A Memoir of Pediatric Nuclear Medicine: Part III: Finding a Place for Nuclear Medicine

A major impediment to the utilization of pediatric nuclear medicine techniques occurred in the mid-1970s with the introduction of competitive imaging technologies such as CT and ultrasound. Although the early versions of these technologies were somewhat primitive, the use of these modalities increased with technological advances, innovative upgrades, and newer devices. My personal experiences in practice, research, and teaching in nuclear medicine spanned 3 1/2 decades. I would remind readers that any memoir is merely one individual's viewpoint on complex and multifaceted events that might be recounted differently by others. I also want to express my gratitude to all the individuals whose collegial contributions are recognized or inadvertently omitted in this account.

Introducing New Technologies to Pediatrics

I was fortunate to participate in a 4-year training program in radiology from 1964 to 1968 at the Hospital of the University of Pennsylvania (HUP) in Philadelphia, PA, where nuclear medicine was the focus of intense research and development. The radiology training program included an extraordinary 6-month nuclear medicine rotation under the guidance of pioneer nuclear medicine practitioner David Kuhl, MD. After completing residency training in July 1968, I accepted a position in pediatric radiology at the Children's Memorial Hospital (CMH) in Chicago, IL.

From the Newsline Editor:

*This is the last in a 3-part series from James J. Conway, MD, a distinguished pioneer in pediatric nuclear medicine and past president of the SNM. In the first part of the series (*J Nucl Med. *2006; 47[4]:12N), he recalled the individuals and early advances that contributed to the introduction of pediatric applications into the mainstream of nuclear medicine practice. In the second (*J Nucl Med. *2006;47[5]:22N), he looked at the establishment of the Pediatric Nuclear Medicine Club within the SNM and at the challenges faced by the subdiscipline in its formative years. In the final installment, he offers a personal memoir of his experiences as a researcher, clinician, and educator.*

Conrad Nagle, MD

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In 1968, when I arrived at CMH, efforts to introduce nuclear medicine techniques in pediatrics were already underway. Harvey White, MD, a pioneer in pediatric radiology and chair of the department of radiology, had already initiated thyroid uptake studies in 1955 with ^{131}I-sodium iodide, using a scintillation detector that was custom designed for small children. It had a 1-inch scintillation crystal and collimator aperture. White recognized the potential for nuclear medicine in pediatrics. In 1967, he persuaded the hospital administration to purchase a Pho Gamma III Nuclear–Chicago camera, the first commercial gamma camera to be installed in a pediatric hospital. The camera cost $34,440, with a yearly service contract of $1,420. My introductory experience with the gamma camera as a resident trainee at HUP led White to assign me to the new apparatus. He said, "The camera is yours; see what you can do with it." We were the only 2 attending physicians in radiology, so in addition to promoting the new technology and developing protocols for various studies, I also routinely performed my share of pediatric radiology (including the novel Seldinger catheter technique for angiography, for which we made our own catheters) and radiotherapy with a 200-MeV orthovoltage therapy unit. The gamma camera was in a small room 2 floors above the main radiology department, and I spent my days running up and down stairs. After 9 months, White went on a well earned 7-month sabbatical, leaving me in charge along with an early pediatric radiology resident, Arnie Shkolnik, MD. That first year was a very hectic but rewarding learning experience.

Within a year, we were acquiring 663 studies annually, a volume that promised to continue to increase. I also wanted to perform bone scintigrams with ^{18}F for children with osteogenic sarcoma and other bone tumors and metastases. The higher energy radiopharmaceuticals were not ideal for the thinner crystal of the gamma camera, so we purchased a Nuclear–Chicago Pho-Dot II rectilinear scanner for $11,500. Children were not tolerant of the tap-tap-tap of the scanner as it traversed the field of interest, so we often silenced the tapper, giving up the print matrix despite its worth as a back-up for the photo matrix. Rectilinear studies took a long time with the low radiopharmaceutical doses administered. It was difficult

for the child to remain motionless for long intervals, so we became adept at using the so-called "scintillation cocktail" adapted from the cardiac cocktail of demerol, phenergan, and thorazine. Nurses assisted us in monitoring children, with the appropriate resuscitation equipment at hand. Although we had no serious problems with the scintillation cocktail, it was abandoned several years later after an adverse event in the CT suite. Our use of sedation decreased dramatically in later years as our technologists developed more sophisticated handling techniques. I once was accused of using anesthesia on all our children because of the high quality of images that we routinely obtained.

One of my objectives was to promote the use of radionuclide techniques in children, and the pediatric staff also wanted to know more about the new gamma camera, so in the late 1960s and early 1970s, I attended as many case conferences and presented as many grand rounds as possible. I frequently commented at these conferences on ways in which a specific nuclear medicine study benefited or might be of service in the management of a child's problem. One of the first local barriers that I encountered in introducing nuclear medicine to the staff was an older pediatrician who had served on the War Department Hiroshima Damage Survey team at the end of World War II. He came to every presentation I gave and would describe to his fellow pediatricians and trainees in lurid detail the effects of atomic bomb radiation on Japanese children.

Despite this challenge, continuing beneficial advances were clear to many of my pediatrician colleagues. The results of early brain studies with ^{99m}Tc-pertechnetate were so clearly superior to the risks associated with invasive pneumoencephalography and/or direct carotid or vertebral angiography that the use of "noninvasive" radioisotope studies in children rapidly increased. Brain imaging was the predominant study in our field in the early years, but radioiosotope-based renal studies soon were recognized as having major advantages over radiographic techniques.

Competition from New Technologies

White was a champion for other new technologies at CMH well before most other pediatric hospitals ventured into new imaging territory. In 1974 he persuaded the administration to install a very early Rohe ultrasound scanner and in 1977 an EMI 5050 CT unit. Although each of these devices produced images that left much to the imagination, rapid advances over the next decade would affect the numbers and types of studies referred for nuclear medicine imaging.

Shkolnik, the radiology colleague in charge of the ultrasound unit, subsequently proved its immense value in pediatric imaging. We shared research studies and reported on the advantages of each modality. Shkolnik was honored several years ago by the Society for Pediatric Radiology as a distinguished pioneer.

The rapid development of CT had a much more profound effect on nuclear medicine practice than did comparative developments in ultrasound. Nuclear medicine studies of the brain, which were primarily acquired for anatomic information, were rapidly replaced by CT. Renal scintigraphy and renogram studies, however, provided functional information that ultrasound could not offer. The result for all imaging modalities, however, was a period in which we "competed" to provide evidence of the utility and benefits of specific approaches. The numbers tell a part of the story. In 1968 at CMH, we performed 444 nuclear medicine studies: 275 brain, 35 liver, 24 renal, 35 lung, 10 cerebrospinal fluid, and 2 thyroid studies. By 1970, this number had risen to a total of 871 studies. Our peak load occurred in 1975, with 619 brain, 244 renal, 237 liver, 354 bone scintigram, and miscellaneous other studies for a total of 1,854 procedures. After the installation of CT in 1977, nuclear medicine brain studies decreased to 131 in 1978 and by 1983 numbered only 33 (for early viral encephalitis and in symptomatic children with normal CT studies).

During the same period, the numbers of nuclear medicine renal and bone studies continued to grow. In 1982, we requested that the hospital purchase a SPECT unit, but we were informed that we could not justify the cost of such a unit based on any projections that business would increase sufficiently. So we embarked upon a personal solicitation to local businesses, and, in 1984, we eventually raised sufficient donated funds to support a field upgrade of an existing older single- head large-field-of-view (LFOV) gamma camera. That was a tactical mistake. The studies took forever to record (thank heavens for the invention of Velcro straps), and the quality of the images was marginal at best. After prolonged negotiation, Siemens Corporation retrieved the field-upgraded SPECT camera, and we purchased a dedicated ZLC SPECT camera that served us well for several years. As the requests for brain, bone, and other SPECT studies increased, we eventually purchased a Picker triple-head SPECT camera and a dual-head total-body imaging camera.

Our most versatile camera was the low-energy small-FOV mobile camera (LEM) by Searle Radiographics (successor to Nuclear–Chicago), with converging–diverging and pinhole collimators. It had high resolution and was a good size for babies. All of our Legg–Calve–Perthes studies were performed with this camera. We also obtained high-resolution renal scintigrams with ^{99m}Tc-glucoheptonate using the pinhole or converging collimator for babies. The camera was also important for portable brain death studies in intensive care and even on occasion in surgery to localize hard-to-find osteoid osteomas (*1*).

Radionuclide cystography spurred major growth in nuclear medicine at our institution, with 92 studies performed in 1971 and 595 studies performed in 1981. At the same time, the numbers of x-ray cystography studies did not decrease significantly. It is my belief that the pediatricians who ordered the majority of the initial urinary tract

studies were accustomed to ordering the x-ray studies and found this anatomic information easier to understand. Some urologists preferred the anatomical and functional components offered by ordering both studies. The radiologic literature persisted in promoting the x-ray cystogram, favorably comparing its capabilities with those of ultrasound (but not nuclear medicine!) as a better technique for anatomy and detection of vesicoureteral reflux. Many such reports came from adult institutions or from pediatric institutions that lacked onsite nuclear medicine facilities.

Bone scintigraphy also grew from 1973 to 1983 after the introduction of ^{99m}Tc-polyphosphate and ^{99m}Tc-diphosphonate radiopharmaceuticals, along with improved gamma camera resolution, total-body imaging, and SPECT capabilities.

A major scientific and technologic regret and disappointment was that I could never convince the administration to purchase a PET camera. Instead, the hospital administrators turned to MR imaging. Every breakthrough in PET imaging that I promoted was sidelined by money for a major upgrade in MR capacity. Interventional radiology and upgrades in ultrasound also demanded the hospital's resources. After a second sophisticated CT device was purchased in the 1980s, the volume of nuclear medicine studies declined steadily. It became obvious that each imaging modality has its special niche for specific questions that need answers. For nuclear medicine, this niche continues to be the elucidation of function.

Research and Education as Part of Pediatric Nuclear Medicine Practice

Finding a niche for the specialty of pediatric nuclear medicine meant promoting our successes and reporting on challenges through research, presentation, and publication. Many of the early nuclear medicine pioneers joined multiple subspecialty societies purposefully to disseminate information about pediatric nuclear medicine. At times we had to persuade their societies' leadership and committees to get our material on the programs at meetings. Although my colleagues at CMH often grumbled and commented on my frequent absences to attend such meetings, they graciously gave me permission to do so.

I felt that presenting our work as scientific papers only at the SNM was somewhat like "bringing coals to Newcastle." I often would offer the first presentation of our work at a pediatric, orthopedic, urologic, or subspecialty radiology meeting rather than at the SNM to spread the word outside our field about the value of nuclear medicine. The policy of many scientific organizations and journals

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Monkey Business

In addition to memories of accomplishments and challenges, every medical career has odd or out-of-the-ordinary moments that stand out in reminiscence.

CMH contracted with Chicago's Lincoln Park Zoo to provide diagnostic and surgical services for small animals in distress. We were asked to perform a brain scintigram on an infant gorilla who had suffered a seizure. They suspected that the gorilla had been injured and wanted to rule out a subdural hematoma. We were not allowed to sedate the little ape, who was quite frightened and restless. Sue Alice Hamilton, one of our senior technologists, climbed onto the imaging table and cuddled the gorilla in her arms while Sue Weiss obtained the images (see figure). We did not find a subdural hematoma or other abnormality. The little gorilla grew up at the zoo and became the proud mother of her own little gorillas.

Technologist Sue Alice Hamilton sooths an unsedated baby gorilla undergoing a brain scintigram.

On another occasion, zoo vets brought over a somewhat larger gorilla with a fever of unknown origin. On a weekend day, Weiss performed a ^{67}Ga scintigram and discovered a focal lesion in the abdomen. Surgery revealed a perforation of the small bowel by an ingested foreign object. We saved that gorilla's life with a nuclear medicine study that localized the site of infection.

Not everyone was as well behaved as our animal patients. In the early days, we contracted for prepared radiopharmaceuticals from Jim Quinn's radiopharmacy at Northwestern Memorial Hospital. We were preparing for a ^{131}I-macroaggregated albumin lung scintigram on an 8-year-old boy. The radiopharmaceutical arrived in a shielded syringe and was placed on a tray next to the child and the camera. The technologist turned to set the camera parameters, and the boy grabbed the syringe and squirted the entire radioactive dose into the room.

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restricting presentation and/or publication to only new materials inhibited the dissemination of important information to the many types of specialist physicians who ordered our studies. Over the years, I published scientific abstracts or papers in 37 different subspecialty publications and scientific journals in an attempt to promote pediatric nuclear medicine as widely as possible.

In 1970, I prepared "Radionuclide Angiography of Chest Masses in Children" as a poster presentation for the annual meeting of the SNM, where it was awarded a silver medal. The same exhibit subsequently received a certificate of merit award at the Radiological Society of North America (RSNA) meeting, a silver medal at the American Academy of Pediatrics meeting, and an honorable mention award at the American Medical Association meeting. I mention this to emphasize that the same scientific exhibit, unlike a scientific paper, was welcomed at different meetings and provided a useful way to spread the visual word about our field. The scientific exhibit promoted pediatric nuclear medicine in a more visual and memorable form to larger audiences than could be achieved through a single-delivery scientific paper presented to a limited audience.

For the 1971 SNM meeting, Sue Weiss, CNMT (who was my chief technologist), and I presented a scientific exhibit and handout booklet on "Sedation and Injection Techniques in Children," and the exhibit was awarded a bronze medal. Nuclear medicine practitioners were anxious to introduce radionuclide techniques for children in their hospitals, but managing children was often disruptive to adult schedules. Our techniques for handling children proved especially helpful for technologists, and in 1972 we published "Considerations for the Performance of Radionuclide Procedures in Children" (*2*).

Between 1970 and 1979, we presented 12 exhibits on various aspects of pediatric nuclear medicine at professional society meetings. Of note, in 1972, our first submission of a scientific paper on radionuclide cystography was rejected for oral presentation by the program committee of the SNM, but our scientific exhibit on the topic was awarded medals by the SNM and RSNA the same year. I often said that if a scientific paper is rejected by a program committee for oral presentation but is accepted as an exhibit and given an award, then the topic must represent an important advancement.

A good example of a rejection was our frustrating experience in attempting to publish our paper on "The Localization of Urinary Tract Infection with ^{99m}Tc-Glucoheptonate Scintigraphy" (*3*). Previous developments had been reported by Hirsch Handmaker, MD, Joe Leonard, MD, and John McAfee, MD (*4–6*). Around 1980, I presented a few pediatric studies with ^{99m}Tc-glucoheptonate at a small think-tank conference in Santa Barbara, CA. Pyelonephritis, especially in the neonate and infant, frequently does not reflect the severity of infection, and, at the time, most initial urinary tract infections (UTIs) were treated with oral antibiotics for a short interval. Intravenous pyelography and x-ray cystography were routine follow-up studies when infants did not respond to initial treatment. These studies frequently failed to detect pyelonephritis as the underlying disorder. After the conference, I persuaded Edward S. Traisman, MD, a pediatrician on the CMH staff, to refer infants with UTIs for a research study that began in 1981 and was finalized in 1983. We studied 55 children with ^{99m}Tc-glucoheptonate scintigraphy and found the technique to be a major breakthrough in differentiating pyelonephritis from simple UTI. The ramifications of this finding were immense: it meant that those infants with pyelonephritis could receive more intense intravenous therapy and that perhaps we could prevent the ravages of unrecognized and/or undertreated pyelonephritis, including recurrent pyelonephritis and hypertension.

In 1983 I was invited to an international symposium on pyelonephritis at the University of Munster, Germany. Eight of the cases we had collected in the previous 2 years were presented there and subsequently published in the conference proceedings (*7*). We submitted our final report on the 55 cases to the journal *Radiology* in the same year. After nearly 8 months, the reviewers rejected it as "too clinical" for a radiology journal. We then submitted the report to the *Journal of Pediatrics*, where, after almost 6 months, it was rejected as "too radiological" for a pediatrics journal. In 1986, almost 3 years after initial submission for publication, the research was published in *Pediatric Radiology* (*3*).

The paper provoked controversy and turmoil. The description of a nuclear medicine scintigraphic test that accurately differentiated pyelonephritis from simple UTI or cystitis made both the pediatric and urologic communities question which diagnostic tests were most appropriate. The intravenous pyelogram (IVP), x-ray cystogram, and ultrasound were the conventional studies obtained in a child with urinary tract symptoms. Although radiologists reported that the IVP was as sensitive as ultrasound, they ignored renal scintigraphy's significantly greater accuracy than either in recognizing renal involvement with infection. Even treatment management became controversial. Some infectious disease gurus even proposed that all UTIs be treated with a short intravenous course of antibiotics to be followed by oral antibiotics, eliminating diagnostic imaging entirely. Because of the continuing controversy, Richard Cohn, MD, a pediatric nephrologist at CMH, and I published an editorial on the role of cortical renal scintigraphy for the diagnosis of pyelonephritis in the *Journal of Pediatrics* (*8*). That article stimulated more positive and negative responses from pediatricians and urologists than any other article that I have written.

Other scientific exhibits we presented covered the topics of lymphosarcoma in children (*9*), renal transplants in children, Polaroid film artifacts (*10*), oral ^{99m}Tc in the differentiation of epigastric lesions (*11*), soft tissue localization of bone-imaging radiopharmaceuticals, neonatal osteomyelitis (*12*), and Legg–Calve–Perthes disease (*13,14*). Our recognition of predictive scintigraphic patterns for Legg–Calve–Perthes disease was derived over many years of observation working with orthopedic surgeons Mihran

Tachdjian, MD, and Lou Dias, MD, at CMH. Our observations allowed the first reliable predictable outcome early in the disease using a diagnostic imaging test. The implication from our study was that when the scintigraphic pattern indicates a poor prognosis, an intervention can be initiated at an earlier interval before irreversible damage occurs in the epiphysis.

In 1976 we presented an exhibit and paper on pulmonary perfusion distributions in congenital heart disease in the neonate with transposition of the great arteries. That exhibit and subsequent publication (*15*) demonstrated that the pulmonary blood flow is equally distributed between both lungs in the newborn with d-transposition of the great arteries but that within weeks the pulmonary perfusion distribution becomes permanently asymmetric. Thus, a very early correction of the transposition within the first weeks of life is necessary to maintain equal distribution of blood flow into both lungs. I believe that our study accelerated the pediatric cardiac surgeons' approach to correction of the defect at an earlier age.

The advantage of noninvasive diagnostic imaging significantly aided in the early development of renal transplantation in children. Among the pioneers in pediatric renal transplantation were Ovar Swenson, MD, a pediatric general surgeon and chair of surgery at CMH; Lowell King, MD, and Casimir "Casey" Firlit, MD, pediatric urology surgeons; and myself. We quickly learned how to differentiate the various severities of acute tubular nephropathy from acute and chronic rejection. We also performed research to determine how long dog kidneys could remain viable on a Belzer pump oxygenation machine (Fig. 1). We found that creating an infarction of approximately one-sixth the mass of the kidney would result in a rupture of the kidney with time. Whenever we detected in vivo partial infarct in a kidney with the gamma camera, we were alert to a potential rupture of the transplant. That research also led surgeons to transplant even the smallest accessory arteries whenever possible and to refuse donor kidneys with multiple small arteries into the kidney.

In 1968, Ranos Rado, MD, had introduced diuretic renography in nuclear medicine. (*16*). We began to use the technique with the gamma camera in the late 1970s but soon found that many factors profoundly influenced the final results and interpretation of the study. We continually modified our technique to minimize those factors that we could control, such as hydration. For example, many babies presented for their studies with minimum liquid input as if they were undergoing an intravenous pyelogram. Their urine output was so minimal even with the diuretic response that false-positive responses misled interpretation. We eventually published an article that discussed the many factors that affected the diuretic renogram (*17*). Max Maizels, MD, a pediatric urologist and cofounder of the Society for Fetal Urology (SFU) expressed his concerns to me that diuretic renography was being performed with a variety of differing techniques at other institutions with variable results. He pointed out that the results on a given patient from one institution could not be reliably compared with results on the same patient from another institution. Pediatric urologists in the SFU were reported to be so frustrated that they began to doubt the value of the diuretic renogram. We felt the need to standardize the technique, and, in October 1989, Maizels, Weiss, and I organized a conjoint meeting of interested practitioners from the SNM Pediatric Nuclear Medicine club and the SFU to meet at CMH (Fig. 2). Approximately 30 physicians, with Weiss as the lone technologist, attended the meeting. Joining me as nuclear medicine physicians were Massoud Majd, George Sfakianakis, Douglas Eggli, Andrew "Tip" Taylor, Ben Greenspan, Eugene Anandappa, and Rick Shore. We attempted to define a standardized technique by considering all of the variables, including bladder catheterization, hydration, diuretic dose, time of injection, radiopharmaceutical, and analysis of half-time response. The result of our deliberations was "The Well-Tempered Diuretic Renogram" (*18,19*). Maizels suggested evoking Bach's "tempering"—tuning a variety of instruments in different keys to play together and produce a pleasing sound.

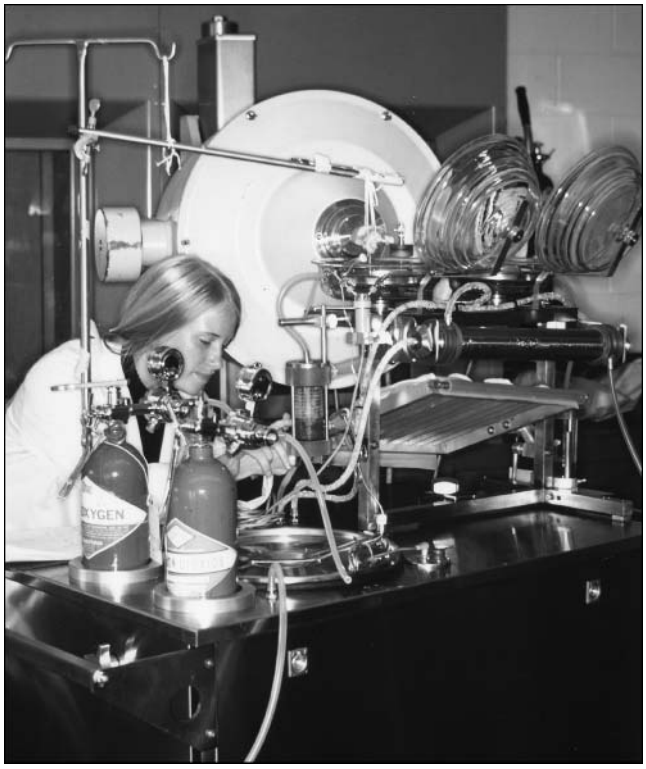

FIGURE 1. A research study of a dog kidney being perfused on a Belzer perfusion pump and imaged with the pinhole collimator.

We subsequently established a central repository for data collection at CMH and created a standardized reporting system for ultrasound studies of the hydronephrotic kidney in the infant (*20*). We also standardized the use of

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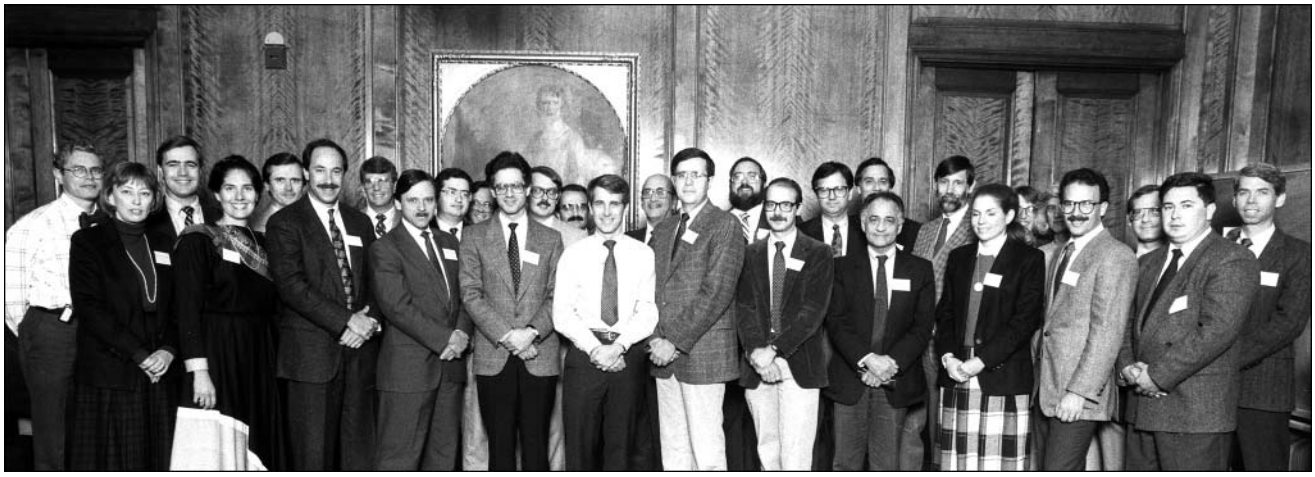

FIGURE 2. Members of the Pediatric Nuclear Medicine Club and the Society for Fetal Urology on October 20, 1989, during their conjoint meeting at Children's Memorial Hospital in Chicago, IL.

surgical terminology to describe findings in obstruction at the time of surgery and the pathological reporting of the tissues comprising the obstruction. However, although everyone was in a compromise mode of agreement at the meeting, only a few institutions actually adopted the "well-tempered" renogram as the standard for their institution.

I must confess that outside of the regulatory impediments, trying to standardize the diuretic renogram technique for neonatal hydronephrosis has been the most frustrating and disappointing experience of my entire professional career. The technique for performing diuretic renography remains an issue even today, and the "most ideal" method is still debated at almost every meeting of the SNM Pediatric Council. It is my contention that nuclear medicine practitioners are artisans and will perform a technique on the basis of their training or their own developmental experiences in practice.

To illustrate the point, Weiss and I conducted a survey in the 1980s. We wanted to prepare a handout booklet on techniques for performing pediatric studies, featuring pediatric nuclear medicine and unusual nuclear medicine studies, to present to attendees at an SNM Central Chapter meeting. We surveyed a dozen full-time pediatric nuclear medicine practitioners on how they performed 10 common procedures. We were surprised to find that only a single individual performed his studies in ways similar to ours—and he had received initial training in our department! The rest of the practitioners had been trained at different institutions or learned on the job, and each performed these common procedures in different ways. It is my belief that physicians are loath to change practices learned during their training. When a modicum of success is achieved in following old beliefs, change will not occur without extraordinary effort. Perhaps this is one explanation for regional variations in surgical procedures or medical treatments in our country and why many physicians cling to "outmoded" procedures and techniques.

With the Help of Friends and Colleagues

I was fortunate to have supportive referring pediatricians and other specialty physicians on our CMH staff. Without their willingness to explore new techniques, such as radionuclide cystography, renal scintigraphy for transplantation and infection, and Legg–Perthes, our techniques would have taken much longer to develop. Shore and Anandappa were my nuclear medicine colleagues for many of the years that I served patients at CMH, and they tolerated my many absences to spread the good word about pediatric nuclear medicine. My technologists labored long and arduously. Among the many that spent many years and tears with me were Weiss, Hamilton, James Everett, and Lolita Fong. The last one to turn out the lights every day was Weiss.

It was my greatest pleasure to introduce and teach pediatric nuclear medicine to perhaps 2,000 trainees, including nuclear medicine residents, fellows, and radiology residents from Northwestern Memorial Medical Center, Loyola Medical Center, Hines Veterans Hospital, Cook County Hospital, the U.S. Army and Air Force medical services, and other Chicago medical institutions. Many of the residents and fellows joined with me in publishing our work. We hosted visiting physicians and technologists from all over the world, including many of the very early pioneers. Weiss was primarily responsible for the training of countless nuclear medicine technologists from the Northwestern Memorial Hospital, Triton College, the College of DuPage, and other programs. Each and every student maintained a log of the studies that they encountered and were quizzed by Weiss at the end of the rotation.

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May all of you be as fortunate as I in associating with such a colleague in your work.

This memoir has been about the early years of pediatric nuclear medicine, its trials, tribulations, and wonderful successes. I leave the memoirs of current practice to my colleagues who are still in the trenches.

Finally, nothing that I may have accomplished could have happened without the behind-the-scenes support of my wife, Dolores, who for 50 years has put up with my shenanigans, late hours, frequent travels, and bringing home "strangers" from all over the world for dinner.

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