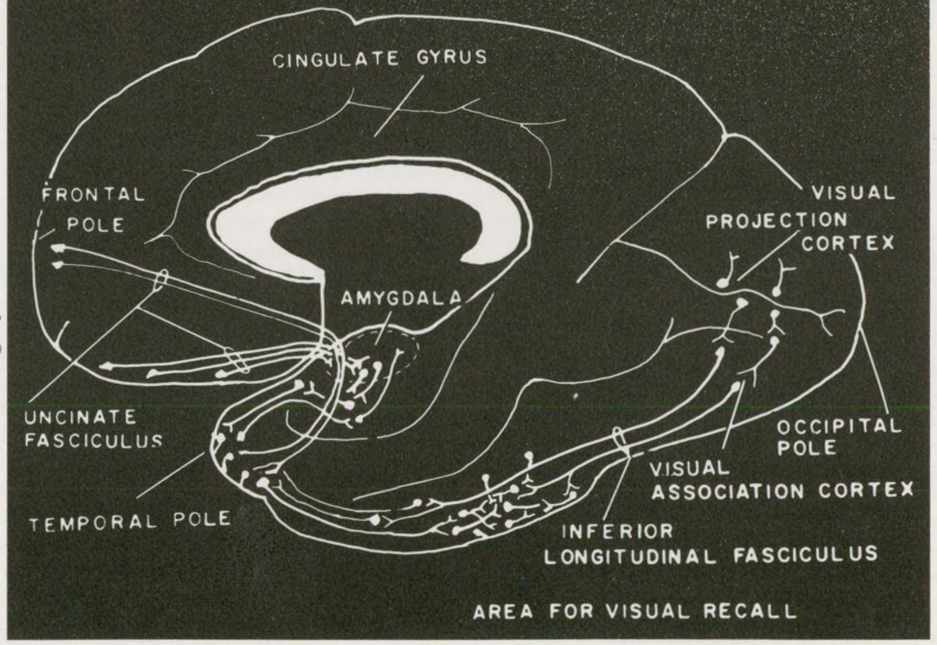
Muriel Ross, a U–M professor of Anatomy, earned her Ph.D. under Elizabeth Crosby. Ross has studied the effects of aging on the human ear, and has developed a theory of the ear's involvement in space–sickness. She is preparing an experiment to travel on an upcoming Space Shuttle flight.

Ten women wrote their doctoral dissertations under Elizabeth Crosby. For these women, her example must have shown that a productive professional life could be combined with motherhood. Though she never married, Crosby brought up two Scottish girls, one of whom she adopted during World War II.

After her retirement, Crosby wrote to a friend about life after retirement. "For people like you and me, who made their own way and have done what they liked for a good many years, independence is a very nice thing."

Crosby worked in Neurosurgery for 23 years after she retired, independent to the end. Before her death, she was honored by every major professional organization in her field. Many universities offered her honorary degrees, and President Jimmy Carter presented her with the National Medal of Science Award in 1980. Perhaps best of all was an honorary Doctor of Medicine, which allowed her to write "M.D." after her name on the last edition of *Correlative Neurosurgery*. Elizabeth Crosby had come a long way from the "scared, not–too–well–prepared little country girl"—her description of herself arriving at the University of Chicago in 1910.

An Anatomist Serves in the Operating Room



From *Correlative Neurosurgery*

As Crosby settled into work at U–M, she was soon noticed by Michigan's pioneering neurosurgeon Max Minor Peet. Oddly enough, her connection with Peet came through a colleague at the University of Chicago. Then "dean" of American neuroanatomy, Stephen Ransom told Crosby that Peet was "interested in people who wanted to relate anatomy to neurosurgery." Crosby met Peet, and thus began a long, informal training in the clinical aspects of neuroanatomy.

Years later Peet was riding the train from a professional meeting in 1932. Also on board was Ransom, who asked Peet, "Do you know that you have the finest neuroanatomist in the country at U of M?" Peet did not, but returned to U–M "beaming," according to Edgar Kahn, a U–M neurosurgeon working with Peet.

"Dr. Peet would call up and show me cases," recalled Crosby. "I saw some of the early cases of pre–frontal lobotomy, which they did for specific clinical disturbances. I remember one case of a woman .... They cut part of her frontal lobe. Well, she quieted down. When her husband came to get her, Dr. Peet asked him, 'How do you like your wife?' The man said, 'Well, I don't know. When I came to visit her, she just read the newspaper.'

"They don't do that any more," Crosby said, with some relief.

After Dr. Peet died in 1949, his successor Edgar Kahn (a student in Crosby's first quiz section, and Peet's first neurosurgical resident) invited Crosby to become more closely involved in the neurosurgical service. Kahn recalls, "When she first came on service, she knew little about neurosurgery. She began by putting on a white coat, and went on the neurosurgical ward for six weeks. She took histories, examined patients, and was checked by staff. She made mistakes, but didn't mind. She just wanted to learn."

When she had completed this period of clinical training, Crosby joined Kahn in teaching rounds. These rounds took place three times a week. Kahn and Crosby visited various patients in the ward, followed by a troop of medical students. The Kahn–Crosby team was probably one of the most famous teaching events in the Medical School's history. Kahn would discover a precise symptom during the neurological examination and Crosby would tie the symptom to an exact locality in the brain or spinal cord. They *correlated* symptoms with anatomy. It was an incredibly exciting process for students, many of whom had recently slogged through two semesters of anatomy courses.

Correlative Neurosurgery: Another Masterwork

When Kahn took over the Neurosurgical Services of the U–M Department of Surgery, the state of the art was still primitive, compared to today's. The trick was to correctly localize tumors and other abnormalities somewhere within the geography of the brain. X-rays were available for locating such problems, but by and large "neurological testing" provided the best diagnostic tool. The reader is probably familiar with one such test—the doctor moves a pen before the patient's eyes to check for specific blind spots, and hence problems in the optic system.

The Crosby–Kahn rounds were the beginning of a new idea in neurosurgery. Up until that time, students had learned neurology and anatomy in two separate departments, and had only put the two together in advanced training. But Crosby and Kahn made clinical symptoms and anatomy inseparable—they *correlated* the two. Eventually, Crosby and Kahn were joined by Richard Schneider, another superb diagnostician. Together they embarked on writing and editing a textbook which would make the correlative concept available to neurosurgeons everywhere. The book's chapters described patients with various tumors, injuries, or other abnormalities. These lesions (a collective term for these medical problems) were correlated with their detailed anatomical and physiological origins and consequences. This was one of the earliest interdisciplinary approaches to neurosurgery, revolutionary in its time.

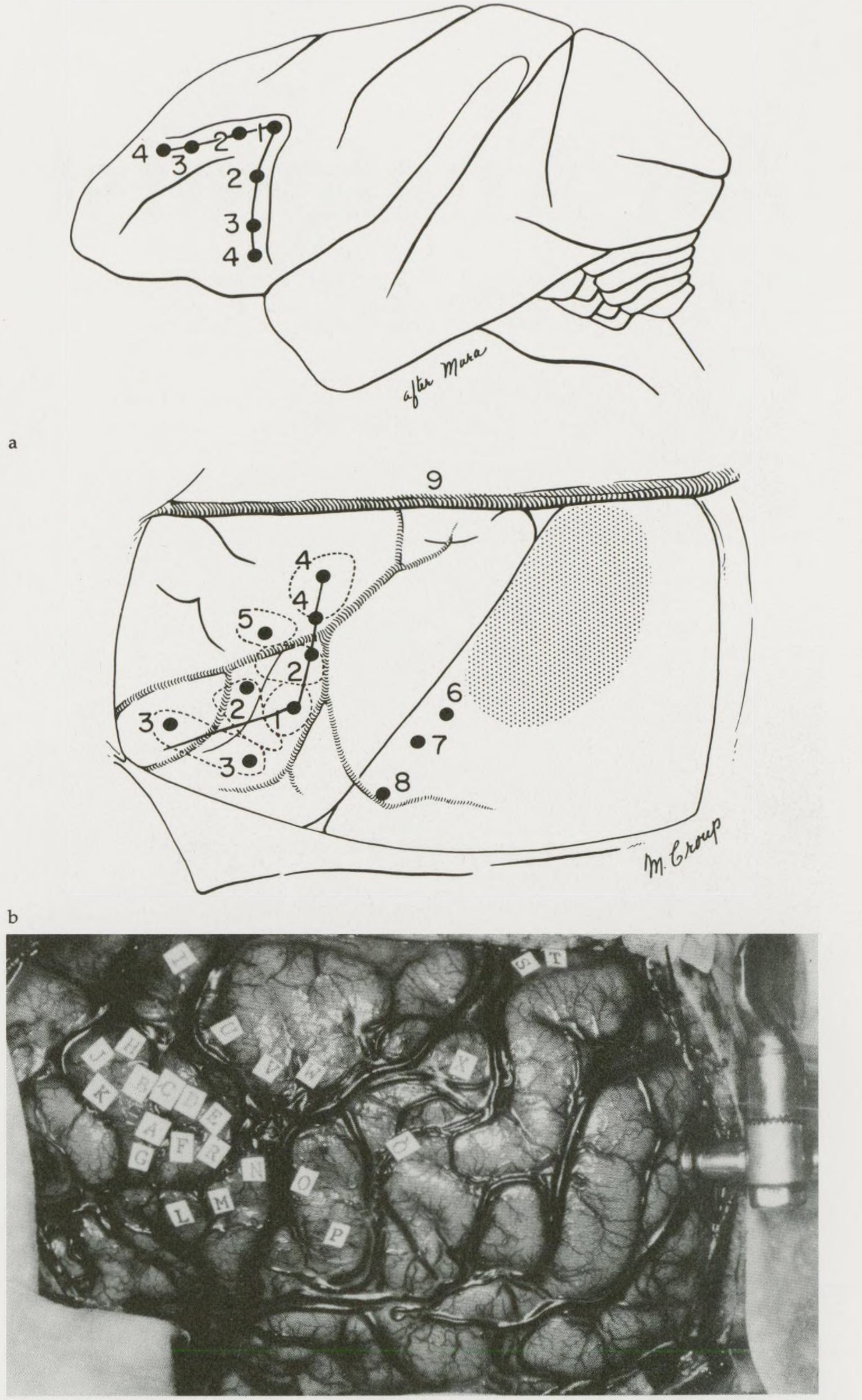
Correlative Neurosurgery has become a staple text in every neurosurgeon's library. Its third edition was published in 1982. U–M neurosurgeon James Taren joined the other authors in the book's second and third editions. The new edition has received favourable reviews, and is a "hot seller" according to Julian Hoff, current chief of the Neurosurgical Service.

Clinical Anatomist

Crosby's training in the service added a new dimension to neurosurgery at U–M. Kahn acknowledges that "She knew so much more anatomy than we knew. Even before she joined the Service I used to call her over to see cases that I couldn't explain."

An example of such help was an eight–month–old child who, Kahn thought, had sustained a head injury upon falling out of bed. He moved his arms and legs equally well on both sides. A day later, the child died suddenly. An autopsy showed that an *entire*

— *Continued on page 16*



Crosby applied her knowledge of vertebrate brain anatomy to clinical situations. Here we see pre-frontal brain sites responsible for eye movements. Crosby located them in the monkey (a), and the human (b) through dissection. The V-shaped pattern was confirmed by stimulating the same sites during an operation on a patient with a convulsive disorder involving eye movement.(c) (From *Correlative Neurosurgery*, courtesy Charles C. Thomas Publishing Co.)

Edgar Kahn: Pioneer Neurosurgeon

Edgar Kahn, described by others as "the master surgeon," "the last of the old-school physicians," and "one of the pioneers," began his career as a neurosurgeon almost by accident. He recalls, " When I was a student, interns and residents did not like to help with brain operations. The operations were so long—up to eight hours—and the mortality so high that it was too depressing.

"Dr. Peet was doing all the neurosurgery in Michigan at that time. He saved the life of a boy that I thought I had mismanaged. I was so appreciative that I said to him, 'If you ever want me to help, just call on me.' So he started calling on me. That is how I got into neurosurgery. The following July, I became his first resident."

Kahn worked with Peet until the latter's death in 1949. He also worked with many others, including leading surgeons in England and Austria. His fascinating 1972 book, *Journal of a Neurosurgeon*, describes medical practice for brief interludes in Bellevue Hospital, in New York City, NY; Russia; a remote area in Persia (now Iran); and service during World War II in France and England.

Kahn sat in Elizabeth Crosby's first neuroanatomy quiz section in 1920. Crosby's memory was phenomenal, he says. "She would lecture for an hour and a half without any notes. She did have notes, but never referred to them, even before a lecture. As I listened to her that Fall, I could not foresee that she would someday be recognized internationally as a neuroanatomist, or that I would later be closely associated with her for over twenty years, or that, together, we would edit two books and many scientific papers."

Kahn's years as a neurosurgeon gained him a reputation for great precision. One operation, a cordotomy (making precisely placed cuts in the spinal cord to relieve intractable pain), was his trademark—his successor Richard Schneider says he could make the maneuver "right down to a half millimeter." This was, of course, before the days of the operating microscope.

Kahn was also known as a curious surgeon, one who conducted careful clinical research. His curiosity lead to the development of many new surgical techniques which later became routine in the field. Working with his wife, internist Dr. Rose Parker, and Dr. Carl Brinkman, he published the first large series of brain tumor X-ray scans using radioactive mercury. The improved accuracy of these brain scans enabled him to open up smaller areas of the skull during operations, thus exposing less brain tissue. The method decreased death rates from tumor surgery, and post-operative recovery went more smoothly.

Kahn is also known for a novel method of dealing with tumors on or near the pituitary gland. These tumors (craniopharyngiomas) are dangerously located at the base of the brain. Kahn used cortisone in the management of these patients, resulting in a reduction from 7 deaths out of 14 cases (in a series of cases before the advent of cortisone) to 1 out of 22 (in a later series). With characteristic humility, Kahn wrote, "Though my technique must have grown somewhat better with experience, there was no doubt that cortisone accounted for the striking improvement."

Kahn's wide-ranging experience enabled him to write about surgery in nearly every section of the brain. In *Correlative Neurosurgery* he and Crosby co-authored five chapters, and he wrote another five alone or with other authors. One of his best-known chapters concerns the diagnosis and treatment of brain abscesses, which somtimes result from ear and nasal infections, as well as from penetrating wounds of the head. Kahn's innovation was to inject a material (opaque to X-rays) into the suspected location of the abscess. This clarified the X-ray image of the region.

Schneider credits Kahn with early use of motorized drills for cutting through the skull. Kahn and Peet were also the first surgeons to operate on the infant skull to remove underlying blood tumors (subdural hematomas).

Kahn has been well-honored by his peers over the years. He is still at work, seeing patients, at the age of 83. He remains one of U-M's most eminent and colorful figures in neurosurgery.

Richard Schneider: Understanding The Spinal Cord

A few weeks before Elizabeth Crosby's death, Richard Schneider, Chief of Neurosurgery between 1969 and 1979, gazed at a photograph of Crosby, Edgar Kahn and himself. The photo shows him and Kahn watching intently as Crosby probes a specimen on a lab bench. Elegantly bow-tied, Kahn stands behind the others, his arms clasped behind his back. Schneider, in surgical garb, sits beside Crosby, still and observant. One can almost hear Crosby's low, gravelly voice as she makes a point about the dissection.

Says Schneider, "It's been like that all our professional lives. A team. I've been privileged to be the junior member."

Schneider began his work with Crosby during an experiment on monkeys. "She said to me, 'You know that the brain controls movement on the opposite side of the brain. But it also controls movement on the same side.' She then stimulated the left side of a monkey's brain in the temporal area and got movement on the same side of the face—this was after removal of the primary motor strip for the facial area cortex, bilaterally." Crosby's understanding of this subtle brain function impressed Schneider so greatly that he "became a believer." And working with Crosby over the years, he became an expert on neurological anatomy in his own right.

Schneider is known for his understanding of cervical (neck area) spinal cord diseases. He defined the range of syndromes affecting the cervical spinal cord, describing various symptoms in tumors, degenerative diseases, injuries, and the courses of these conditions. He worked with Crosby to define in great detail the anatomical correlates of each clinical situation. Schneider wrote two chapters of *Correlative Neurosurgery* concerning the cervical spine. He also wrote, with Crosby, a major chapter on the surgical treatment of epilepsy. In all, he wrote or co-authored eight chapters of the classic volume.

Schneider, Crosby and Kenneth Magee (of U-M's Department of Neurology) described and explained *syringomyelia*, a disease in which the center of the spinal cord is destroyed. Schneider credits Crosby with knowing the complex "wiring" of nerves in the high spinal cord and brain stem extremely well. She explained why people with this disease have superficial pain sensation around their lips and shoulders, while losing it everywhere else.

Julian Hoff, current Neurosurgery Chief, says that Schneider was like Kahn in his ability to recognize signs in a patient that others would miss. "He saw lots of patients and tested them exhaustively. He defined the entire spectrum of spinal cord diseases—something never done before with any sophistication. Schneider's work made neck and spinal cord diseases understandable on an anatomical basis."

Preventing Sports Injuries

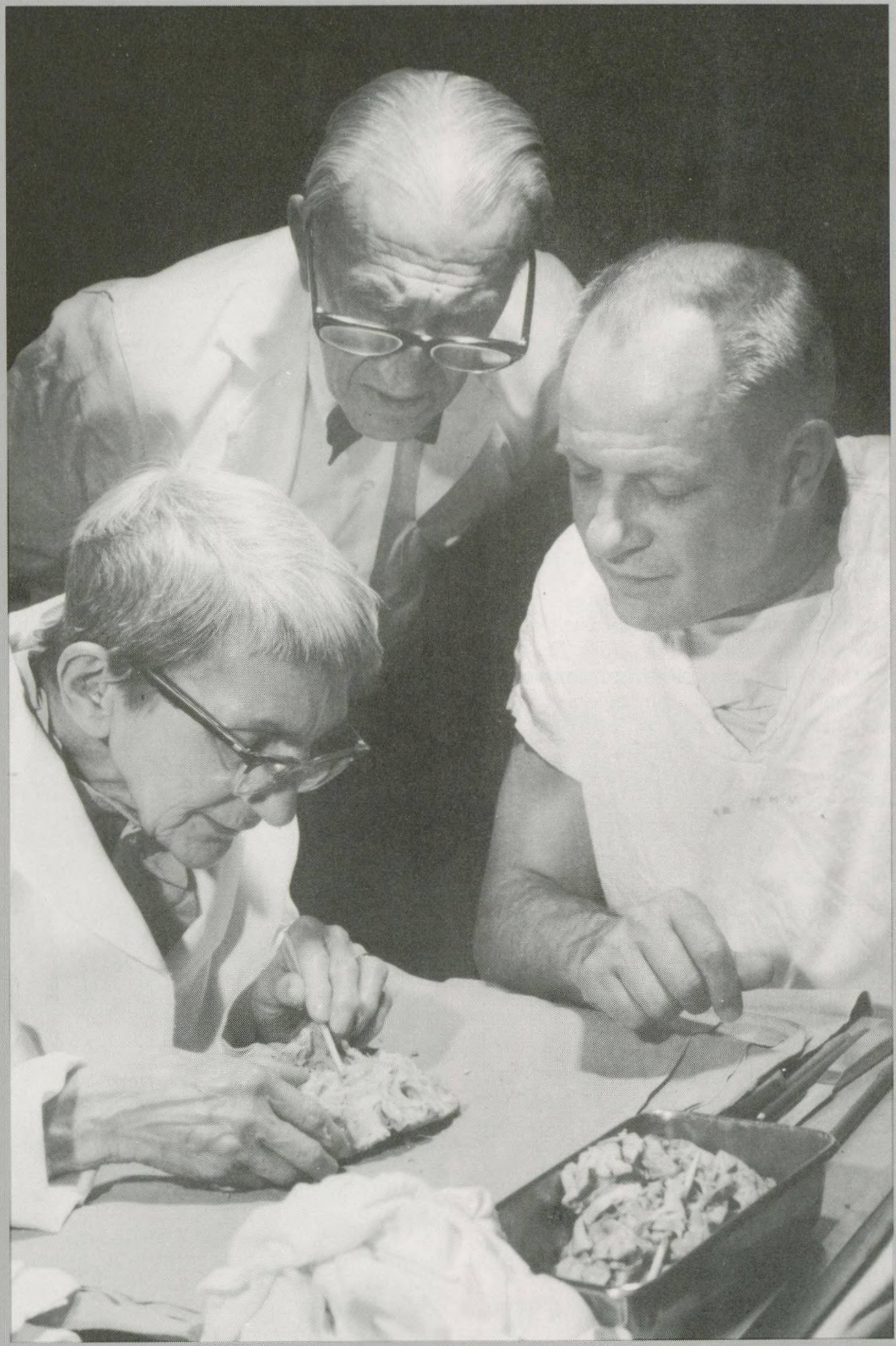
Schneider's avocation, sports medicine, currently has him spending hours in his office writing a veritable tome on the subject. He is working hard to meet the publisher's deadline.

Regardless of how well his book sells, Schneider's most important contribution to sports medicine may never appear in scholarly literature. It appears instead, with great regularity, on the helmeted heads of football players—including the U-M Wolverines. Schneider co-invented an air-cushioned football helmet which has prevented countless possible head injuries to athletes. Working with Hank Gosch, a neurosurgical resident, and an engineer Elwyn Gooding, (both no longer at U-M), Schneider conducted research with anesthetized monkies to find out exactly how head blows affect the brain. His observations enabled the engineer to design headgear which prevents some of the most crippling injuries to gridiron athletes.

Schneider discovered that typical football headblows result in the brain being dashed against one part of the skull. The force of the blow or fall is concentrated on a relatively small part of of the brain, causing massive contusion. He reasoned that a helmet which distributed the energy of the blow over a wider area would prevent the injuries he witnessed in the laboratory and on the football field.

The helmets are air-cushioned with the ability to spread the impact over a broader surface area of the head. They are recognized as one of the best protective headgears.

The patented helmet, manufactured by the Bike Helmet Company, has been a best-seller for six years. In fact, U-M's slice of the royalties adds up to the University's largest patent profit in history. The helmet is so successful in preventing injury that researchers hope to adapt it for other sports.



The Crosby-Kahn-Schneider team described the anatomical basis for neurosurgery. Here, they explore a brain specimen, looking for an association bundle—a nerve pathway which transfers responses from one part of the brain to another.

— *Continued from page 13*

half of the child's brain had been tumor. Nonetheless, the baby had moved its limbs normally. Says Kahn, "I couldn't understand how the child moved his limbs on the one side. Normally, such movements are controlled by brain areas on the opposite side of the body.

"Crosby was surprised too, at first. Then she told me that there were some primitive motor pathways of the brain that were used in lower vertebrates for progressive movements. Humans have a remnant of that primitive brain which is used until children are about eight or ten months old. At that time the voluntary cerebral pathways start to control limb movement. This explained the child's 'normal' limb movement. I could not distinguish movement controlled by this primitive pathway from cerebral-controlled movement in a baby."

Crosby was often called to consult in the operating room—a highly unusual, if not unique, role for anatomists. Her encyclopaedic knowledge of the brain proved invaluable to surgeons. Says Kahn, "When you're doing neurosurgery and working in the region of a tumor, the anatomy can be confusing. The tumor itself puts everything in unusual positions, and hemorrhages may make things difficult to see. We called Dr. Crosby for advice. Even when she was on crutches she'd come around to help." (Crosby suffered several leg and hip injuries as she aged.)

Richard Schneider also called upon Crosby for advice in operations for convulsive seizures. He recalls an unusual case. He was puzzled by a woman who showed hallucinatory symptoms: smelling foul cigar smoke, hearing whirling winds, and seeing people with crossed arms where their heads should be. These symptoms would be expected from a problem arising in the *temporal* lobe of the brain—one of two brain areas on either side, at the base of the skull. During an operation, however, Schneider discovered the problem in the patient's frontal lobe, despite EEG readings of pathway "firings" in the temporal lobe. He called Crosby by telephone from the operating room. What was going on? "That's easy," she replied. "Come down to my lab when you're finished with the operation." When Schneider arrived, she showed him a connection between the frontal lobe and the temporal lobe via a fiber path known as the *uncinate fasiculus*, an association bundle. "These are bundles of fibers which connect distant parts of the brain. This was the first time we had really paid much attention to association bundle connections in the operating room. You need an anatomist like Crosby to call attention to such things.

The Bird Man of Neurosurgery

One day I (Edgar Kahn) was doing a trigeminal operation... and was soon in trouble. I asked our nurse to call Dr. Peet immediately, but she could not find him....In a moment of frustration, I said, "I suppose he is over at the museum working on those goddamn sparrows." Two weeks later, history repeated itself. I was doing a left-sided tic operation, the dura was thin and tore, and the temporal lobe under nitrous-oxide anesthesia was extruding. I waited twenty long minutes before Dr. Peet arrived, and I immediately said to him, in angry relief, "Where were you?" He answered, without cracking a smile, "I was over at the museum working on those goddamn sparrows." (from *Journal of a Neurosurgeon*, Edgar Kahn, 1972)

While Max Minor Peet's first calling was undoubtedly medicine, he managed to fit an entirely separate career into his busy life. As an ornithologist—a scientist who studies birds—he was as well known as he was in neurosurgery.

At Peet's death in 1949, Josselyn Van Tyne, Curator of Birds at the U-M Exhibit Museum, wrote, "Dr. Peet was among his generation's most active ornithologists. His study of the ecology of the birds of the Ypsilanti bayou is one of the earliest important studies in avian ecology."

In that study of sixty acres near the Ypsilanti, Michigan, Highland Cemetery, Peet observed bird populations in swamp, willow, forest and meadow habitats. He concluded that "the distribution of birds in any given area is primarily determined by the geological formations, the physiographic changes taking place, and the resulting biota, i.e., the plant and animal societies characteristic of these conditions." The relationship among animal populations and their habitats may seem like old hat today. But in 1908 Peet's conclusions and observations helped move birdwatching from a pleasant pastime into the newly emerging field of ecology.

Van Tyne also acknowledged the museum's debt to Peet for his collection of bird specimens, "the largest and finest private collection of birds in the U.S. and Canada." The collection, donated to the Museum by Peet's widow, contained a hundred kinds (sub species) of birds entirely new to the Museum, six "type" specimens that serve as standards for the species, and 45 specimens of extinct birds.

Robert Storer, Curator of Birds at the Museum today, credits Peet with 32,300 specimens. (The Museum has a total of 150,000 bird skins). "What makes the collection useful to us is that he got specimens from all areas. For instance, he bought a collection from the Queen Charlotte Islands. They differed in many ways from mainland specimens. Also, he got an extensive collection from southwestern U.S., and even some from Greenland."

Peet purchased and traded a large number of specimens to complete his collection. Being a crack shot, however, he collected many himself from the wild. His medical career aided him in obtaining birds from the entire continent. Van Tyne says that he would come back with new specimens or data whenever he travelled to medical conventions, or performed operations and consultations in faraway places.

And what does all this have to do with neurosurgery? Edgar Kahn says that Peet was famous for the speed and accuracy with which he performed certain delicate brain operations, despite his large (size 9) hands. Peet attributes his dexterity to skinning *baby* humming birds. "He could do the procedure for *tic doloureaux* in ten minutes," says Kahn.

Photo courtesy Martha McAndrews

Max Peet pioneered brain surgery in Michigan and the United States. He also pioneered early ecological studies of birds, and contributed a large fraction of the bird specimens now in the U-M Museum of Zoology.

Eventually, we treated quite a number of convulsive seizure cases with association bundle problems."

In addition to this major contribution to neurosurgery, Crosby co-authored many scholarly papers on the subject. Her insights added a basic science component to papers which might otherwise have been limited to clinical observations. Kahn, for instance, was once asked to deliver three papers for a professional group. He consulted Crosby, who "wrote a remarkable paper on facial expression with me. She refused, however, to have her name on it. It was the best paper I ever gave." (Kahn foiled Crosby's modesty by acknowledging her contribution in the first paragraph of the paper.)

Some of Schneider's and Crosby's papers concerned the surgical treatment of epilepsy, after studying 139 cases of intractable convulsive seizures. They also wrote about the voluntary and automatic pathways controlling eye movement, the human olfactory system, and a major paper on treating abnormal muscle tone and movements resulting from cerebral palsy. The latter paper, based on ten years of experimental and clinical work, addressed patients suffering from spasticity. Their muscles are so tense and rigid that their bodies are "tied up in knots." Crosby and Schneider explored surgical methods of destroying specific parts of the brain to balance and overcome the spasticity. The paper, according to Kahn, was based on cases of heart-breaking difficulty, and only began to solve some of the problems in palsy cases. However, the paper is a classic from an anatomical point of view. U-M Anatomy Professor Muriel Ross says that she bases several classes each semester on discussion of that paper alone. Schneider and Crosby also published three papers on a theory of space space sickness based on related symptoms in certain brain tumors.

Great Strides in Neurosurgery

"Max Peet, Kahn, and Schneider spent their careers puzzling out two major problems," says Julian Hoff, who now chairs the Neurosurgical Service. "First, they used anatomy to locate the site of the disease. The second thing they learned, basically, was how to operate on someone safely. Both contributions were tremendously important, and they learned then mostly by trial and error—doing the best they could with the knowlege of the times."

These surgeons' anatomical approach to neurosurgery has now become so integral to the field that students rarely take the extensive anatomy courses required in the past. They learn anatomy in conjunction with other disciplines such as neurochemistry and neurophysiology. "Students must know as much anatomy as in the past—they are tested for it in board examinations. But they pick it up along the way now, by studying books such as *Correlative Neurosurgery* and in clinical work." Crosby and Kahn's revolutionary ideas have quietly become institutionalized in the practice of the 1980s.

Kahn recalls that when Peet began neurosurgery in the first decades of the century, brain tumor surgery had a 30 percent mortality rate. Hoff says that now, less than one percent of patients with neurosurgery die from the operation. "Neurosurgery had a bad name until recently," he acknowledges. "Anyone considering brain surgery faced the likelihood of death or, if they survived, serious disability. That's largely changed now. Mortality is an unusual result, and disability is substantially better, though not as much as we'd like. And for those with disabilities, rehabilitative medicine has made enormous strides."

The figures on elective versus emergency surgery indicate neurosurgery's new respectability. In the past, high mortality must have discouraged most people from willingly undergoing brain surgery. Hoff says that today, 85 percent of such operations are elective. Only a small portion are do-or-die emergencies where the patient is chosing surgery or certain death.

Hoff attributes the current high level of surgical success to technical lessons learned in the past, including better anaesthesia, better operating instruments, operating microscopes, and earlier diagnosis. He points to mortality rates for surgery on tumors of the hearing nerve as an example of recent rapid advances. Until the 1960s, says Hoff, 50 percent of these patients died. Now, less than five percent do.

Another positive factor is that fewer types of neurological disease require surgery. "There used to be a lot of surgery for seizures," says Hoff. "Now, potent medicines have reduced the volume of such cases." He says that the notorious "psychosurgery"—frontal lobe destruction, or lobotomy—is carried out only extremely rarely. "It's a good thing it got such a bad name," he asserts. "It smacked very much of Orwell's 1984."

New Frontiers for Neurosurgery

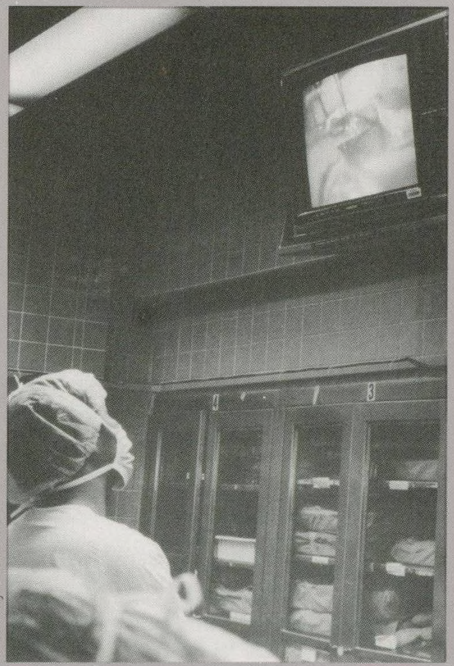
Some have dubbed the 1980s as "The Neuroscience Decade." Just as in the decade when Crosby began her work, neuroscience is glamorous and exciting. This time, though, it is not neuroanatomy hitting the headlines and winning Nobel prizes. New tools such as PET (positron emission tomography), CAT (computerized axial tomography) scanners, and NMR (nuclear magnetic resonance) enable scientists to explore the basic chemistry or structure of the nervous system without surgery. Reports of the links between body chemistry and psychological states fill academic journals and popular science magazines.

In neurosurgery, Hoff sees four major problems still defying practitioners. The most progress has come in the prevention of stroke. Aided by public education and earlier diagnosis, surgeons can now bypass occluded blood vessels in the brain, thus preventing otherwise-likely damage. On the other hand, physicians are discouraged by the prospects of finding effective cures for malignant brain tumors. The third area, traumatic head injuries, has witnessed significant improvements. In the fourth, spinal cord injuries, little progress has occurred. Hoff says, "Generally, there is no surgical solution to a broken spinal cord. As a matter of fact, there isn't even a glimmer of hope towards this problem. We are still having to deal with patients only in rehabilitation. All those kids that go out drinking and take a midnight dive into a shallow lake and break their necks—their lives are irrevocably changed. There is not much we can do now for them."

Neurosurgery *Then & Now*

Reading Edgar Kahn's diary of neurosurgery during 1930, one can't help marveling at the his courage in the face of such discouraging odds. Besides intelligence and sensitivity, he had little to go on in many cases. Diagnostic tools were not only primitive but dangerous. Anaesthetic drugs and technology were unreliable. During the operations, it was hard to see the region being explored, not only because bleeding was difficult to control, but some of the brain parts and nerves are so tiny. To top it off, tools for the various procedures were crude, at best.

Below, we will juxtapose excerpts from Kahn's diary with the situation today in neurosurgery.



Photos by Leslie Lin

A medical resident watches details of the operation on a video monitor whose camera is incorporated into the operating microscope. Tapes of such operations are also used for instructing medical classes.

Diagnosis

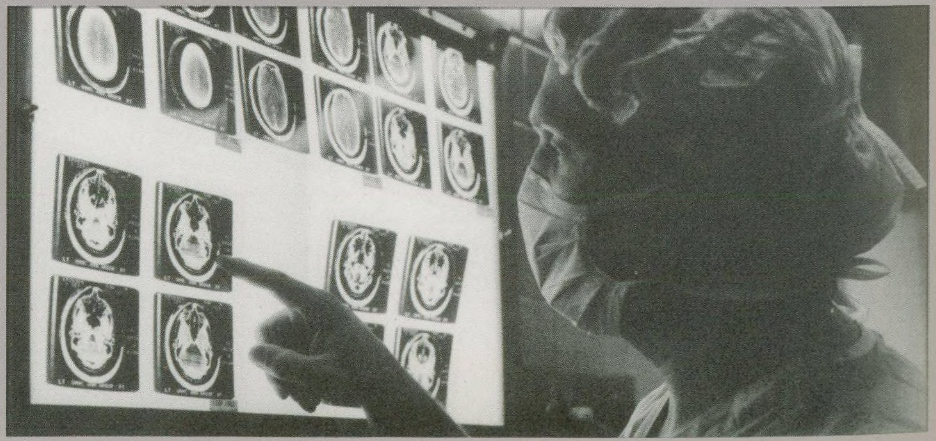
...Elizabeth R., 9, returned for check–up. I operated on her in June with a diagnosis of cerebellar tumor. Took off almost entire cerebellar hemisphere thinking it contained tumor. None was found on examination. ...she is now symptom free except for some optic atrophy. ...feel she will get a return of symptoms.

...made an incision in the frontal and parietal areas but found no tumor. Took off the bone flap and closed. Felt rotten over case.

....When I commenced my training, "exploratory craniotomy" was as frequently seen on the operating schedule as any other procedure."

Today, U–M neurosurgeons never open up the brain as a method of finding out what is wrong. Julian Hoff says that before an operation now, neurosurgeons are 99 percent sure of where the problem lies, and 90 percent sure of what it is. Since the early days of Kahn's practice, CAT scans have replaced *ventriculography*, the practice of blowing air into the brain's cavities so that things would show up better on X–rays. Kahn says that ventriculography itself had an eight percent mortality; patients sometimes died the night after being diagnosed with this procedure. "Neurosurgery evolved only in small steps, and some of the steps were backward."

Arteriography with thorotrast, another old diagnostic tool, involved injecting radioactive materials into brain blood vessels. They would show up nicely on X–rays, but the radioactive materials could themselves cause cancer. Today, a non–radioactive iodine dye is used.



◄ In the operating room, a medical student discusses the case of a young auto worker with chronic vertigo. Here, he checks CAT scans to see if any other brain abnormalities might be present.

Anaesthetic

...(He) is a big Czechoslovakian with thirteen kids. We gave him a large dose of Avertin rectally and he went right to sleep. While I was putting in the local, and Peet was telling the visiting doctors how wonderfully the anaesthetic worked, the fellow raised his head up and said: "S—t, give me some ether." We had to sit on him. The operation was technically beautiful.

According to Hoff, "Better anaesthetic is one of the biggest reasons for neurosurgery's current success. We have better anaesthetic drugs, we understand the lungs better as well as the theory of how anaesthesia works. For about the last 15 years, we've had sophisticated machines for monitoring the patient's vital functions. Also, the anaesthesiologist uses various stimulators to check out the patient's responses, to be sure he or she is unconscious."

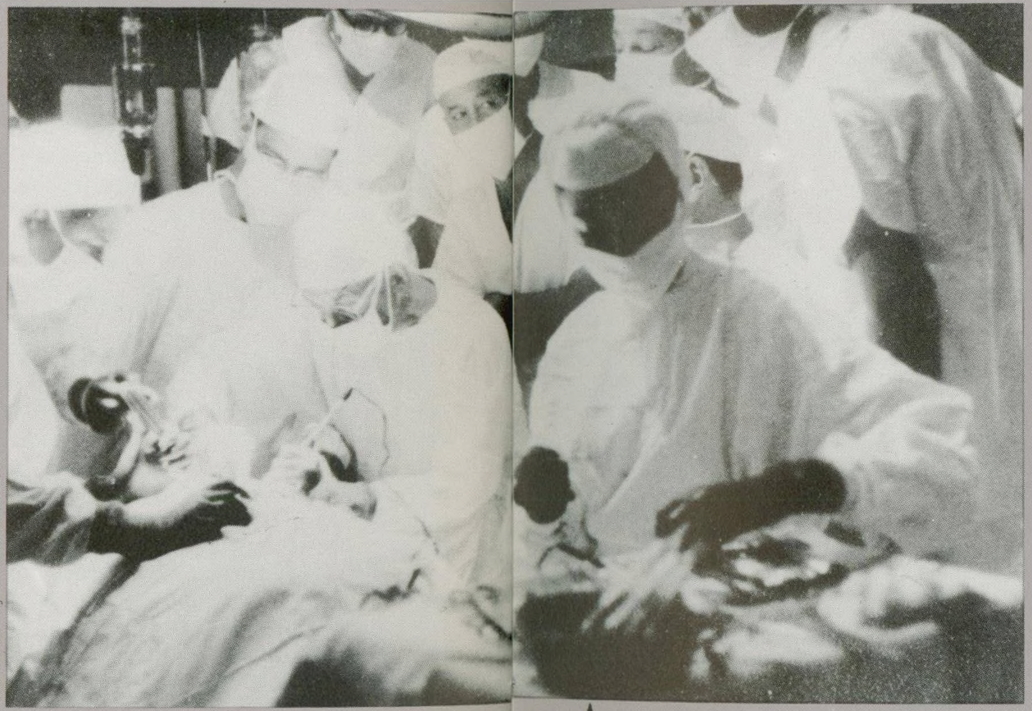


Photo courtesy Richard Schneider

▲ Neurosurgery in 1955—without benefit of operating microscope, good anaesthesia, or brain dehydrating agents. The crowd of residents and students around the suregon had a poor view of the operation, a less-than-ideal learning situation.

Pre–Operative Procedures

...We had no urea and mannitol, which when given intravenously, shrink the brain tissues, facilitating tumor removal.

...When the dura (a tough sheath covering the brain) was opened over the cerebellar hemispheres, the most unbelievable herniation (ballooning out) developed, and this could not be relieved by tapping the small ventricles. This complication was almost invariably fatal.

According to Kahn, such intravenous infusions were not begun until 1950 in neurosurgery. Now they are routine. Patients are at far less risk of damaging or fatal pressure build–ups occurring when swollen brain tissues press against the cranium.

Operative Procedures

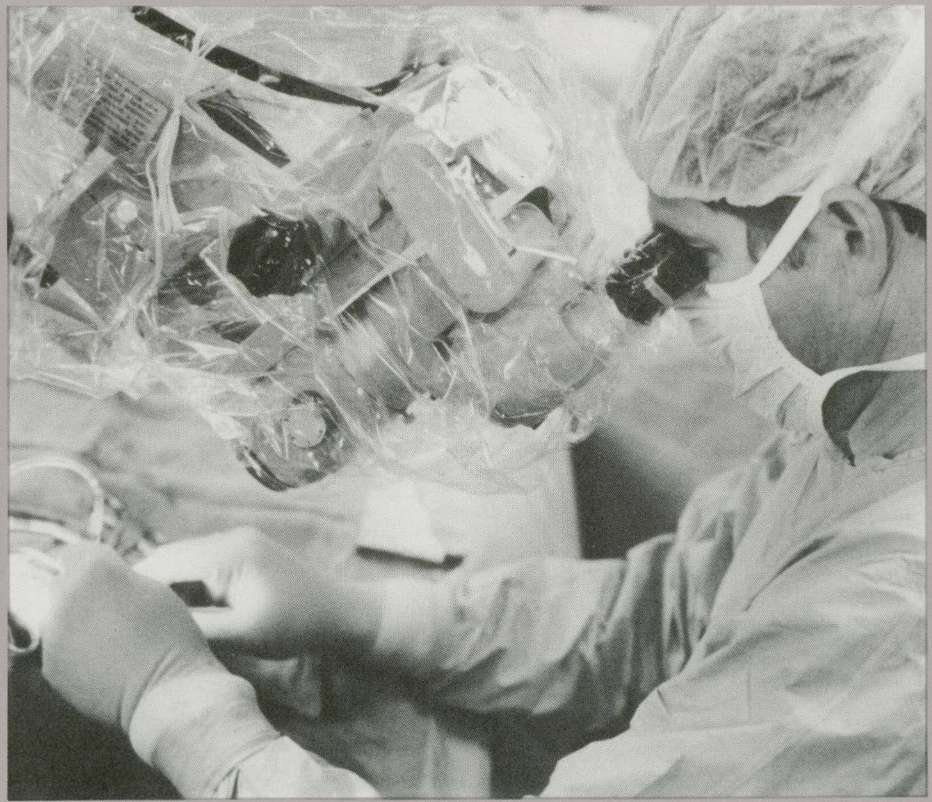
...There sure is a lot of grief in the work I'm doing. My philosophy is that I'm probably doing no harm, as you "can't spoil a bad egg"; while frequently I really do some good.

...I've got to operate on a 14–month–old baby in the morning. I'm in such a rotten mental state that I'm nervous as the night before I did my first appendix about five years ago. The mother wrote me a letter about operating on the baby saying that she prayed to God my hand would be steady. It's rather funny but not so to me because this is an only child and my nerves are on the ragged edge. I've got to get away from here in a few days to forget the bleeding and swearing, mortality, etc.

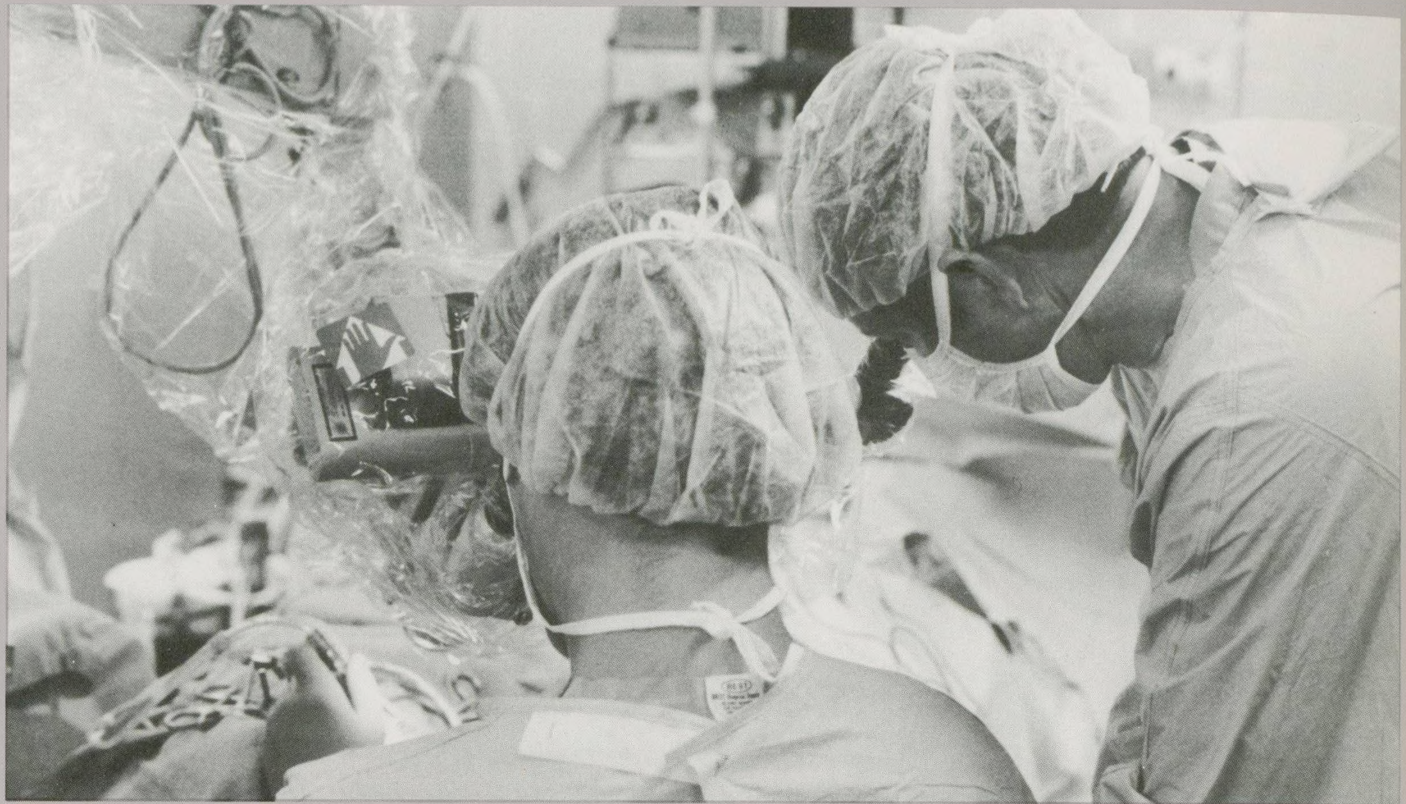
Neurosurgery itself pushed its practitioners to their limits of skill and nerve. Bleeding was a high risk, especially because in the very early days there was no cautery (closing bleeding blood vessels by electrical burning), and no suction to draw off obscuring fluids. Surgeons used hand tools; today, most instruments are power–operated and very precise. (Kahn was one of the first to use powered instruments for opening the skull.) Above all, surgeons had trouble seeing what they were doing because the operating microscope had not yet been introduced. Today, neurosurgeons use binocular microscopes focused on brightly–lit fields. Their highly refined tools and the microscope enable them to operate on the tiniest nerves and blood vessels. Kahn points out, however, that the operating microscope doubles operating times, thus increasing fatigue and chance of infection.

"Neurosurgery evolved only in small steps, and some of the steps were backward."

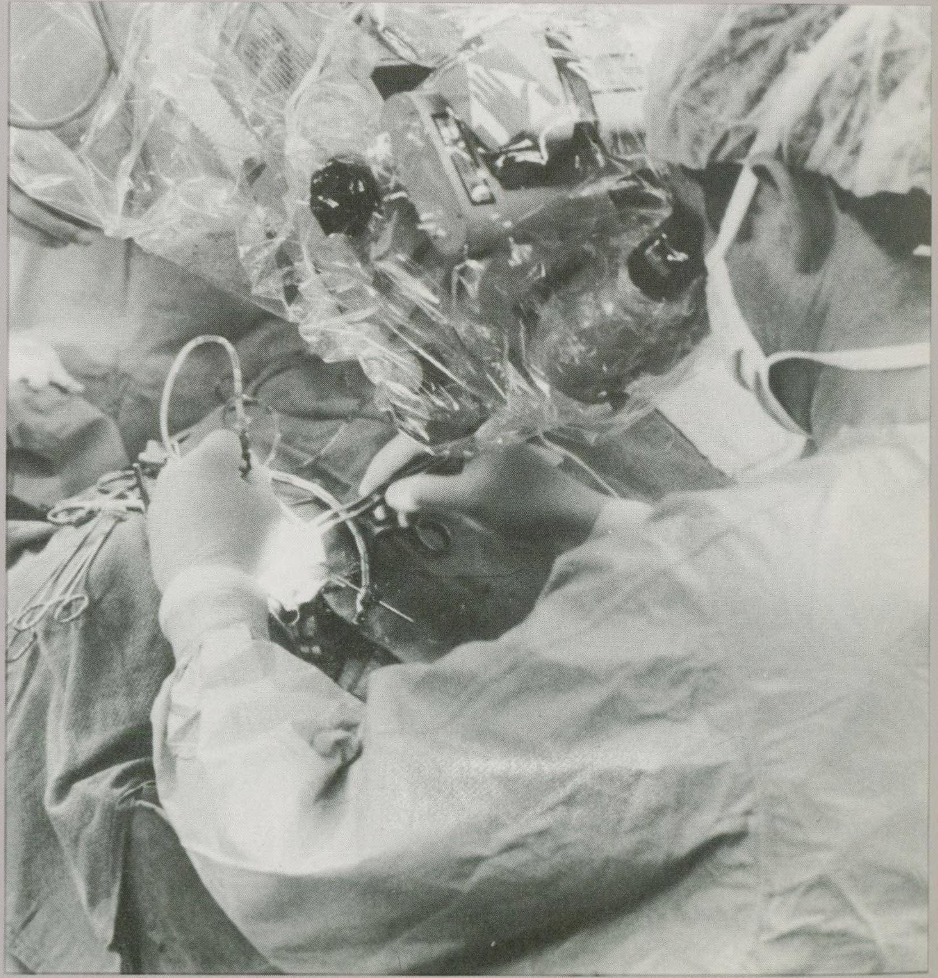
—Edgar Kahn



▲ The operating binocular microscope enables surgeons —here neurosurgeon Julian Hoff—to perform delicate procedures. Hoff is splitting the two parts of the eighth cranial nerve (hardly even visible to the naked eye) in order to relieve chronic vertigo in the patient.



Hoff (right) watches as his resident exposes the cranial nerve. Later, he takes over for the critical cutting of half the nerve. A mistake at that point could disable the patient's ability to control facial expression.



Julian Hoff makes the all–important cutting of the nerve which controls the patient's balance. He has a clear field of vision, thanks to a suction device (in his left hand) and a binocular operating microscope (draped in sterile plastic). The patient has been dehydrated to reduce pressure in the brain, and is monitored carefully by an anesthetist.

JULIAN HOFF:
Wearing the Mantle of Tradition

Physicians line their offices with dignified rows of massive texts. Julian Hoff, current Chief of the U–M Neurosurgical Section, is no exception. But when we visited, it was late in the day. As he leaned back tiredly in his chair, his faded, baggy, hospital greens seemed incongruous in his learned study.

"I've got a hard act to follow in this Section. I'm only the fourth section chief in neurosurgery here.

"The neat thing about U–M is that neurosurgery began here around the time it began in the whole world. We've always been right on the frontier since then. Peet began as a general surgeon, and did the first real neurosurgery in Michigan. He was one of the few people who pioneered the field in the U.S. He, and later Kahn and Schneider, helped establish the anatomical basis for neurosurgery—with Crosby, of course.

"The emphasis now is changing. I'll be pushing the department in the direction of incorporating the new knowlege of chemistry and physiology in our work."

Hoff is interested in two types of surgery. He treats difficult–to–reach tumors at the base of the skull. He operates, for instance, on tumors of the nerve which links the ear and the brain (the eighth cranial nerve). Until the 1960s, half the patients undergoing such surgery died. Now, according to Hoff, less than 5 percent die.

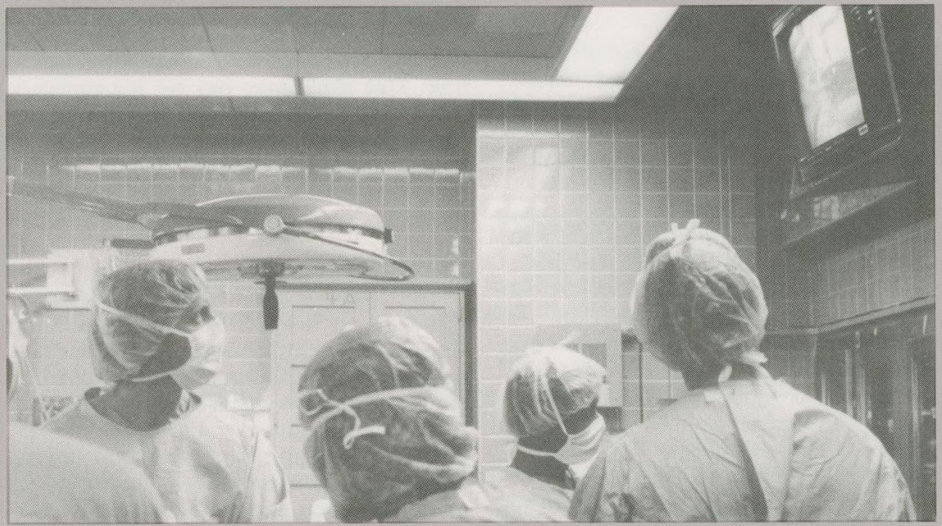
Hoff also treats diseased blood vessels in the brain. These vessels sometimes become aneurysms—typically, a weakened artery which balloons out with blood, threatening its victim with a sudden hemorrhage.

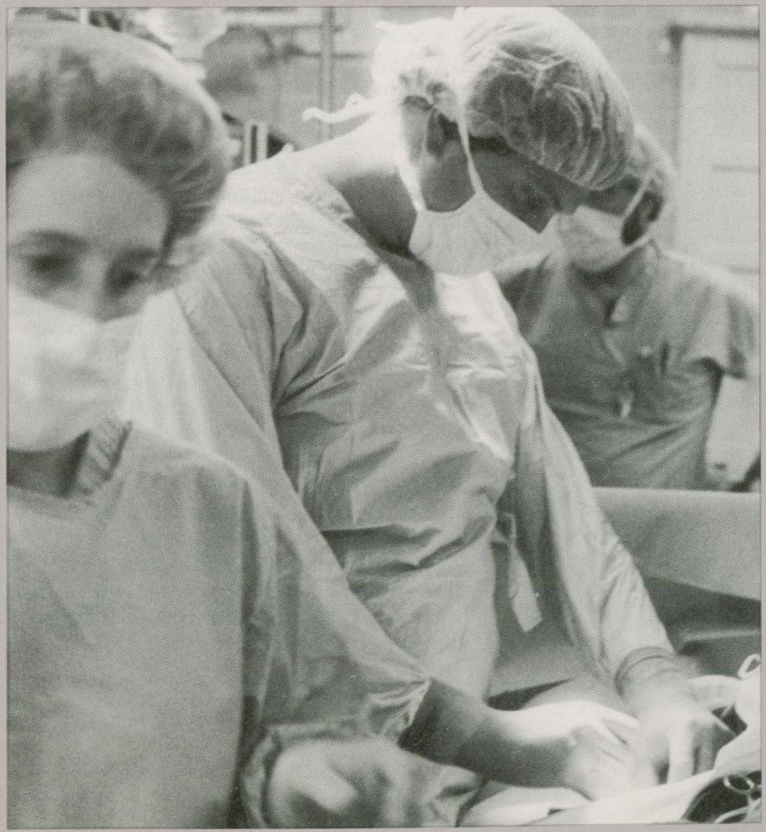
Hoff has also performed a new technique known as the "brain bypass." In this procedure a blockage, such as a clot, prevents circulation in a brain blood vessel, and the area of the brain it serves suffers from oxygen deprivation. Hoff locates the blockage, and then connects a healthy artery from the scalp "upstream" from the blockage. The scalp artery is detatched from the scalp and then re–routed through a small window cut in the skull. Hoff guides it into the brain and sews it onto the ailing vessel with 10 or 12 tiny stitches. The skull is patched up with the original bone, leaving a tiny notch for the new blood vessel. The bypass improves brain blood flow.

Hoff's interest in circulation processes within the brain have involved him in an experimental project funded by the National Institutes of Health. Using laboratory animals, he is examining how the swelling of brain tissues affect pressure in the brain, circulation, and other factors. Such reseach threatens one of neurosurgery's most ancient foes—excessive pressure in the brain, which can kill or cripple a patient quickly.

In the crowded operating room, everyone can learn by watching the operation on the television monitor. The camera is attached to the operating microscope.

While surgeons, residents, and interns take turns at various tasks during the operation, the scrub nurse works throughout. Behind her, a medical student—the low man on the totem pole—removes belly tissue for replacing lost tissue in the patient's skull.





Proton Decay: The Theorists Respond

This is the third in a series of articles about the IMB Proton Decay experiment. Here, U–M theorists discuss the experiments and its implications.

Skeptics: Proton Decay as E.T.

Martinus Veltman and Edward Yao stand firmly in the sceptic camp, *vis a vis* proton decay. They trust only those theories with solid mathematical foundations, capable of yielding precise predictions. Veltman is renowned for developing gauge theory, the framework for much of grand unification. While he stands by gauge mathematics, he does not expect protons to decay.

People tend to like science with speculative elements. But nature rarely works that way. Through the ages, physics has progressed with careful step-by-step work. The last ten years have seen many wild speculations in physics and proton decay is one of them. It is an unbelievable extrapolation from known physics. A scientific version of E.T.

"Our knowledge currently stretches to energy levels around 200 to 300 billion electron volts, or GeV. Proton decay requires 10^{15} GeV. Personally, I consider that wild."

Yao, whom Veltman cheerfully pegs as a "notorious sceptic," agrees. "To extrapolate from what we know by 12 to 15 orders of magnitude without some drastically new theoretical ideas--it's just prepostrous. I have a gut feeling that we just won't see it. Even if we did, it would tell us nothing about the real puzzles in physics today; for example, we know almost nothing about why various particles possess the masses they do."

Both Veltman and Yao look forward to further news from the salt mine. Says Veltman, "The proton decay experiment is in the best tradition of physics. It is a careful experiment, investigating detailed and precisely-formulated questions--not the wild goose chase variety. It is looking at cosmic rays in a way no one has ever been able to see them before. This alone may pay for the experiment in the end. And if no proton decay is observed, the experiment will have a healthy, sobering effect on physicists."

Optimists: More Than One Way to Skin a Cat

Just across the hall from Veltman, Gordon Kane and Stewart Raby appear unperturbed by Veltman and Yao's incredulity. "The original model may be ruled out, but lots of variants are still viable," says Kane. Only the most obvious and easily observed proton decay mode has been eliminated. Actually, we would be disappointed if they had found it, since it would have eliminated the more sophisticated 'super symmetry' theories that have been developed since the first scheme. I think that the majority of physicists believe that proton decay occurs, whether or not it can be observed in this experiment."

Raby, along with two other physicists, has predicted a supersymmetry theory in which protons would decay into different particles (characterized by a muon) different from the mode that Vandervelde *et al* have not found. Says Raby, "We should know in two or three months if this occurred during the first running period." A less-powerful proton decay experiment in Europe has some inconclusive evidence of Raby's decay mode. A *series* of the same event in the salt mine is necessary to prove that this result was not just a fluke. Unfortunately, says Raby, the muon decay may occur so rarely that it will not show up in the salt mine within two or three years.

Kane and Raby maintain that not observing proton decay in the salt mine experiment would only alter proton half-life estimates, but would not endanger GUTs (Grand Unified Theories). Kane notes, "When the theory is not well enough understood to calculate precise lifetimes, negative results constrain you, but don't necessarily alter the fundamental theory. Once we get some positive results, we can constrain the theory better."

One of the chief reasons Kane expects proton decay is evidence that we all experience daily--we live in a universe of matter rather than anti-matter. This reality has puzzled physicists ever since Paul Dirac discovered anti-matter in the 1930s. Kane says, "Proton decay, as predicted by GUTs, can yield this universal assymetry. We hope it can be observed in the window open to the experiment."

Moderates: Proton Decay Possible but Unlikely

Martin Einhorn has been impressed by some initial successes of GUTs, but hesitates in light of the high odds against seeing proton decay. This dichotomy makes him Randall Hall's resident moderate.

"Nature would have to be very kind to grant us this," he says with regret. "But besides addressing the anti-matter/matter asymmetry, GUTs explains several other known phenomena. It explains why the charge of electrons are equal and opposite to protons, and why quarks, which are constituents of protons, have charges of either 1/3 or 2/3. Most convincing is that GUTs predicts an extremely precise, experimentally confirmed number for the ratio between the strengths of electromagnetic and weak interactions."

Einhorn has examined the monopole issue, including one prediction that monopoles are catalysts for proton decay. He doubts that further running of the salt mine experiment will discover monopole interactions. "Recent astrophysical arguments suggest that monopoles are so rare that the resulting proton decay would not show up in the salt mine experiment."

Psychological Impact

According to Einhorn, continued negative results from the salt mine could have a profound psychological impact on physics. "The experiment gives us a 'window of observability' up to a proton lifetime of 10^{33} years," he says. Some of the more speculative theories predict up to 10^{38} years." Since no other technology is likely to exceed the salt mine experiment's power, Einhorn says that it is seen as a "last chance" to observe proton decay. "If proton lifetimes run beyond 10^{34} we'll never know if it is stable or if it decays. The theory would leave the range of observability, thus becoming natural philosophy, not an experimental science. That would be very sad."

Ed Yao says that further negative results would undermine GUTs because "Belief or non-belief in a theory is a function of time. Physicists are human too. If there are no results after three or four years, it will be less profitable to be a believer. It would not lead us any closer to the most challenging problems in physics today."

How do people of such divergent views manage to work together from day to day? Yao enjoys the diversity. "It's good to have different ways of looking at things. It helps to eliminate the really crazy ideas." He says that the theorists pay close attention to each other's work, and that disagreement does not prevent them from being fair.

Kane admits, with a grin, "We agree to disagree. But when one of our ideas proves correct, we really rub it in!"

CASE Award to *The Research News*

The Research News received the 1983 Citation Award for research periodicals from CASE, the national Council for Advancement and Support of Education. The award judges noted that the publication "represented a good use of institutional resources and treated one topic quite well in an in-depth way. In addition, it deals with scientific issues, as well as the research itself, which many publications fail to do."

Blanchard Hiatt Moves On

Writer Blanchard Hiatt, whom readers have enjoyed for the past ten years, has left *The Research News* for a position as a medical writer in private industry. Hiatt's efforts here won him two CASE awards, and set standards for interpreters of science at U-M. He is a hard act to follow. We wish him well in his new endeavors. Meanwhile, Lee Katterman has joined the *RN* quill-pushers. Katterman comes to us from science broadcasting for National Public Radio and WEMU, the radio station of Eastern Michigan University. He is currently preparing his first issue, about U-M research on aging.

To the Editor:

I want to tell you how much I have enjoyed reading the April–May issue of *The Research News*, concerning literary translation. It was sent to me by a friend and fellow former U–M grad student. Please send another copy so that I can share it with my instructor of Biblical Hebrew at the University of Minnesota. I know that she would enjoy it also. She has continually recommended Anchor Bibles (edited by Dr. Freedman, one of the consultants listed in the issue.)

I continue to be interested in research and scholarship at the University of Michigan.

Sue Groth Kloker

Minneapolis, MN

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