AJNR

PEDIATRIC NEURORADIOLOGY

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AJNR Am J Neuroradiol 2000, 21 (1) 29-36
http://www.ajnr.org/content/21/1/29

PEDIATRIC NEURORADIOLOGY

The history of any subspecialty in the field of neuroradiology is often determined by the prominence of personal figures who contributed to and shaped its creation. There is little doubt that pediatric neuroradiology has flourished, in part, because of the contributions of individuals such as Harwood-Nash, Naidich, Fitz, Zimmerman, and Barkovich, to name but a few. But it is the literary history of a subspecialty that truly defines its character for all individuals outside of neuroradiology, and that provides definitive evidence of the contribution of a subspecialty to all of neuroscience. In this regard, the *AJNR*, since its inception in 1980, has played a significant role in defining and shaping the subspecialty of pediatric neuroradiology. During the past 20 years, the *AJNR* has chronicled a remarkable change in how we image children.

The First 5 Years (1980–1984)

The Golden Age of Sonography and CT

I was surprised to find, when undertaking this assignment, that the first 5 years of pediatric neuroimaging in the *AJNR* were not defined by conventional angiography, pneumoencephalography, or ventriculography, as we might expect, but rather by sonography and CT. No less than approximately one third of the major articles in this early period related to the use of neurosonography for the evaluation of the neonatal and infant brain and spine. This may be surprising to some, but clearly defines the importance of neurosonography to all of neuroimaging, which continues even today in the hands of both pediatric neuroradiologists and pediatric radiologists.

Perhaps the historical interest in the use of neurosonography to image neonates and infants is not surprising because, from the very beginning, sonography required minimal or no sedation, was portable, and was without the biological effect of ionizing radiation. Whatever the reasons, neurosonography helped shape the literary heritage of pediatric neuroradiology as much as any other imaging technique in use then or today.

The first article in the *AJNR* on neurosonographic applications was published in 1980. Appropriate to pediatrics and using what then were state-of-the-art static B-mode scanners, it centered on the evaluation of congenital abnormalities of the brain. Oddly enough, CT, also new at that time, was quoted as the standard of reference despite its own recent introduction to the field of neuroimaging. This article was also noteworthy in its reference to the use of neurosonography for sequentially following ventricular dilatation in the neonate, which eventually was to become a frequent use of sonography. This article was soon to be followed by others, which defined the use of sonography for the evaluation of normal anatomy of the brain, the infant cranium, and congenital vascular malformations. It was, however, a series of articles on the use of sonography for diagnosing and following intracranial hemorrhage (ICH) and its complications in the neonate that was to contribute most to the use of sonography in pediatric neuroradiology in these early years. Sonography showed ICH with great sensitivity and specificity and could accomplish this portably as many times as necessary without the use of radiation and at a lower cost. The versatility of neurosonography to diagnose CNS infections and abnormalities of the spine was also introduced to the readership—practices which continue today in the modern neonatal intensive care unit.

In the same period of time, CT began to emerge and significantly impacted the practice of pediatric neuroradiology. CT was to have an even greater impact than sonography owing to the number of children of all age groups it would eventually reach. In a similar fashion to sonography, CT proved very versatile for the evaluation of congenital malformations of the brain, CNS infections, trauma, and primary brain tumors. One of the very first articles to come from the *AJNR* described the use of CT for evaluating congenital absence of a vertebral pedicle. Articles followed shortly thereafter, showing the superiority of CT over traditional methods of myelography for evaluating congenital malformations of the spine. CT was obviously a natural combination with intrathecal contrast for the evaluation of the cisternal and other CSF spaces. CT was quickly shown to be of value for the intracranial diagnosis and evaluation of primary tumors of the brain and surrounding structures. CT also offered us the ability to image in direct coronal and sagittal projections to see anatomy from perspectives never before realized. The use of CT to evaluate perinatal intracranial hemorrhage compared with pathologic analysis earned Ludwig the Dyke Award during the 1982 annual meeting of the ASNR.

CT further contributed to our understanding and appreciation of two major concepts in pediatric neuroradiology; that of the effect changing development has on the appearance of the child's brain and how the attenuation characteristics of tissue and fluid could be used to assess both congenital and neoplastic processes. In a classic series that was to be repeated many times, investigators revealed how the CT of normal development could be used to assess abnormal cranial development in patients with microcephaly. CT also clearly opened up new vistas in the evaluation of the pediatric spine, and allowed us a look at disease processes previously only seen by the neurosurgeon and pa-

thologist. Classic imaging descriptions of processes such as lipomyeloschisis and primary tethered cord syndrome extended our ability to serve the patient, and extended the influence and respect of pediatric neuroradiology among our clinical colleagues.

The first 5 years also brought to our attention pediatric applications of the new and developing field of neurointervention. The use of embolic methods to treat juvenile angiofibromas was to be described early in the *AJNR*, and was to be followed in later years by even greater and more complex applications of neurointervention in children.

It was during these early years that we also were first introduced to disorders that previously were only the domain of the pediatrician and neuropathologist. Metabolic disorders of the brain were, until now, read about but seldom seen by the neuroradiologist. CT played an essential role in introducing us to metabolic disorders in these early times—a role that eventually was to be totally replaced by MR imaging. Descriptions of unusual conditions such as fucosidosis, neurofibromatosis, adrenoleukodystrophy, methylmalonic and proprionic acidurias and Krabbe's disease were to enter the vocabulary of the neuroradiologist as CT, and eventually MR imaging, entered the picture.

This was truly an exciting time for pediatric neuroimaging that had built a firm foundation not only for a developing subspecialty, but also for the personal careers of many individuals in pediatric neuroradiology. As this period began drawing to a close in 1984, evidence of an even a greater future in the use of magnetic resonance imaging to diagnose cerebral disorders in children, began taking shape.

The Next Five Years (1985–1989)

The Contribution of MR Takes Shape

This period, as much as any other, truly shaped modern pediatric neuroradiology. This period was the prelude to the decade of the brain and the emergence of MR imaging as the dominant technique in pediatric neuroradiology. The important roles of CT and sonography were not to be lost, however, as can be easily seen as this period began. Rather than to focus on the technical aspects of a technique, imaging began focusing more on disease processes. The diagnostic potential of imaging for characterizing and staging primary brain tumors, such as the primitive neuroectodermal tumor, and determining the effect on tumor patient management. Through CT, we could not only now tell the clinician that a tumor existed, but what its likely histologic characteristics would be. Early recognition of complications related to various disease states were now also possible, which, until now, could only be identified in the very late stages of the disease process. With the use of CT, new and exotic illnesses were defined, such as disorders in neuronal migration, that eventually would emerge as a significant cause of childhood morbidity and mortality. Our vocabulary soon included terms such as lissencephaly and schizencephaly that before were terms only mentioned to us by the developmental pediatrician or the pathologist. It now became obvious that even the neuroradiologist must be able to understand and classify malformations of the brain based on embryologic development. Such classifications, as published in the *AJNR* of van der Knapp and Valk, were paramount to our understanding of these conditions. The ability to recognize even minor malformations in vivo changed the shape of genetics.

It was, however, the diagnosis and management of intracranial tumors that was to dominate the CT literature during this period of time. Tumors such as choroid plexus papilloma, optic pathway gliomas, and gangliogliomas were regarded very differently based on what was recognized through imaging. An easy way to follow the effect of therapy now emerged through CT, and imaging eventually was to become part of every treatment protocol.

The key to the diagnosis of childhood disease has always been, and always will be, first the recognition of the normal appearance. Not surprisingly, the process of defining normal brain maturation and recognizing variations in brain development as seen by CT, sonography, and, later, MR imaging was the topic of numerous investigations. From asymmetry in the temporal lobes, to the size of the normal pituitary stalk, the normal process of development was further defined through imaging. This process was to become even more important with the emergence of MR imaging, with its improved resolution and ability to reveal not only tissue structure but also characteristics of tissue composition. MR imaging emerged as a new way of following maturation through depicting the T1 and T2 characteristics of myelination. Landmark articles that remain standards of reference were published throughout this 5-year period. No longer was the term ''developmental delay'' to be determined by physical examination alone. The impact of such contributions was to have a far greater reach than just in neuroradiology, but impacted all of pediatrics.

It was during this period that we also witnessed a significant shift of attention in pediatric neuroimaging techniques. Sonography continued in the first half of this period to play a strong role in pediatric neuroimaging. No less than 20 articles for its use in hemorrhagic disorders in the premature infant, follow-up of neonatal hydrocephalus, and evaluation of infections of the infant brain were to be published in the years 1985–1987. By the end of this period, however, this publication record for sonography fell to only five to eight articles, which were nonetheless important contributions to neuroimaging. Despite this decline, sonography was clearly established in the armamentarium of the neuroradiologist and pediatric radiologist as the principle technique for assessing the preterm infant and the follow-up of neonatal hydrocephalus. CT was also clearly established in the evaluation of the

pediatric head and neck, the bony calvarium, and pediatric head trauma, including that secondary to abuse.

By the end of this period, however, it was clear that MR imaging was to become the primary focus of interest in pediatric neuroradiology for the next decade. As early as 1985, MR imaging of the pediatric spine clearly emerged as the primary technique for assessing spinal soft tissue. This included the recognition of malformations of the craniocervical junction, such as the Chiari I malformation, with far greater frequency than was previously recognized. The presence of syringomyelia and hydromyelia of the cord, as well as defects such as diastematomyelia, could easily be recognized by MR imaging without the need for myelography or ionizing radiation. This was to change the very way we screened the pediatric spine for disease. Myelography no longer was to be performed with its previous frequency. Reports in the *AJNR* regarding the use of spinal MR imaging in children testified to this trend toward less invasive and more accurate diagnoses achieved by MR imaging.

In the time that was to follow, the use of MR imaging to diagnose primary brain tumors, congenital malformations, vascular malformations presenting in childhood, metabolic diseases, and childhood cerebrovascular disease were the focus of numerous contributions to the *AJNR.* MR imaging was not only a more accurate way to make a diagnosis, but also provided insight into the actual classification and pathophysiology of such malformations, such as dysgenesis of the corpus callosum and disorders of neuronal migration. As in the previous 5-year period when many anatomic abnormalities became ''newly'' discovered through imaging, MR imaging allowed neuroradiologists to diagnose and recognize many metabolic and neurodegenerative disorders unfamiliar to most. Names like Pelizaeus-Merzbacher disease, Leigh disease, oculocerebrorenal disease, and Menkes disease began cropping up with increasing frequency in journal articles with every issue. We were soon to learn from this experience that conditions such as these were not as rare as previously thought, but only perhaps unrecognized with sufficient frequency. MR imaging was clearly here to stay, and was clearly to remain a significant part of our literary history in the *AJNR* for the decade to come.

The Decade of the Brain (1990–1995)

The Early Years

With the beginning of the 1990s came the beginning of what was to be referred to as the *Decade of the Brain.* This period was as productive for pediatric neuroradiology as it was for all of neuroradiology and for the Journal. By 1990, MR was clearly the dominant imaging technique used in pediatric neuroradiology. This period was to continue with the trend of shifting from the technical aspects of imaging to categorizing disease processes. Several relatively new sections were to emerge in the Journal, encompassing some familiar and some not-so-familiar conditions. An entire section was devoted to imaging of the phakomatoses, in part because of the number of good publications submitted and in part owing to the fact that this group of conditions, perhaps more than any other in children, lent itself well to MR imaging. Never before had we realized the scope of CNS involvement in the phakomatoses by diseases such as cutaneous melanosis, neurofibromatosis, epidermal nevus syndrome, Sturge Weber syndrome, and tuberous sclerosis. Rare phakomatoses, such as segmental neurofibromatosis, now approached center stage through publication. Excellent scientific reports introduced us to exotic conditions such as Lhermitte-Duclos disease and linear sebaceous nevus syndrome, allowing readers to recognize them by example.

During this period, acceptance of papers for publication played on the strengths of MR imaging to explore new territories, especially in the area of metabolic and neurodegenerative disease. Reports on the MR imaging findings in phenylketonuria, Refsum disease, glutaric and methylmalonic acidurias emerged that would be joined later by even newer developments in MR spectroscopy. The visual display of such conditions would later play a significant role in their differential characterization. More common conditions, such as the mitochondrial leukodystrophies and Krabbe's disease, were described in sufficient detail to allow their identification by all of neuroradiology and not just a few. As these conditions are very rare and seldom present in a single institution, the publications of high-quality images representing these disorders began to serve as pictorial references for comparison by many investigators as they might encounter them in their own practice. As if to appear in groups by chance, entities such as Kallmann syndrome, with its array of imaging findings, began appearing in a number of excellent descriptive articles. More advanced imaging, such as spectroscopy, also appeared to show promise in the evaluation of neurodegenerative disorders for which anatomic imaging alone still provided incomplete information.

It was, however, in 1992 that the field of pediatric neuroradiology truly came into its own as a subspecialty, with significant literary exposure to the readership of the *AJNR.* It was the year that Dr. Michael Huckman took two bold steps. The first was to change the appearance of the journal (for the better, I might add). The second was to publish, in its entirety, a symposium on pediatric neuroradiology created by Dr. Thomas Naidich and given by foremost and upcoming experts in the field of pediatric neuroradiology at the 1992 annual meeting of the ASNR. This symposium, perhaps more than any other format at the time, defined the broad scope of what was then pediatric neuroradiology. It also indicated to all in the ASNR and in neuroscience that this subspecialty had finally matured into a significant part of neuroradiology. Volume 13,

number 2 was, as published, not just another issue of the Journal, but a concise textbook on pediatric neuroimaging. It remains so even today an excellent source for review and pathologic correlation.

Conditions that were to play a large role in pediatric neuroimaging were the topics of numerous reports published over this period in the *AJNR*. Migrational disorders were defined to the point of classification based not on pathology, but according to patterns seen on imaging. Neonatal brain imaging advanced to the point that imaging allowed a better definition of the pathologic changes in infants with cerebral palsy and developmental delay. Cocaine abuse and its effect upon the developing brain was just one example of how imaging added to the total body of knowledge within well-defined areas. Most importantly, articles published in the *AJNR* continued to advance our understanding of how significant brain injury often had its origin in utero, and this understanding was based on recognizable patterns of abnormalities seen with imaging. Imaging began to support the clinical work of clinical pediatric pioneers such as Nelson and Ellenberg who sought to prove that in utero injury was in fact the leading cause of postnatal developmental delay. Neuroradiology responded by many articles in support of this concept.

The anatomic virtues of MR imaging were fully explored over this period. Primary CNS neoplasms in childhood were further characterized to the point of common recognition. Less common tumors in childhood such as meningiomas and oligodendrogliomas were the topics of excellent reports in the *AJNR*. Although less common than in adults, a literary focus on cerebrovascular disease in children began to emerge after a long hiatus. Congenital malformations such as those found in the region of the vein of Galen were better characterized to allow for specific neuroradiologic intervention. The wide variety of causes of cerebrovascular disease in children such as mitochondrial disease, moyamoya, and aneurysm was becoming more obvious in practice by the increasing number of reports on these and other subjects that were to continue to increase over the next 5 years.

Of particular note was the emergence of a relatively new method to pediatric imaging, that of MR spectroscopy (MRS). Its use in the evaluation of childhood metabolic disorders, and specifically neurodegenerative disease, became the topic of several major articles and short reports. The use of MRS, as opposed to standard laboratory methods, could actually establish the diagnosis for conditions such as nonketotic hyperglycinemia. Other uses of MRS to assess heterotopias and HIV infections in neonates were also published. It was during this time that the *AJNR* published its first article on the pediatric use of diffusion-weighted MR imaging to assess brain maturation. By the close of this first half of the decade of the brain, anatomic imaging by MR imaging was clearly established, and the stage was set for the next major advance in pediatric neuroradiology, that of imaging brain function as well as form.

The Decade of the Brain (1995–1999)

Prelude to the Future

By 1995, the *AJNR* clearly led the way in publishing on all aspects of pediatric neuroradiology. MR imaging now was the most often used technique in pediatric neuroimaging, but CT and sonography both maintained well-deserved strong niches for specific clinical indications. It was also clear that we no longer viewed imaging strictly from a technical perspective, but rather as a vehicle to uncover new and important information about the physiology of the pathologic condition. Imaging became firmly entrenched in the management of patients, as it now became a part of almost every treatment protocol to screen for and follow neurologic disease. The focus of the pediatric neuroradiologist was no longer just on diagnosing the presence or absence of a disorder, but rather in uncovering information about its physiology, natural history, and the direct effect treatment had on the underlying pathology. During this period, literary documentation clearly demonstrated that we no longer viewed pathology as purely anatomic in nature, but as a complex process consisting of cellular metabolism, vascular perfusion, and diffusion of water. If literature is to be considered a roadmap of where we are and where we are going, the changing course of pediatric neuroradiology was clearly set in the literary record of this period.

Sonography, which began the first decade in the *AJNR* with one third of the manuscripts, by the last 5 years had dropped to less than 10 papers. Although the quality of these papers stand as evidence of a strong continued role for sonography in pediatric neuroradiology, I can only say that the numbers of currently submitted sonographic investigations in no way equal those of the past. Although sonography has certainly given way to MR for the imaging of all age groups, it remains a very useful method to evaluate and screen for CNS disease in neonates and infants. Several articles during this period investigated sonography of the infant spine; one of these articles clearly demonstrated a role for sonography in screening the infant spine to identify the level of the conus. Sonography of the brain, like other techiniques, continues to expand its abilities to depict pathophysiologic changes beyond its traditional role of anatomic imaging. In one study, investigators clearly demonstrated the promise of quantitative analysis of the infant brain for the detection of hypoxic-ischemic encephalopathy while maintaining the portability and low cost inherent to this method. Investigators also demonstrated the future of contrast enhancement in sonography in one report on neonatal hydrocephalus. Such advances are likely to continue. Although sonography is not likely to be as widely used in the future as it was in the past, technical advances provide clear evidence that its role, while changing, is

likely to remain strong in the neonatal intensive care unit for years to come.

In a similar fashion to sonography, articles reporting the benefits of CT also dramatically declined mostly because of increasing MR imaging. A number of excellent correlative articles were published during this period in which MR and CT scanning were performed in the same subjects. Although these were not direct statistical comparisons, it is clear that a role for CT of the brain, secondary to that of MR imaging, had developed by 1996. CT did, however, solidify its niche in the evaluation of the skull base and cranium, and maintained a hold as well on the evaluation of the pediatric head and neck. Articles defining the normal anatomy of the skull base and larynx were published, and became the anatomic standard for defining both normal and abnormal morphology of these regions in children. CT still proved to be quite useful in the evaluation of the neck for conditions, such as fat necrosis and congenital anomalies of the pediatric spine. By 1999, the hint of new applications for pediatric CT began to emerge, as they did for the imaging of adults, through the application of CT angiography. Helical CT angiography may eventually prove as useful as MR angiography as the range of cerebrovascular disease in children widens and increases in clinical importance.

Nevertheless, it was MR imaging that clearly emerged as the leader in pediatric neuroimaging by the end of the millennium, and it is unlikely that this trend will be altered in the near future. Leading the applications of MR imaging was its continued use for exploring metabolic and neurodegenerative disease in the pediatric age group. The use of MR imaging for evaluating demyelinating disorders, such as multiple sclerosis in children, paralleled its similar use in adults; however, the balance of MR imaging applications in metabolic and neurodegenerative disease in children focused on developmental metabolic defects. MR imaging and advanced methods such as MR spectroscopy were used to study a wide range of conditions, including the phakomatoses, mitochondrial disorders, adrenoleukodystrophy, lysosomal disorders, and Pelizaaeus-Merzbacher disease. MR imaging improved our understanding of the development of many of these conditions as well as provided morphologic information regarding their course. Advanced imaging, such as MR spectroscopy of adrenoleukodystrophy, was shown to be more sensitive than physical examination for following up patients with metabolic diseases. By the end of the decade of the brain, MR imaging and MR spectroscopy had advanced to the imaging method of choice in the evaluation and follow-up of children with a wide variety of metabolic and neurodegenerative diseases.

The role of MR imaging in the evaluation of childhood epilepsy also surged forward in the latter half of the decade. The value of high-resolution imaging for detecting structural causes of epilepsy improved lesion detection. Other reports better defined the range of developmental abnormalities that might contribute to childhood epilepsy by using MR imaging. The multiplanar capabilities of MR imaging also allowed better definition of cortical dysplasias and migrational anomalies that contribute to neurologic disease in the pediatric population.

The importance of understanding normal development and anatomy depicted on MR images led to numerous reports on the subject in the latter half of the decade. Both normal and abnormal development of the temporal lobes were highlighted as examples of what we may still learn from such anatomic investigations. Other reports touched on a wide range of developmental issues, including that of normal formation of the pituitary gland, the operculum, the corpus callosum, the hippocampus, myelination, and supratentorial parenchyma.

Neonatal imaging continued with a strong showing in this period as well. Reports improved our understanding of perinatal asphyxia and its appearance in both the term and preterm infant as well as in neonatal trauma. Kernicterus appeared again to be on the rise after a decrease in previously published reports. The evolution of the germinal matrix hemorrhage was better identified by careful comparison of imaging with the pathologic condition, as was the relationship between structural injury and metabolic conditions, such as neonatal hypoglycemia. More careful analysis of the imaging patterns of birth asphyxia led to the development of image-based scoring systems that may in time prove valuable in the assessment of severity and have improved our ability to predict outcome.

By the close of this period, the use of advanced MR applications such as MR spectroscopy, perfusion, and diffusion set the tone for what neuroradiologists must be capable of understanding if we are to continue as imagers in the future.

In summary, this has been an interesting 20 years of literary growth in pediatric neuroradiology. The publication record of the *AJNR* shows us where we began and how we got to the beginning of the future. Neuroradiologists developed and defined what is the subspecialty of pediatric neuroradiology. Our literary contributions far surpassed any other literary contributions in pediatric neuroscience. Our future is to be considered bright only if we can continue in this role.

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