Otology & Neurotology
22:113–122 © 2001, Otology & Neurotology, Inc.

Harold Schuknecht and Pathology of the Ear

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Background: Like Joseph Toynbee and Karl Wittmaack before him, Harold Schuknecht understood that studying pathology was the key to advancing the scientific basis of neurotology. His work elucidated the pathophysiology of the most common neurotologic disorders, including benign paroxysmal positional vertigo, Ménière's disease, and viral neurolabyrinthitis. Schuknecht was a tireless crusader against medical and surgical treatments that he considered to have little scientific foundation. His textbook *Pathology of the Ear* remains the definitive work in the field. **Key Words:** Vertigo—Neurotology—Biography.
Otol Neurotol **22:**113–122, 2001.

In 1928, John Lindsay arrived at the newly established Medical Center at the University of Chicago as an assistant professor in the Division of Otolaryngology (1,2). Lindsay had grown up on a farm in Ontario, Canada; attended a 6-year medical program at McGill University; and then entered private practice in the office of a country doctor. He quickly realized that he didn't know enough about medicine to be effective with most of his patients, so he decided to stick to one specialty, entering a residency in otolaryngology first at the University of Toronto and then at McGill University. With the support of Dallas Phemister, Chief of Surgery, a year of sabbatical leave was arranged so that Lindsay could visit Europe to learn the latest developments in otologic surgery. He spent most of the time in Zurich, Switzerland, working with F. R. Nager, Chief of Otolaryngology at the University of Zurich.

In the tradition of Wittmaack, Nager had his practice in a small house just down the hill from the university buildings. His patient examination rooms were next door to his research laboratory. Nager had learned the art of processing temporal bones and had begun to develop his own temporal bone library. John Lindsay was given a desk in the laboratory and was called next door to the examination rooms whenever Nager had a patient worth seeing. In this setting, Lindsay became fascinated with the pathology of the temporal bone. He watched the technician process and cut the bones, and he routinely reviewed the histologic sections with Nager. When Lindsay returned to the University of Chicago, he established a temporal bone research program of his own. "When I got back from Europe, I started to save, from the morgue, every ear I could get my hands on–or anybody else could get their hands on. The processing took about a year after you got the ears; then you could study what was going on" (1).

At that time, a debate was beginning regarding whether biomedical research should be relegated to full-time basic researchers or whether physicians in clinical practice had a role to play. John Lindsay believed that physicians knew the clinical expressions of disease and therefore were best able to establish and maintain a relationship between clinical medicine and research. He recruited several like-minded physicians on the otolaryngology faculty, and he insisted that his resident physicians were exposed to research during their training (2). On the other hand, he was well aware of the competing forces of the need to make a living. "Some people are naturally interested in doing high quality research, making a reputation through what they do, what they produce, then there are others who get their satisfaction out of making money. There seem to be two sets of ideals, one set being for those who make the big money and just can't resist it. Money is useful, of course, but it is much more satisfying to go after knowledge" (1).

Into this fertile environment, a young doctor just back from the war in Europe, Harold Schuknecht, began his residency training in January 1946. While stationed in Italy, Schuknecht had enjoyed his work in an eye clinic and had decided to apply for an eye residency when he returned to the United States. When he attempted to apply to the eye, ear, nose and throat residency at the University of Chicago, he was told that during the war, the eye residency program had become separated from the ear, nose, and throat (ENT) program. All of the eye residency positions were full, but there was still a position in

Supported by NIH grants AG 09693 and DC 02952.
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ENT. He decided to take the position because he didn't want to delay his residency training. Before coming to the University of Chicago, Schuknecht had had no formal exposure to research and had planned on a career in the private practice of surgery. He soon came under the influence of John Lindsay, Henry Perlman, and Heinrich Kobrak, who encouraged him to become involved in a research project. Perlman and Kobrak were young academic-oriented otolaryngologists recruited by Lindsay in the early 1930s, who along with Lindsay formed the backbone of the Otolaryngology Division (3).

During his residency, Schuknecht examined the temporal bone specimens from several patients who had experienced severe head injuries and noted a characteristic pattern of cochlear damage primarily involving the basilar turn of the cochlea (4). This led to his first series of scientific experiments, in which he tested hearing and examined the cochlea for damage after delivering blows to the exposed skulls of anesthetized cats (5). In collaboration with William (Dewey) Neff, an experimental psychologist, Schuknecht developed a method to obtain pure-tone hearing thresholds in the animals using behavioral methods (6). After the blows to the head, he found that the cochlear damage was greatest in the upper basal turn and that the hearing loss affected a greater range of frequencies as the cochlear damage became more widespread. This first experimental study, which was published in the *Annals of Otology, Rhinology and Laryngology* in 1951, stimulated Schuknecht's interest in the relationship between the locus of cochlear damage and the frequencies at which hearing loss occurred. To conduct his research during his busy surgical residency, Schuknecht did most of his experiments in the evening and on weekends. Basic researchers were amazed to see this young surgeon testing hearing in cats late into the evenings (7).

HAROLD SCHUKNECHT–AN AMERICAN SUCCESS STORY

In many ways, Harold Schuknecht had grown up as a prototypical American boy. He was born in a small farming community in Chancellor, South Dakota, in 1917 (8). His father, also born in South Dakota, had quit school after the sixth grade to work on the family farm. Despite his lack of education, his father was known for his knack with numbers, being able to add long columns in his head. Schuknecht's paternal grandfather was also a farmer, who had migrated to South Dakota from a German community in Wisconsin. He had no formal education and had never learned to read. Schuknecht's mother's family had come to South Dakota from Germany when she was 4 years old. They were Baptist fundamentalists who had left Germany in part because of religious persecution. Schuknecht's early family life was dominated by his mother's strong fundamentalist beliefs. She regularly attended prayer meetings, and the whole family was expected to attend Sunday services and Sunday school. Hal's father had to stop playing baseball in a semiprofessional league because his wife did not allow him to play on Sunday. Every morning the family gathered together, and Hal's father read a section from the Bible, the only book in the house.

Harold worked on the farm from morning to night, 6 days a week, except for the time he was at school. He developed a work ethic that would stay with him throughout his life. The family was poor and in constant danger of losing the farm during the Depression years. The father took on an additional job operating a grain elevator in town to make the mortgage payments. He expected Harold to stay on and take over the farm, as he had done with his father's farm, but Harold's mother encouraged him to go to college so that he could become a teacher. Hal made his choice on a hot dusty summer day in the middle of a prolonged drought. Walking behind five horses dragging a field that had just been plowed, he decided that this was not what he wanted to do for the rest of his life.

Schuknecht went off to the University of South Dakota in 1934. At that time, the tuition was $35 a semester—a major factor in his choice of schools. He picked premed as a major because a friend of his from high school, and his roommate at the university, had done so. The two young doctors-to-be were able to obtain a room rent free from an aging and ailing retired doctor in return for helping him around the house. Their only expense was an average of $2 a week for food for both of them. For entertainment they played handball and swam in the school pool, and occasionally on weekends they would sneak into the local movie theater. Harold began medical school in 1936 after cramming 3 years of premedical training into 2 by attending summer classes. The tuition in medical school increased to $50 a semester, so Schuknecht had to work at several part-time jobs to meet the increased payments. The University of South Dakota offered only the first 2 years of medical school, so he had to apply to another medical school for the final 2 years. He was accepted at Rush Medical College at the University of Chicago, but this meant a dramatic jump in tuition to $450 a year. With his mother's help, he was able to arrange a loan through a cousin, and he paid it back over several years after he had finished his medical training. He graduated from Rush Medical College in 1940 and then spent a year doing a rotating internship at Mercy Hospital in Des Moines, Iowa. On his first day of work, he met his wife-to-be, Anne Bodle, who had just come to work at the hospital as a laboratory technician. They were married exactly 1 year later and had their first child, a daughter, 1 year after that.

With World War II heating up, Schuknecht joined the reserves and was shortly called to active duty. After 2 years in the United States, he spent 2 years as a flight surgeon with the 15th Air Force in the Mediterranean theater. While stationed in Italy, he was in the first ambulance to arrive as a B-24 crash landed, setting off a fire and several explosions. All of the crew were able to get out except for the pilot, who was trapped in the burning cockpit. Schuknecht climbed onto the plane, pulled the

pilot out, and rolled him on the ground to put out the fire. Shortly afterward, the plane exploded. For his heroism in rescuing the pilot, Harold Schuknecht received the Soldier's Medal, the highest U.S. award for noncombatant action. Schuknecht loved to fly, having obtained his pilot's license during his internship. While in Europe, he frequently went on "milk runs" just for the fun of flying. The practice came to an abrupt end, however, when a routine "milk run" turned into a major battle with the Luftwaffe. The bomber next to his was shot down, and his plane barely made it back to the airfield.

After completing his residency in 1949, Schuknecht stayed on at the University of Chicago, first as a clinical instructor and then as an assistant professor. His clinical activities were largely directed at general head and neck surgery and endoscopy, and he continued his experimental work on the relationship between the locus of cochlear damage and the frequencies of associated hearing loss. He made precise surgical lesions in different parts of the cochlea and carefully measured the effect on hearing after the animals had recovered (9). Consistent with the resonance theory of Helmholtz, animals with lesions at the base of the cochlea showed a characteristic high-frequency hearing loss, whereas those with lesions at the apex had a low-frequency hearing loss. Schuknecht then conducted a series of experiments testing hearing in animals after lesions of the auditory nerve. He eventually developed a complete map of the cat's cochlea that showed the relationship between hearing loss and locus of cochlear damage (10).

Despite the heavy surgical workload, Schuknecht was making less than $15,000 a year as a young assistant professor at the University of Chicago. Money began to be an issue, because he was still repaying his medical school debts and had a wife and two young children to provide for. Furthermore, he was concerned about bringing up young children, particularly a young daughter, in the rough neighborhood around the University of Chicago. When the opportunity of a higher-paying position at Henry Ford Hospital in Detroit came up in 1953, he decided to take it even though he was unsure about what effect this might have on his promising academic career and the experimental research he was conducting at the University of Chicago. An unexpected benefit of the move to Henry Ford Hospital was that Schuknecht was able to drop the head and neck work, focus his clinical activity on otologic surgery, and establish an experimental research laboratory on his own. At Henry Ford Hospital, he was in the forefront in developing new otologic surgical techniques, including stapedectomy surgery, which revolutionized the management of otosclerosis. Over his career, he would perform more than 1,000 stapedectomy surgeries, gradually refining the technique.

THE SEARCH FOR THE CAUSE OF BENIGN POSITIONAL VERTIGO

In 1956, John Lindsay, along with one of his residents, Garth Hemenway, reported the case of a 65-year-old woman who, without any previous illnesses, suddenly experienced severe vertigo, nausea, and vomiting, which gradually resolved over several weeks (11). About a month after the onset of this acute prolonged episode of vertigo, she experienced brief recurrent attacks of positional vertigo, triggered by turning onto her right side while in bed or when getting in and out of bed. When examined, she had a bilateral sloping sensorineural hearing loss, slightly greater in the right ear, but she had not noticed any change in hearing with her vertigo symptoms. Positional testing triggered positional vertigo and nystagmus when she was turned onto her right side and when she sat up from the recumbent position (no description of the nystagmus was given). There was no response to caloric stimulation of the right ear, even with ice water. The patient died of a coronary thrombosis about 13 years after the acute prolonged vertigo episode. On postmortem examination of the temporal bones, there was a remarkably selective degeneration of the superior division of the vestibular nerve and the sense organs supplied by it: the macule of the utricle and cristae of the horizontal and anterior semicircular canals. In the same article, Lindsay and Hemenway described an additional six cases with a similar clinical picture of acute vertigo followed by positional vertigo. They concluded that the cause of the acute prolonged vertigo in all these cases was a vascular accident affecting the vestibular mechanism on one side. Regarding the delayed onset of positional vertigo, they thought that a utricular macular origin (as proposed by Bárány and Hallpike) was unlikely because the macule of the utricle was degenerated in the case they had studied at postmortem. "The explanation appears to lie in the fact that part of the labyrinth remained active, in this case the saccule and the posterior canal" (11).

Harold Schuknecht reviewed the temporal bone specimens from the patient reported by his former mentor John Lindsay and from the patients reported by Hallpike and colleagues. He was struck by the remarkable similarity in the pathologic changes (12). Each had a selective degeneration of the superior part of the labyrinth, including the superior branch of the vestibular nerve, the utricle, and the cristae of the horizontal and superior semicircular canals. He concluded that in each case the damage to the labyrinth resulted from occlusion of the anterior vestibular artery, the branch of the internal auditory artery that supplies the superior division of the vestibular nerve, the utricular macule, and the cristae of the posterior and anterior semicircular canals (Fig. 1). Schuknecht thought that the paroxysmal positional nystagmus in those cases must have originated from the posterior semicircular canal, because it was the only peripheral sensory organ capable of generating nystagmus that was still functioning. He dismissed the saccule as a possibility because it had never been shown to generate nystagmus.

With this hypothesis in mind, Schuknecht attempted to produce paroxysmal positional nystagmus in cats by cutting off the blood supply in the left anterior vestibular

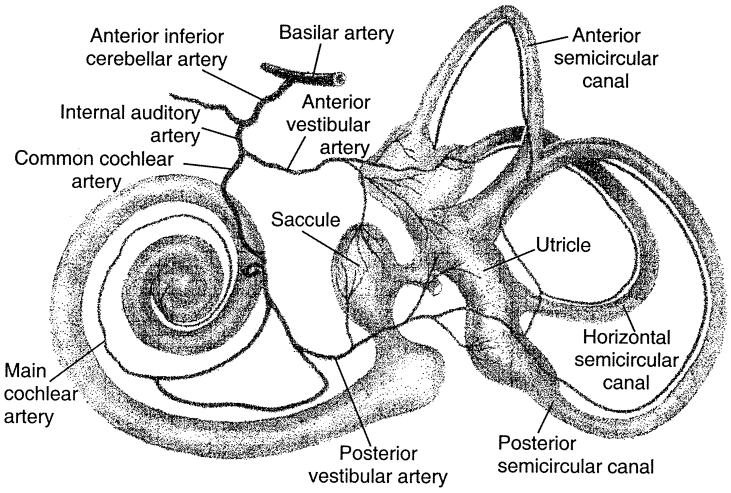

FIG. 1. Arterial circulation of the inner ear.

artery (12). The superior division of the left vestibular nerve was cut, along with the artery, because it was not technically possible to block the artery alone. He studied four cats and observed in each the development of the expected acute vestibular syndrome with horizontal nystagmus and imbalance in the immediate postoperative period. After these acute vestibular symptoms gradually subsided over several days, typical benign paroxysmal positional nystagmus developed in one of the animals 3 months after the operation; the condition persisted until termination of the experiment at 7 months. The animal exhibited a rotatory clockwise nystagmus when placed in the supine position with the left ear undermost. There was a latency and fatigability with repeated positioning. When the animal's temporal bones were examined 7 months after the operation, all showed severe atrophy of the superior division of the vestibular nerve and the sense organs supplied by that nerve. The posterior semicircular canal cristae and the inferior division of the vestibular nerve were intact. Thus, Schuknecht was able to reproduce the clinical picture of an acute vertiginous syndrome followed by the delayed onset of positional nystagmus in one of four cats that had undergone sectioning of the anterior vestibular artery. He argued that collapse of the superior part of the inner ear might have interfered with the function of the posterior semicircular canal in the animals that did not have positional nystagmus.

SCHUKNECHT SUGGESTS A NEW MECHANISM FOR BENIGN PAROXYSMAL POSITIONAL NYSTAGMUS

Schuknecht presented the results of his studies on benign paroxysmal positional nystagmus at the 66th annual session of the American Academy of Ophthalmology and Otolaryngology in October 1961 in Chicago. The article was published in the *Transactions of the American Academy of Ophthalmology and Otolaryngology* the following year (12). Schuknecht effectively argued that the only logical source of the paroxysmal positional nystagmus was the posterior semicircular canal, based on his review of the human temporal bone specimens and his animal experiments. He reasoned that with degeneration of the superior vestibular labyrinth, otoconia would be released from the otolithic membrane and that, in certain positions of the head, the otoconia would respond to gravity and thereby displace the cupula of the posterior semicircular canal (Fig. 2).

John Lindsay was asked to discuss Schuknecht's article at the Academy meeting in 1961 (13). Lindsay acknowledged that Schuknecht's theory could simplify a complicated problem, but he rejected the theory because he thought it was too simple. He argued that there are many different types of positional nystagmus associated with many different ear diseases. "It is a well-established law that stimulation of any semicircular canal causes eye movements in the plane of that canal. Therefore, the

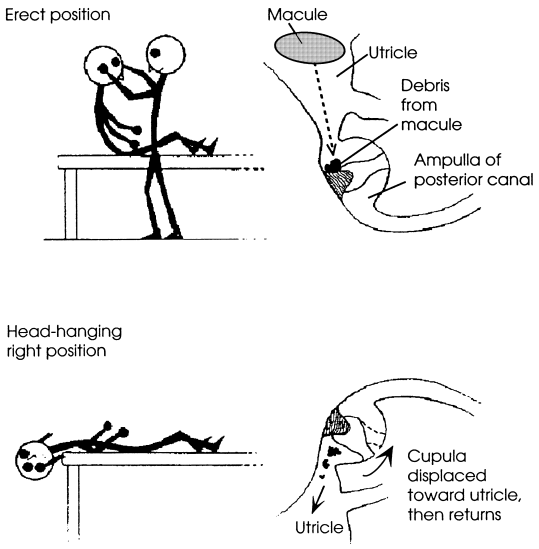

FIG. 2. Proposed mechanism for benign paroxysmal positional nystagmus in Schuknecht's 1961 presentation (12).

variation in the plane and direction of the positional nystagmus which has been observed in many peripheral lesions seems to refute the theory of origin from the posterior canal." Lindsay pointed out that a colleague at the University of Chicago, Cesar Fernández, produced positional nystagmus of the paroxysmal type in cats when he ablated the nodular lobe of the cerebellum. Furthermore, this clear central type of positional nystagmus was abolished if the peripheral vestibular apparatus was destroyed. Therefore, the observation that benign paroxysmal positional nystagmus disappears after destruction of the peripheral labyrinth was not proof of a peripheral origin of the positional nystagmus. It could be a central type of positional nystagmus requiring peripheral input. Lindsay objected to the use of *benign* in describing the paroxysmal nystagmus; he argued that many central lesions that caused paroxysmal positional nystagmus were not benign. In support of his argument, he mentioned three cases of so-called benign paroxysmal positional nystagmus that turned out to be caused by tumors of the cerebellar vermis. Lindsay had a way of presenting his comments in a constructive rather than a critical tone, always careful not to challenge or offend a colleague. But these criticisms by his former mentor strongly motivated Schuknecht to search for more compelling evidence for his new theory on benign positional vertigo.

SCHUKNECHT MOVES TO BOSTON

Harold Schuknecht was initially approached to become Chief of Otolaryngology at the Massachusetts Eye and Ear Infirmary at Harvard in 1959, but he had just completed his new research laboratory at Henry Ford and was uneasy about leaving, even though the Harvard position was the opportunity of a lifetime. Fortunately, Harvard was not able to decide on a new chief in 1959 and appointed an interim chief (7). Two years later, Schuknecht reconsidered and took the position at Harvard.

When Harold Schuknecht arrived at Harvard to chair the Department of Otolaryngology in 1961, he immediately set up a temporal bone laboratory and began collecting temporal bone specimens. His close friend Richard Gacek later stated that "It is safe to say that Schuknecht's main hobby was the temporal bone, and he took great joy and satisfaction not only in deriving knowledge of human otologic disease from the temporal bone, but in sharing it with his staff and trainees." He was known to have said that studying the temporal bone on Sunday morning was closer to religion than attending church services (14). His "Sunday school" temporal bone sessions with the resident physicians were a regular feature of his early years as Chief of Otolaryngology at Harvard.

Without a doubt, Harold Schuknecht was a workaholic. He typically left for work between 6:00 and 6:30 in the morning and did not return until after 7:30 in the evening. Saturday was also a working day, although he usually went in a little later in the morning. Sunday was his leisure day; he usually spent only about 4 hours in the hospital on Sunday. He worked on reading manuscripts and writing research papers when he was at home. He slept 5 or 6 hours a night at most but not infrequently would awaken early—as early as 2:00 A.M.—particularly when he was working on his textbook *Pathology of the Ear*. Schuknecht did not consider himself intellectually gifted, but he was proud of what he called his "intellectual stamina" (Anne Schuknecht, personal communication, 1998). He just worked harder and stuck with things longer than others.

Despite his heavy workload, Harold Schuknecht maintained a fascination with sports. He had a lifelong interest in fishing and hiking inspired by his childhood in rural South Dakota. He took great pride in the Boston Marathon, regularly filming the runners and keeping detailed records on all of the marathons he had seen. He liked to wait at the halfway point and encourage the runners whom he knew in the marathon. Every year he held a cookout at his home for friends as they returned from viewing the marathon. Like most Americans, he had a fascination with the professional sports teams in his home city. He had season tickets to the Boston Celtics basketball games during the 1960s and 1970s, when the Celtics dominated professional basketball. Dick Gacek noted that "one of his fondest memories and most prized trophies was catching the game ball after the final seventh game of the 1965 championship series with the Los Angeles Lakers, when the ball was thrown into the stands by Sam Jones. The ball was subsequently autographed by all of the Celtics players and occupied a favorite spot in his den" (14).

MORE TEMPORAL BONE SPECIMENS FROM PATIENTS WITH BENIGN PAROXYSMAL POSITIONAL NYSTAGMUS

All three temporal bone specimens from patients with benign paroxysmal positional nystagmus that Schuknecht reviewed in his 1962 article showed degeneration of the superior part of the labyrinth with sparing of the inferior part. However, as Dix and Hallpike noted, benign paroxysmal positional nystagmus usually occurs as an isolated finding without other damage to the inner ear (15). These cases, therefore, were not representative of the usual case of benign positional vertigo.

In his Boston temporal bone laboratory, Schuknecht obtained two temporal bone specimens from patients with a more typical clinical picture of benign positional vertigo (16). Both had shown a clockwise rotary nystagmus when positioned with the left ear down. Schuknecht identified a prominent basophilic staining mass attached to the cupula of the left posterior semicircular canal in these two patients (Fig. 3) (16). In the second case only, there was also a thin layer of similar material located on the membranous wall of the posterior semicircular canal in its most inferior location. Schuknecht did not find similar material, either attached to the cupula or on the membranous wall of the posterior semicircular canal, on

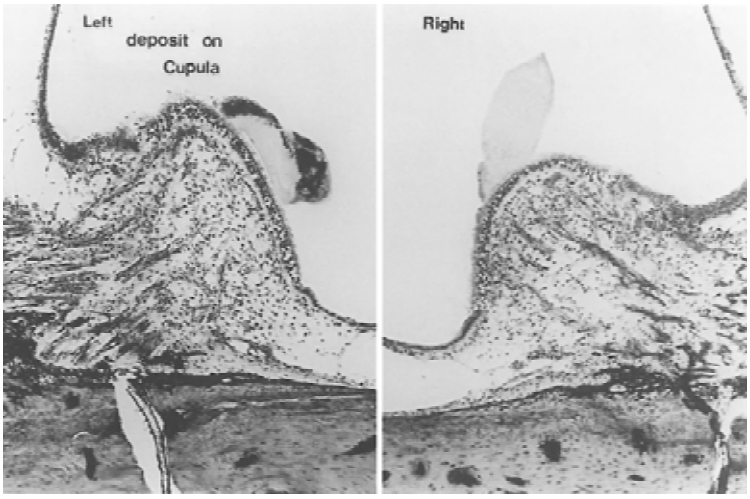

FIG. 3. Histopathologic section through the cristae of the posterior semicircular canals of a patient who had typical benign paroxysmal positional vertigo and nystagmus in the head-hanging left position before death of unrelated causes. Note the granular, basophilic deposit attached to the cupula of the left posterior canal and the normal cupula on the right. (Courtesy Harold Schuknecht.)

the right side (the normal side). The sensory epithelia of the utricle, saccule, and the three cristae of the semicircular canals were completely normal in both ears from both specimens. The nature of this basophilic deposit on the cupula of the posterior canal was not clear, but Schuknecht thought that it was probably derived from otoconia that had been detached from the otolithic membrane. Calcium would have been resorbed during the decalcification process, so he assumed that it was the matrix in which the calcium carbonate was embedded that stained with hematoxylin. He mentioned that in a study of 550 specimens at the Massachusetts Eye and Ear Infirmary examined by his associate, Ralph Ruby, similar deposits on the cupulae of the posterior canals were found in only 15, and he suggested that some of these deposits might have resulted from postmortem degeneration of the utricular otolithic membrane.

On the basis of the findings in these two postmortem specimens, Schuknecht coined the term *cupulolithiasis* to explain the clinical syndrome of benign positional vertigo (16). He assumed that "substances having a specific gravity greater than endolymph and thus subject to movement with changes in the direction of gravitational force come into contact with the cupula of the posterior semicircular canal. Presumably these particles may exist free in the endolymph or may become attached to the cupula. With the head in the erect position, the posterior canal ampulla is located inferiorly, whereas in the provocative test position (supine, head hanging, ear down), the posterior canal assumes a superior position." He assumed, as in the 1962 article, that the limited duration of the vertiginous attacks resulted from "the return of the cupula to a normal position after the particles have left it," so even though he used the term *cupulolithiasis,* he was aware that the mass must float away from the cupula when the critical position was reached; otherwise, the cupula would stay deviated, and the positional nystagmus would last longer. Fatigability could be explained on the basis of dispersion of the particles in the endolymph, and repeatability after rest could be explained by the particles again settling into the posterior canal ampulla so that they could again act en masse when the critical position was achieved.

In his 1969 article on cupulolithiasis, Schuknecht recognized that movement of the head from the erect position to the provocative head-hanging position (with the standard Dix-Hallpike positional test) must result in an ampullofugal (away from the utricle) displacement of the cupula of the posterior semicircular canal to explain the observed nystagmus (17). Yet, in his 1962 article, he had concluded that the critical position change resulted in an ampullopetal (toward the utricle) displacement of the cupula of the posterior semicircular canal (see Fig. 2). This confusion regarding the expected direction of the cupular deviation with his cupulolithiasis theory would continue to haunt Schuknecht. In the first edition of *Pathology of the Ear* in 1974, he used the earlier figure showing ampullopetal displacement of the cupula (18). In the second edition of *Pathology of the Ear,* he recognized that he had inadvertently reversed the position of the utricle relative to the crista of the posterior semicircular canal in his earlier figure (Fig. 4 A) (19). By this time, however, it had become clear that the calcium carbonate debris was not usually attached to the cupula but rather was freely floating within the canal on the other side of the cupula (Fig. 4 B) (20,21).

Although the otolithic debris mechanism for the generation of benign paroxysmal positional nystagmus is generally attributed to Schuknecht, he was not the first to consider this mechanism. Karl Wittmaack performed a series of experiments on guinea pigs in 1910 during which he rotated them at a very high speed, dislodging the heavy otolithic membrane from the macules of the utricle and saccule. On histologic examination, Wittmaack noted pieces of the otolithic membrane scattered throughout the inner ear. In a comment on an article published by Nylen on positional nystagmus in *Acta Otolaryngologica* in 1927, Wittmaack noted that "in guinea pigs whose otolithic membrane has been rotated off you can sometimes observe a sudden nystagmus

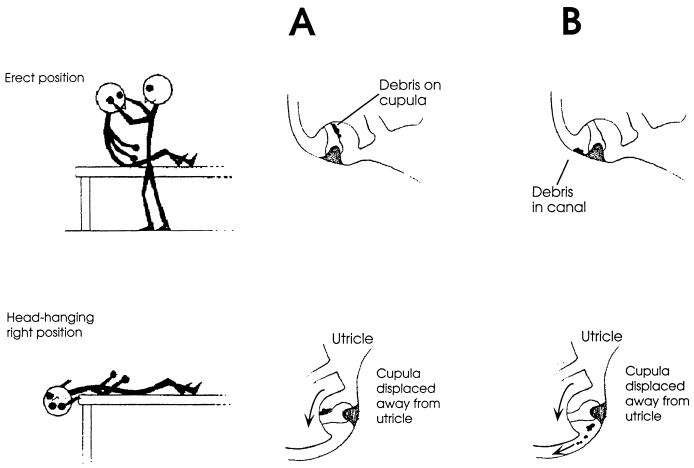

FIG. 4. **A:** Schuknecht's revised cupulolithiasis figure after he recognized that earlier figures (e.g., Fig. 1) had reversed the position of the utricle relative to the crista of the posterior semicircular canal (19). **B:** Currently accepted mechanism for benign paroxysmal positional nystagmus (canalithiasis) (20,21).

with changes of head position. This phenomenon occurred only when the otolith membrane was lying on or adjacent to the cupula, so that the phenomenon was undoubtedly explained by a pathologic loading of the cupula with the otolithic membrane. Therefore, the possibility of a such a loading with concretions or something similar has to be considered as an explanation for this phenomenon in certain cases (particularly when the origin is posttraumatic)" (22). This series of experiments was never published because they were interrupted by the World War I. Harold Schuknecht was unaware of Wittmaack's brief comment, which had been published in German.

PATHOPHYSIOLOGY OF MÉNIÉRE'S DISEASE

Harold Schuknecht studied numerous temporal bone specimens from patients with Ménière's disease. As did Hallpike and Cairns and Yamakawa before him, he concluded that the principle pathologic finding was an increase in the volume of endolymph resulting in enormous distension of the endolymphatic system (23). He noted that the earliest changes were a ballooning of the cochlear duct and dilatation of the saccule. As the disease progressed, the cochlear duct occupied the entire scala vestibuli, and the saccular wall made contact with the footplate of the stapes. Dilatation of the utricle and semicircular canals was usually less severe, and often the utricle was displaced posteriorly by the enlarging saccule. Schuknecht emphasized that there were frequent breaks in the continuity of the membranous labyrinth, which could take the form of herniations or frank ruptures. The ruptures were sometimes followed by a collapse of the entire membranous labyrinth or of just part of the membranous labyrinth, such as the saccule. Although there was occasional atrophy of the sensory hair cells and neurons, particularly at the apex of the cochlea, in most specimens Schuknecht found no changes in the sensory or neural structures.

Schuknecht grappled with the problem of how to explain the abrupt episodes characteristic of Ménière's disease on the basis of endolymphatic hydrops. Deformation of the membranous labyrinth by the increased pressure was not a good explanation. A more likely explanation was rupture of the membranous labyrinth with spilling of potassium-rich endolymph through the rupture, causing a potassium intoxication of the vestibular nerve. In support of this argument, Schuknecht cited animal work showing that perfusion of the perilymphatic space with artificial endolymph rich in potassium caused a severe nystagmus reaction (24). Over the following 2 to 3 hours, the nystagmus subsided as the potassium concentration decreased to the normal level for perilymph. In 1936, Tumarkin described dramatic falling spells in patients with Ménière's disease, which he called otolithic catastrophes (25). Patients felt as though they were being pushed to the ground. Schuknecht suggested that these sudden falling attacks might be explained by a collapse of the utricular wall onto the utricular macule.

In 1927, Stacy Guild, an anatomist at Johns Hopkins University, reported on his studies of endolymph flow in the guinea pig (26). Guild injected Prussian blue granules into the cochlear duct of guinea pigs and then killed the animals at various time intervals, demonstrating that the granules of Prussian blue moved down the cochlear duct into the saccule and then into the endolymphatic duct and sac. On the basis of these observations, he developed the theory of longitudinal endolymph flow, in which endolymph is produced in the cochlea, flows through the ductus reuniens into the saccule, and then finally reaches the endolymphatic sac, where it is resorbed. Guild concluded that the endolymphatic sac "serves as the principal place of outflow of the endolymph; not, as some have thought, as the place of origin of endolymph" (26). Based on an analogy with hydrocephalus, a logical interpretation of Guild's endolymph flow theory was that blockage of the endolymphatic duct and sac would lead to an increase in endolymphatic volume and pressure (endolymphatic hydrops).

Harold Schuknecht, with John Lindsay and William Neff and a young student, Robert Kimura, were among the first to attempt to produce an animal model of en-

dolymphatic hydrops at the University of Chicago in the early 1950s (27). However, their efforts to obliterate the endolymphatic sac in the cat and monkey did not produce hydrops. Kimura joined Schuknecht at Harvard in the early 1960s, and the two again began the quest to find an animal model of Ménière's disease. Finally, in 1965, they reported the successful production of membranous hydrops in guinea pigs after obliteration of the endolymphatic sac (28). A few years later, they were able to produce a similar result in cats (29). An increase in endolymphatic pressure and volume with ballooning of the membranous labyrinth, particularly the cochlea, developed in these animals. However, with rare exceptions, the animals with experimental hydrops did not have episodic symptoms. Furthermore, in the animal model, ruptures were never seen in the vestibular labyrinth and only rarely seen in the cochlear duct.

SCHUKNECHT'S CRUSADE AGAINST MYTHS IN OTOLOGY

Like Joseph Toynebee, Harold Schuknecht thought that the only way to develop rational treatments for inner ear diseases was to understand the pathologic changes occurring in these diseases. Schuknecht noted that "regardless of how mysterious a disorder may be, most physicians feel obligated to counter with some form of medical or surgical treatment. The empirical approach to therapy is acceptable to many physicians, particularly if it can be based on an attractive, even unproven, concept of pathogenesis. The hypothetical explanation of disordered function can become widely accepted in spite of a serious lack of scientific support. When evidence emerges however that refutes the logic of a concept of pathogenesis, then that concept becomes a myth. No specialty in medicine, including neuro-otology, is immune to myths" (30).

More than 4,000 people in the United States every year are stricken with "sudden deafness," usually involving just one side although rarely involving both sides. Otologists had traditionally considered sudden deafness to result from blockage of blood supply to the inner ear, so frequently patients were hospitalized for the administration of anticoagulants, vasodilators, and blood viscosity reducing agents. Over the years, Schuknecht collected a total of 12 temporal bone specimens from patients who had experienced sudden unilateral deafness. None of these specimens showed abnormalities in the vascular systems. What he did find was a selective degeneration in the organ of Corti, primarily involving the sensory cells (31). These changes were identical with those seen in specimens from patients with hearing loss caused by known viral diseases, such as mumps and measles, and completely different from those seen in specimens where there was known vascular occlusion. Schuknecht concluded that the vascular hypothesis "was a myth for most cases of sudden deafness and that aggressive vascular therapies caused more harm than benefit" (30).

Although some patients with sudden deafness also experience vertigo, the majority have hearing loss alone. This suggests that certain viruses have a preference for the sensory epithelium of the cochlea. The reciprocal of this concept is that other viruses have a predilection for the vestibular end organs. This clinical syndrome, which was called vestibular neuronitis by Dix and Hallpike in their classic article in 1952, is characterized by acute prolonged vertigo with normal hearing and otherwise normal neurologic function (15). On studying the temporal bones of numerous patients with vestibular neuronitis, Schuknecht noted a consistent pattern of atrophy of vestibular nerve branches and of the vestibular sensory epithelium. Again, these changes were identical with those associated with known viral inner ear syndromes, such as those associated with herpes zoster infection of the vestibular system. He therefore preferred the name *vestibular neuritis* to refer to a discrete degenerative neuropathy of the vestibular nerve trunks (32). There was no evidence of vascular disease in any of his specimens, and he pointed out that the selective atrophy was not consistent with a vascular mechanism.

In later years, Schuknecht coined the term *neurolabyrinthitis* to cover the spectrum of viral inner ear disorders (31). He argued that viruses can selectively involve the vestibular and cochlear nerves and their branches and any of the sensory receptors, so that any combination of vestibular and auditory symptoms is possible. Certain viruses seem to be selective for the vestibular and/or cochlear part of the inner ear, but many affect both parts. He thought that because viral labyrinthitis and viral neuritis could not be separated on clinical grounds, and often there was some combination of both nerve and end organ involvement, *neurolabyrinthitis* was a more practical clinical term.

On the basis of his later experience of temporal bone studies in patients with viral inner ear syndromes, Schuknecht reassessed his interpretation of the patients with benign positional vertigo reported by Lindsay and Hemenway in 1956 (11). These cases, which Schuknecht initially ascribed to occlusion of the anterior vestibular artery, provided the impetus for his theory of cupulolithiasis. On rereviewing the temporal bone specimens of Lindsay and Hemenway and of Hallpike and colleagues, Schuknecht concluded that the pathological changes were most likely secondary to a viral rather than a vascular cause (32). He could find no evidence of vascular occlusion, and the atrophy of the vestibular nerve terminals and vestibular end organs reminded him of the changes seen with viral neurolabyrinthitis in other patients. A remarkable feature in these cases, which Schuknecht did not address, is the selective involvement of the superior part of the vestibular labyrinth with sparing of the inferior part. This indeed was the feature that had initially led Schuknecht to speculate on an occlusion of the anterior vestibular artery. This dichotomy between involvement of the superior and inferior parts of the vestibular labyrinth has been consistently seen in patients with the clinical syndrome of vestibular neuritis

or neurolabyrinthitis. If the syndrome is indeed secondary to a viral infection, then the virus or viruses must have a predilection for the superior part of the vestibular labyrinth.

Like Ménière, Schuknecht tried to save patients from needless and potentially dangerous treatments. When he was asked to recommend the best treatment among the many treatments recommended for these presumed viral inner ear disorders, he commented that "there is no treatment I'm aware of. Certainly vasodilators, antibiotics, probably steroids–none of these drugs are really effective drugs for the treatment of viral disorders, as you all know. So all I'm making a plea for is a more logical approach to these disorders and for us not to be carried away by some therapeutic concept that's being imposed upon us by well-meaning colleagues, maybe pharmaceutical houses, and others" (33).

Schuknecht was a tireless crusader against surgical procedures that he considered to have little scientific underpinning but carried significant risk to the patient. Two popular surgical procedures that he considered to be in that category were vascular loop surgery and perilymph fistula surgery. Schuknecht pointed out that vascular loops are common in normal subjects without symptoms (34). On reviewing his temporal bone specimens, he observed such loops in the internal auditory canal in 12.3% of 1,327 temporal bones. Of those, 5 had unexplained unilateral hearing loss, but in 3 of them the loops were located in the opposite ears, and 2 had the loops in both ears. Two of the patients with vascular loops had unexplained tinnitus, but in one it was in the uninvolved ear. Schuknecht concluded that there were no clinical manifestations that could be attributed to vascular loops in the internal auditory canal and that his temporal bone observations seriously challenged the concept that arterial loops anywhere along the course of the auditory and vestibular nerve trunks were the cause of auditory-vestibular disorders. "The practice of performing a suboccipital craniotomy for the purpose of cushioning these nerve trunks against the pulsation of arteries does not seem reasonable in view of these findings" (30).

Traumatic rupture of the inner ear membranes produces a perilymph leak called a perilymph fistula. Schuknecht had done extensive work on trauma to the inner ear in animals, and he was highly skeptical of the concept of a spontaneous perilymph fistula. He was particularly struck by the fact that when he intentionally ruptured the membranous labyrinth when performing a cochleosacculotomy operation for Ménière's syndrome, patients rarely had auditory or vestibular symptoms as a sequela, and less than 25% even showed evidence of postoperative sensorineural hearing loss. Also, the perilymphatic space is routinely entered during stapedectomy surgery for otosclerosis, while postoperative auditory or vestibular symptoms are unusual. Schuknecht concluded that "perilymph fistula is a proven reality following several different types of stress-related incidents. However, the idea that it is a common cause of audio-vestibular symptoms that are not related to a stressful incident is a myth" (30).

THE FINAL YEARS

Harold Schuknecht's scholarly productivity included over 300 original articles, editorials, and reviews and 7 books on the anatomy, pathology, and surgery of the ear. His temporal bone collection at the Massachusetts Eye and Ear Infirmary contained more than 1,500 sets of clinically well documented specimens. Without doubt, his most lasting contribution is his textbook *Pathology of the Ear*, the second edition of which was completed in 1993 just 4 years before his death (19). Schuknecht began the second edition of his text with a quote from Joseph Toynebee: "If we carefully survey the history of the rise and progress of aural [surgery] as a distinct branch of scientific surgery, one main cause of the disrepute into which it has fallen may be traced to the neglect of the pathology of the organ of hearing." Throughout his career, Schuknecht demonstrated a burning desire to understand the pathophysiology of disease processes. As Chairman of the Department of Otology and Laryngology at the Harvard Medical School and Chief of Otolaryngology at Massachusetts Eye and Ear Infirmary from 1960 to 1987, Schuknecht was responsible for training many physicians who now chair departments of otolaryngology worldwide. After retiring from his administrative and clinical activities in 1987, he continued to teach and conduct research, focusing on his temporal bone collection and the second edition of his textbook.

In 1996, while he was attending a medical meeting in Vancouver, Canada, Harold Schuknecht had several recurrent spells of right-sided weakness typical of transient ischemia attacks. He had had an episode of transient aphasia about 5 years previously, but otherwise there had been no previous warnings. He flew back to Boston. Although his physician wanted him to go immediately to the emergency room, he preferred to stay at home overnight and enter the hospital the next day. He had his wife Anne prepare freshly baked cornbread smothered with milk and sugar—his favorite meal or snack since his childhood in South Dakota. He reminded Anne that he wanted to be cremated, because he still had disturbing memories of his mother's funeral and the several days that she was laid out for viewing. Despite his strict religious upbringing, he had lost interest in religion once he had left the farm and started college. He had a peaceful night without any further spells. The next day he entered Massachusetts General Hospital to undergo a carotid endarterectomy. One complication after another followed, so that he was not able to leave the intensive care unit for the next 6½ weeks. After a quadruple coronary bypass, he experienced atrial fibrillation and a massive stroke, which left him paralyzed and unable to communicate. Day after day, he sat in a chair in the intensive care unit, watching the activities going on around him but unable to respond. His wife knew that he wanted out of the situation, and she was finally able to arrange for

him to leave the intensive care unit and enter a private room with hospice care, where he died peacefully.

Acknowledgment: Much of the personal data on Harold Schuknecht was obtained from conversations with Anne Schuknecht and Dave Dahlin in 1998. Dick Gacek provided helpful comments.

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