History of surgery for cerebrovascular disease in children.

Part I. Intracranial arterial aneurysms

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✓ Intracranial aneurysms are rare in children, and their origins and treatment methods tend to be different from those in these same entities in adults. These lesions tend to be congenital or to have an infectious or traumatic origin. In the current paper the authors trace the historical evolution of the diagnosis and treatment of intracranial aneurysms in children. Based on the literature, these lesions appear to occur in children in less than 3% of all series. The literature also supports the suggestion that symptoms from these aneurysms are often from mass effect and that giant aneurysms and lesions in the posterior cranial fossa are relatively more common in children than in adults. The termination of the carotid artery and the anterior cerebral artery seem to be disproportionately common sites of aneurysm formation in this cohort. Interestingly, surgical outcomes in children appear to be moderately better than in adults. Based on the literature, the claim can be made that a multidisciplinary approach to the management of such aneurysms can yield good outcomes in a very high percentage of children treated.

KEY WORDS • aneurysm • subarachnoid hemorrhage • pediatric neurosurgery • history of neurosurgery • children

ALTHOUGH there are a myriad of conditions in children that can affect blood delivery to the brain, the three major categories of surgically treatable cerebrovascular disease in children are cerebral aneurysms, vein of Galen malformations, and cerebral arteriovenous malformations (AVMs). In this three-part review, each of these will be considered with regard to the historical evolution of contemporary management options, strategies, and principles. Intraventricular hemorrhages in premature infants, ischemic strokes, and arteriopathic hemorrhagic strokes will not be reviewed because surgical and endovascular techniques are presently ineffective or are aimed primarily at treating secondary complications arising from these phenomena (for example, hydrocephalus following intraventricular hemorrhage).

The topic of cerebrovascular diseases in children is lacking in the writings of the great pioneers of neurosurgery. Cushing^{16,19} wrote of tumors arising from blood vessels (hemangiomas and hemangioblastomas) and described AVMs of the orbit. His principal writings on pediatric topics included hydrocephalus, medulloblastomas, cerebellar astrocytomas, and studies of the physiology of cerebrospinal fluid, but vascular problems in

children were not addressed.^{17,18} Bartholow⁶ first described Sir Victor Horsley's use of CA ligation in an adult patient in whom an intracranial aneurysm was discovered at surgery. Dott²² first reported wrapping an aneurysm that had bled three times in an adult patient. According to Albright,¹ Dandy was the first to use aneurysm clips to treat an adult patient who presented with spontaneous third cranial nerve palsy. Olivecrona and Ladenheim⁵² wrote an original and seminal treatise on the treatment of cerebral AVMs that featured almost exclusively adult patients.

The earliest descriptions of each of the major cerebrovascular diseases of childhood that are now surgically treatable are case reports in the pathology literature. Most date back to the nineteenth century, but isolated case reports from antiquity can be found. The twentieth century brought a better understanding of the nervous system and greater surgical capability to address problems within it. Nevertheless, it was not until pediatric care was centralized in large children's hospitals that sufficient numbers of these patients were recognized and case series collected to enable insight into their unique pathophysiological features and response to treatment efforts. Early surgical attempts to treat all of these lesions were met with high mortality rates, and it was not until the middle to latter part of the twentieth century that meaningful therapeutic interventions were realized. Advances in adults were modified and applied with varying degrees of success to pediatric patients. In the last 25 to 30 years (since the most

Abbreviations used in this paper: ACA = anterior cerebral artery; AVM = arteriovenous malformation; CA = carotid artery; CT = computerized tomography; HIV = human immunodeficiency virus; ISAT = International Subarachnoid Aneurysm Trial; MR = magnetic resonance; SAH = subarachnoid hemorrhage.

recent review by Humphreys, et al.,²⁸ of cerebrovascular disease in children), greater understanding of these lesions, coupled with technological advances, have yielded great advances, so that meaningful diagnostic and therapeutic interventions are now possible for the majority of children who harbor these complex and dangerous lesions.

Cerebral Aneurysms of Childhood

Earliest Reports

Although aneurysmal SAH was documented as early as the 1760s, the intracerebral aneurysm and resulting SAH is a disease entity that came to be understood in the twentieth century. Contributions from the nineteenth century established the correlation between clinical decline from apoplexy and the presence of a hemorrhage adjacent to an intracerebral aneurysm. Confirmation that an observed clinical apoplectic event arose from a hemorrhage became possible after Quincke⁵⁹ introduced the technique of lumbar puncture in 1891. At this time, aneurysms were treated surgically only when they were mistaken for tumors, and CA ligation was the primary modality of treatment. Seminal firsts in the care of aneurysmal SAH in adults included Dott's²² direct attack for wrapping intracerebral aneurysms in 1931, Dandy's use of a clip for obliteration of an intracerebral aneurysm in 1928,¹ then his use of a silver clip in 1943, and Moniz's development of effective techniques for cerebral angiography in 1931⁴⁹ and safe and effective contrast material in the 1950s.

The first report of an aneurysmal SAH in a child was published in 1871 in the German pathology literature, when Eppinger²³ detailed the case of a 15-year-old boy, a gymnast who collapsed while exercising. Postmortem analysis revealed an intracerebral hemorrhage associated with an aneurysm as well as a stenosis of the aorta. Matson,⁴³ in the first peer-reviewed paper describing a series of intracranial aneurysms in children, quotes McDonald and Korb,⁴⁴ who allude to an earlier description of a ruptured intracranial aneurysm by Biumi of Milan in 1778. A similar report by Strassman⁶⁷ appeared in the German literature in 1922. In this paper the author detailed the case of another German youth with aortic coarctation who suddenly died of a ruptured cerebral aneurysm while playing a vigorous sport (football). The association with aortic coarctation captured the interest of many workers in the field and caused the aneurysmal diseases to be considered a secondary complication of the aortic condition, which largely prevented recognition of the importance of the cerebrovascular disease.

The next significant event in the evolution of the understanding of pediatric intracranial aneurysms came with the publication of a combined series by McDonald and Korb⁴⁴ in 1939. These investigators collected 1125 verified aneurysms from 407 sources reported prior to 1938. Only one infant (1.5 years old) and two patients younger than 5 years of age were encountered in the entire series. Only 28 patients, which is slightly less than 2.5% of the entire series, were noted to be younger than 15 years of age. Thus, the rarity of intracerebral aneurysms in children was established with this early publication.

Other large population-based reviews have supported

this early finding. Locksley, et al.,⁴² reported on 2627 patients with intracranial hemorrhage in the cooperative study of this disease published in 1966, and these authors observed a 1.9% annual incidence in children. Patel and Richardson⁵⁵ later summarized the British combined cohort of patients with aneurysms treated by McCissock at Queen Square and the Atkinson Morley Hospital. Between 1944 and 1968, 58 cases (1.9%) in a total of 3000 ruptured intracranial aneurysms were recognized in children (< 19 years old). Laitinen³⁶ summarized the data of 1175 Finnish patients who were treated for SAH and noted that 35 (2.9%) were children. Similarly, Ostergaard and Voldby⁵³ reviewed 1368 patients treated at a single university setting in Denmark and noted that 43 (3.1%) were children. The rarity of aneurysms in childhood is further accentuated when the patients are further substratified by age. Of the 43 children reported by Ostergaard and Voldby, only nine (0.7% of all cases) were 12 years of age or younger. Only one patient in the large series from Finland reported by Laitinen was younger than 10 years of age. Similarly, in the report by Patel and Richardson, only 16 of the 58 reported pediatric cases were found in children younger than 14 years of age (0.5% of the total). Thus, the exact incidence varies from series to series and is reported to be between 0.5 and 4.6%, but a baseline incidence of 2 to 3% in adult series appears accurate. Perhaps more importantly, it is clear that the great majority of aneurysms occurring in children are found in teenagers and that they are exceptionally unusual in young children.

The existence and rarity of aneurysms in children has fueled a controversy surrounding the pathophysiological features of intracerebral aneurysms. Those embracing the concept that these are developmental lesions emphasize the presence of aneurysms in children as supporting evidence for their point of view. Any aneurysm found in an infant or neonate could not reasonably be said to arise as a result of atherosclerosis and hemodynamic stresses. By contrast, those embracing the concept that aneurysms arise from degenerative hemodynamic stresses point out the remarkable rarity of these lesions in young children. Others have critically reviewed published cases of lesions occurring in infancy and childhood and have called into question the legitimacy of claims that the aneurysms were characteristic of the berry aneurysm of adulthood.⁶⁵ Regardless of one's point of view, it is apparent from a review of large series that aneurysms in children do occur at all ages but are exceedingly uncommon in the youngest patients. Infectious and traumatic causes of aneurysms are addressed later in this paper.

Case Reports and Case Series Published Before the Era of CT and MR Imaging

A series of isolated case reports of aneurysms in children appeared during the early 1960s. Kimbell, et al.,³³ reported on a 16-month-old girl who suffered an aneurysmal SAH in the middle cerebral artery in 1960. In 1961, Jane³⁰ reported on a 1-year-old child who died of a ruptured posterior inferior cerebellar artery aneurysm. Jones and Shearburn³¹ reported clip occlusion of a middle cerebral artery aneurysm in a 4-week-old infant in 1961.

The first purely pediatric series of intracerebral aneurysms was published by Donald Matson⁴³ from Children's

Surgery for cerebrovascular disease in children: intracranial aneurysms

Hospital Boston in 1965. By this time several important events had occurred. First, pioneers of microsurgery had begun studies that would culminate in widely accepted and implemented techniques of microsurgery. Microsurgical instruments, clips, and continuously improved illumination and magnification were shortly to follow. Second, tools and techniques had advanced to enable widespread use of high-quality angiography. Third, most large cities in North America had a children's hospital and there was increasing recognition of the value of subspecialization of pediatric care. Such specialized centers promoted the collection of experience in rare disease processes such as intracranial aneurysms in children.

Other cerebrovascular centers evolved and made important contributions. Matson's initial report detailed findings in 14 patients who were seen and evaluated between 1955 and 1968 at the pediatric neurosurgery service Children's Hospital Boston. Matson noted that only two patients with intracerebral aneurysms had been followed at Boston Children's Hospital before 1954. Seven of the 14 patients were younger than 12 years of age, and 12 of the patients were boys. This observation, which was repeated in several but not the majority of subsequent series, introduced the concept that intracerebral aneurysms are more common in boys. Review of the approximately 700 children with intracerebral aneurysms whose cases were subsequently reported in the literature revealed that differences in incidence between the sexes were inconsistent and probably minimal. All patients except one in the Matson series presented with spontaneous hemorrhage. One patient received no treatment, two underwent ligation of the CA, the aneurysm was excised in three, and seven underwent ligation or clip placement to occlude the aneurysm. In this cohort, three patients died and 11 survived. Matson drew two simple conclusions: 1) intracranial aneurysms do occur and rupture in children and should be considered when intracranial hemorrhage is encountered; and 2) surgical results appear to be at least as good as or better than in adults.

Since Matson's initial report there have been approximately 10 others detailing large pediatric series of intracranial aneurysms. These are summarized and briefly reviewed in Table 1.

Amacher and Drake³ reported a series of 16 children with intracranial aneurysms in 1975. Only three were younger than 15 years of age and none had coarctation of the aorta. Giant aneurysms were seen with increased frequency, and they were treated with clip occlusion in seven of 16, excision in three, and trapping of the parent vessel in three. There was a striking incidence of aneurysms observed at the CA termination and along the ACA complex. In virtually all of the early series (before 1985) the vast majority of patients presented with SAH. The London, Ontario series of Amacher and Drake is unique in that a significant number of their patients had giant and/or posterior fossa aneurysms and presented with symptoms of local mass effect. The difference was probably due to referral patterns and selection issues, but later series published in the era of CT and MR imaging showed a similarly higher incidence of aneurysms presenting with cranial neuropathy and local mass effect.⁶³

In the large British series reported by Patel and Richardson,⁵⁵ there were 58 cases in patients younger than 19

years of age. This remains a landmark contribution because of the large size of the patient group (it remains the largest series reported to date) and because of several insights that arose from the review of the series. Sex distribution showed minimal male predominance (32 male and 26 female patients). The series only addressed aneurysms that ruptured, so by definition all patients presented with SAH. The circumstances were usually benign (walking, standing, or sitting predominated the reported activity).

That 54 of the 58 patients in the series underwent angiography attests to the advances in angiographic capability during the study interval (1944–1968). This is particularly notable when direct CA puncture in children was necessary. A high incidence of aneurysms at the CA bifurcation and ACA complex was noted. Children were found to demonstrate vasospasm less frequently than adults. In later series it was suggested that children experienced vasospasm but tolerated it without neurological decline better than adults. Twelve percent of patients in this series had coarctation of the aorta. The less aggressive role of surgical therapy is evident in that 21 of 58 patients did not undergo this treatment despite harboring a known ruptured aneurysm. Seven died acutely and five died later; only eight of the 21 treated conservatively attained long-term survival with good neurological outcome. Of the 37 patients who underwent surgery, 19 were treated with CA ligation and 15 had intracranial surgery. The latter comprised a heterogeneous group of treatments ranging from drainage of hematoma through a bur hole to direct intervention with wrapping or clip occlusion (in 12 patients). Outcome was not precisely described with regard to choice of intracranial procedure, but the authors concluded that CA ligation is safer and preferable to other modes of surgical treatment.

Storrs, et al.,⁶⁶ reported the early results in the series of pediatric patients with aneurysms who were treated at the Hospital for Sick Children in 1982. Like Matson's early work from Boston, this report attested to the lack of recognition of aneurysms prior to the latter half of the twentieth century. Only one patient with this entity had been cared for at the Hospital for Sick Children prior to 1950. In this series of 29 patients the sex distribution was even, and approximately 75% presented with SAH. These authors also found an elevated incidence of CA bifurcation, posterior fossa, and giant aneurysms. Clip placement, ligation, and parent artery occlusion were all used, but outcomes were not stratified by surgical choice.

In 1977 Almeida, et al.,² reported a series of 11 intracranial aneurysms in children younger than 15 years of age. Boys predominated, and the most common location for aneurysms was the termination of the CA. The authors concluded that direct surgical clipping was preferable to CA ligation in their experience. Ostergaard and Voldby⁵³ reported another pediatric series from Denmark in 1983. Collectively these series attest to the existence (however rare) of pediatric aneurysms, and mirror the North American studies. Ostergaard and Voldby noted the relative tolerance to angiographically apparent vasospasm that pediatric patients demonstrated, which was previously noted by Patel and Richardson.⁵⁵ Despite an incidence of 53%, there was no increase in the mortality rate in the group demonstrating vasospasm, and none of the patients who died had evidence of cerebral infarction on post-

TABLE 1
Literature review of intracranial arterial aneurysms in children*

Authors & Year	Center	No. of Pts†	Yrs Reviewed	Observations
Matson, 1965	Children's Hospital Boston, Boston, MA	14	1955–1964	distribution no different than expected in any other group aneurysms occur in all ages & are cause of intracerebral bleeding/should be considered surgical treatment well tolerated; results as good as/better than adults M/F ratio 12:1 (sex not reported for one patient)
Patel & Richardson, 1971	Queen Square & Atkinson Morley, London, United Kingdom	58	1944–1968	high incidence at CA termination & ACA vasospasm occurs less often than in adults CA ligation recommended for treatment: safer than direct attack
Amacher & Drake, 1975	London, Ontario, Canada	16		high incidence of giant aneurysms M/F ratio 11:5 VA occlusion well tolerated
Almeida, et al., 1977	São Paulo, Brazil	11		all pts except 1 presented w/ SAH
Storrs, et al., 1982	Hospital for Sick Children, Toronto, Ontario, Canada	29	1950–1970	high percentage of pts w/ aneurysm have symptoms prehemorrhage M/F ratio 13:16 high incidence of lesions in CA bifurcation (9 of 29 [31%]) & PF (10 of 29 [35%])
Ostergaard & Voldby, 1983	University of Aarhus, Denmark	43 (51)	1943–1980	no illness or death from vasospasm M/F ratio 25:18 all pts studied w/ angiography except 4 who died w/in 1st day
Pasqualin, et al., 1986	Verona City Hospital, Verona, Italy	38	1965–1984	4 pts < 3 yrs; 29 > 9 yrs old bifurcation aneurysms predominate in adolescents (10–15 yrs); ACoA predominate in teens (16–20 yrs) overall results better than in adults: 73% w/ good outcome, 21% dead
Heiskanen, 1989	Helsinki University, Helsinki, Finland	16	1977–1986	children represent 1.2% total institutional aneurysm experience 14 aneurysms treated: 13 clipped, 1 trapped
Meyer, et al., 1989	Mayo Clinic, Rochester MN	23 (24)	1967–1987	M/F ratio 3:1 PF localization predominates 30–45% giant aneurysms symptomatic aneurysms w/ SAH in 13 of 14 & mass effect in 1 of 14 no instances of coarctation of aorta or connective tissue disease treated aneurysms: 14 clipped, 4 trapped outcome excellent in 87%, good in 8%, poor in 5% aneurysms occur & need to be considered in diff dx
Herman, et al., 1991	Barrow Neurological Institute, Phoenix, AZ	16 (20)	1984–1990	M/F ratio 7:9 7 pts had solitary, saccular aneurysm (simple aneurysm); 9 had giant, infectious, traumatic, or associated w/ AVM (complex lesions) all simple aneurysms presented w/ SAH & were present at arterial bifurcation
Sanai, et al., 2006	University of California, San Francisco, CA	32 (43)	1977–2003	pts w/ simple aneurysms older than pts w/ complex aneurysms rupture of aneurysm not most common presentation; majority SAH were low grade wide distribution of aneurysm sites/locations 13 pts treated w/ microsurgery, 16 w/ endovascular occlusion, 1 observed microsurgery & endovascular therapy both effective in children

* ACoA = anterior communicating artery; diff dx = differential diagnosis; PF = posterior fossa; pts = patients; VA = vertebral artery.

† Numbers in parentheses represent the number of aneurysms.

mortem evaluation. Finally, these observers noted a significant decrease in the overall mortality rate with the late introduction of microsurgical techniques and modern intensive care capabilities. Pasqualin, et al.,⁵⁴ reported a large series from Verona in 1986. Like the Scandinavian studies, their report addressed the pediatric subpopulation receiving treatment at a large European center and demonstrated the rarity of pediatric aneurysms (2% overall in the series), the rarity of deterioration from vasospasm, and the generally better course for children than for adults.

Thus, by the end of the era before CT and MR imaging became available, there had been a number of reports in which the presence of intracranial arterial aneurysms in children was clearly established. Sufficient expertise had been accumulated to allow recognition of pediatric intracerebral aneurysms as a distinct pathophysiological entity.

Based on two reports from pediatric neurosurgery centers (Hospital for Sick Children and Children's Hospital Boston), two neurovascular surgeons (Drake and McCissock), and a number of large European series, the following observations had been made that defined pediatric intracranial arterial aneurysms. These observations are as follows. 1) Pediatric arterial aneurysms definitely occur and result in hemorrhage, but they are rare in teenagers and exceptionally uncommon in children younger than 10 years of age. 2) Data in some series support the suggestion of a predominance of childhood aneurysms in males and at the bifurcation of the CA or ACA complex. 3) Giant and posterior fossa aneurysms are more common in children. 4) The vast majority of aneurysms found in this era presented with SAH. 5) Angiography is useful in defining the aneurysm. 6) Children demonstrate vasospasm but tolerate it

much better than adults. 7) Carotid artery ligation was initially the preferred surgical intervention, but early support for microsurgical exposure and clip placement is being expressed. 8) Outcomes for treatment in children are at least as good as for adults.

Case Series Published in the CT, MR Imaging, and Early Neurointerventional Era

The development of contemporary neuroimaging has contributed greatly to the study, understanding, diagnosis, and treatment of pediatric intracerebral aneurysms. The emergence of CT and MR imaging studies obtained with contrast agents has allowed noninvasive, detailed characterization of aneurysms and the structures surrounding them.^{60,78} The development and widespread adoption of digital subtraction angiographic techniques occurred during the late 1970s and early 1980s.⁷⁹ There were also very significant advances in microneurosurgical techniques during this time that revolutionized the treatment of intracranial aneurysms in adults. Pool and Colton⁵⁸ first emphasized the value of the magnification and illumination that the operating microscope provided. Yaşargil,^{75,76} Sundt,⁶⁹ and others^{21,68} made seminal contributions in texts and papers that promoted direct attack on intracranial aneurysms with the aid of microdissection techniques that centered on the use of magnification and a comprehensive understanding of microneuroanatomy and microvascular anatomy. These are detailed in other parts of this monograph. Advances in technique and materials for treatment of aneurysms in adult patients were applied to pediatric aneurysms, with resulting improvements in outcomes and overall care. The earliest descriptions of endovascular occlusive techniques were also published during this period.^{64,71} Another decade or more would pass before these techniques were discussed specifically in pediatric aneurysms.^{32,39,70}

There were several large series of pediatric aneurysms reported during this time that reflected these general advances and grew increasingly distinct from the early series of pediatric aneurysms. The Mayo clinic series of Meyer, Sundt, and colleagues⁴⁵ attested to the technical advances occurring during this period. This retrospective series of 23 pediatric patients was the first in which direct microsurgical clip occlusion predominated as the primary treatment modality. Those aneurysms that were not directly clipped were trapped via direct intracranial exposure and trapping, or were resected with surgically created vascular anastomoses to reestablish normal flow. Postoperative results were excellent in 21 (87%) of 24 aneurysms. These authors concluded that with “current microsurgical and neuroanesthetic techniques an excellent result can be obtained in the large majority of these patients.”

Herman, et al.,²⁷ reported the Barrow Neurological Institute experience with pediatric intracranial aneurysms in 1991, and in their report they differentiated between simple and complex aneurysms. These authors defined simple aneurysms as solitary saccular lesions arising at an arterial bifurcation and complex aneurysms as a diverse group including giant, infectious, and traumatic aneurysms. Six of the seven patients presenting with simple aneurysms underwent clip obliteration of the lesion. However, due to the large number of complex aneurysms, these authors

emphasized the importance of specialized, individualized, and alternative methods of treatment. Trapping, bypass grafts, and hypothermic cardiac arrest were all used.

The Barrow team is not the only group to report on complex aneurysms that arise from a variety of complex origins in children. Trauma is a very important cause of intracranial aneurysm in this patient group.^{8,12,73,77} Although traumatic aneurysms represent only approximately 1% of all such lesions, they can comprise up to 50 to 75% of pediatric aneurysms in some series³⁷ (this probably reflects the rarity of de novo aneurysms in children). Unusual cases have been presented following nonaccidental injury or birth trauma.⁵⁷ The largest pediatric series was recorded in Los Angeles by Yazbak and colleagues.⁷⁷ Seven children were treated between 1975 and 1992, and all underwent surgical repair of their aneurysm. No patient died or worsened neurologically. Traumatic aneurysms are usually located in the supratentorial space and most often occur at the level of the skull base. Either direct or indirect trauma can result in arterial injury and secondary development of an aneurysm. The incidence of rupture of traumatic aneurysms in adults is estimated to be greater than 50%. Outcome in pediatric patients is most dependent on the outcome of the underlying injury and whether the aneurysm ruptures. Surgical treatment, either by trapping or clip placement, generally results in a good outcome. Endovascular techniques are also of great utility, particularly for lesions involving the cavernous sinus.⁷²

Infectious or mycotic sources are another important cause of aneurysms in children. In adults mycotic aneurysms represent approximately 2 to 3% of the total, but in children up to 10% of aneurysms are mycotic in origin.⁴⁰ These aneurysms are usually fusiform dilations of the vessel wall and were well recognized early in the still evolving understanding of intracranial aneurysms.^{7,50,51} Besides a few small series,¹³ the majority of publications have been individual case reports.^{9,40,74} Children are disproportionately represented, which is probably due to the higher incidence of infectious diseases in this group. The exception to this finding is in infants, who have a high incidence of septic illness but a very low incidence of mycotic aneurysms.⁷⁴ The most common clinical setting for an infectious aneurysm is bacterial endocarditis, but intracerebral aneurysms have complicated a wide range of infectious problems, including sepsis, osteomyelitis, sinusitis, and orbital cellulitis.⁵ The exact pathogenesis is unknown, but the best evidence suggests that the most common sequence is infected emboli lodging within the vessel wall and eliciting an inflammatory response at the level of the adventitia. The fact that most mycotic aneurysms are found on the small distal branches of the cerebral vessels supports the primary role of infectious emboli, but the more difficult to manage proximal mycotic aneurysms may arise as a result of direct extension from an infected space such as the paranasal sinuses.

The natural history of untreated mycotic aneurysms is ominous; they demonstrate a high incidence of spontaneous rupture. The most common presentation for a mycotic aneurysm is intracerebral bleeding or SAH.⁵⁶ In patients with bacterial endocarditis, the aneurysm rupture may be the first clinical manifestation of the illness. The treatment for unruptured mycotic aneurysms is administration of antibiotic drugs and serial imaging with angiog-

raphy to document progressive decrease in their overall size. Surgical treatment is necessary for lesions that progress or fail to show improvement with antibiotic therapy. Rupture may result in an intracerebral hematoma with mass effect that may necessitate surgical intervention. Typical distal mycotic aneurysms can be managed by trapping the parent vessel.⁵⁶ More proximal mycotic aneurysms on parent vessels are more difficult to address. Very little has been directly written about this problem, but encircling aneurysm clips or endovascular techniques are recent developments that may prove useful in this rare though dangerous variant of infectious aneurysms.^{15,34,40}

Another important infectious aneurysm observed in children during this era was the intracranial lesion associated with HIV infection. In the late 1980s and early 1990s, several cases of aneurysms occurring in HIV-infected children were reported.^{29,35,38} Several different types of cerebral arteriopathy related to HIV infection were described over the ensuing few years. In addition to aneurysms, fibrosis, vasculitis, and calcification were all observed.²⁴

Thus, by the mid-1980s a number of additional developments had occurred that were important in pediatric aneurysms. 1) Microsurgical techniques had been developed, disseminated, and recognized as far superior to conventional neurosurgical techniques. Limited numbers of aneurysm series in children showed evolution toward microneurosurgical techniques. 2) Instruments and clips were developed specifically for cerebrovascular microneurosurgery. No specific clips or tools are designed specifically for children. 3) Infections were an important source of aneurysms in children. They appear to be more common in this age group, and treatment is individualized according to the clinical situation and angiographically identified anatomy of the aneurysm. It became known that HIV is an important source of infectious aneurysms. 4) Traumatic aneurysms are common in children after open or closed head injury.

Contemporary Era: Clip Compared With Coil Occlusion

During the last 10 to 20 years there has been an explosion of activity regarding the optimal treatment of intracranial aneurysms. This has been promoted in large part by dramatic improvements in endovascular techniques and materials. The development of subselective catheters, detachable balloons, Guglielmi detachable coils, and other coils has enabled endovascular obliteration of complex aneurysms.¹⁴ Neurointerventional centers have been created to optimize techniques and experience with these methods and materials in the treatment of cerebral aneurysms.⁶¹ Review of the literature published on this disease during the 1990s shows increasing numbers of case reports and small series in which endovascular techniques are used to obliterate aneurysms.¹⁰ All of these reports were from series of adult patients.

Ultimately, a multicenter prospective trial called the ISAT was organized and conducted in Europe. The ISAT trial was a prospective randomized clinical trial in which outcomes from endovascular coil obliteration of intracranial aneurysms were compared with outcomes from microsurgical clip occlusion in adult patients. The initial results were released in 2002, with follow-up data re-

leased in 2005.^{47,48} The results, which showed a relative reduction in dependency and death for patients who underwent endovascular treatments compared with surgery, elicited a firestorm of controversy.^{11,41,46,62} This study has been vigorously criticized by vascular neurosurgeons for its failure to include patients who are elderly and/or who have high-grade or posterior fossa aneurysms.⁴ The observed surgical outcomes were worse than those widely reported from North American centers. Angiographic follow-up data demonstrating occlusion of the aneurysm was not provided. Perhaps most importantly, the study was criticized for not attaining proper "clinical equipoise," which refers to the notion that each patient should be truly equally suitable for clip placement or coil therapy.^{20,26} Nonetheless, the study was a prospective randomized trial with significant numbers of patients and a good design. Despite the vigorous controversy and the study's methodological shortcomings, it is affecting clinical decision making in adult patients with intracerebral aneurysms.²⁵

The applicability of the ISAT data to pediatric patients has not been established. In a single recent large series from the University of California at San Francisco, the investigators compared outcomes in pediatric patients between those undergoing coil occlusion compared with clip placement.⁶³ Thirty-two patients with a total of 43 aneurysms were described. Giant and fusiform lesions were disproportionately represented, and SAH was less common than symptoms from mass effect. A good neurological recovery was noted in 78% of patients. When outcomes were compared by treatment modality, the authors concluded that microsurgical techniques resulted in greater long-term control with less recurrence. There was no randomization in the assignment of treatment, however, and because of that it is highly likely that selection biases entered into the selection process. Therefore, the results need to be interpreted with caution.

Conclusions

After centuries of very limited knowledge about cerebral aneurysms, in the last century there has been a virtual explosion of knowledge and experience. Aneurysms unequivocally occur in children and cause SAH. Recent series support the suggestion that symptoms associated with mass effect are at least as common as hemorrhage. Giant aneurysms and lesions in the posterior fossa are relatively more common in children than in adults. The termination of the CA and the ACA are disproportionately common sites of aneurysm formation in the anterior circulation of children. Traumatic and infectious aneurysms occur more frequently in children than in adults, but this may reflect a relative paucity of spontaneous aneurysms in children. Vasospasm occurs in children but appears to be better tolerated.

The development of microsurgical techniques in neurosurgery was a landmark accomplishment and microsurgical clip placement remains the cornerstone of treatment for intracerebral aneurysms in adults and children. Surgical outcomes in children appear to be moderately better than in adults. Advances in imaging techniques such as CT, MR, and selective angiography studies have enabled visualization of aneurysms with regard to parent vessels

and surrounding structures. Endovascular techniques have recently been developed and are increasingly being used in both adults and children who harbor intracerebral aneurysms. Multidisciplinary management can yield good outcomes in a very high percentage of children treated for these lesions. Cooperative multidisciplinary teams of pediatric neurosurgeons, vascular neurosurgeons, and neuro-interventionalists are best suited to address the many complex issues involved in the important decision making surrounding the child who harbors an intracranial aneurysm.

References

- Albright F: The syndrome produced by aneurysm at or near the junction of the internal carotid artery of the circle of Willis. **Bull Johns Hopkins Hosp** 44:215–245, 1929
- Almeida GM, Pindaro J, Plese P, et al: Intracranial arterial aneurysms in infancy and childhood. **Childs Brain** 3:193–199, 1977
- Amacher LA, Drake CG: Cerebral artery aneurysms in infancy, childhood and adolescents. **Childs Brain** 1:72–78, 1975
- Barrow DL: Bad science ISAT: the impact on neurosurgical practice. **Clin Neurosurg** 51:126–131, 2004
- Barrow DL, Prats AR: Infectious intracranial aneurysms: comparison of groups with and without endocarditis. **Neurosurgery** 27:562–573, 1990
- Bartholow R: Aneurisms of the arteries at the base of the brain: their symptomatology, diagnosis and treatment. **Am J Med Sci** 64:373–386, 1872
- Bell WE, Butler C II: Cerebral mycotic aneurysms in children. Two case reports. **Neurology** 18:81–86, 1968
- Benoit BG, Wortzman G: Traumatic cerebral aneurysms. Clinical features and natural history. **J Neurol Neurosurg Psychiatry** 36:127–138, 1973
- Bohmalk GL, Story JL, Wissinger JP, et al: Bacterial intracranial aneurysm. **J Neurosurg** 48:369–382, 1978
- Bracard S, Lebedinsky A, Anxionnat R, et al: Endovascular treatment of Hunt and Hess grade IV and V aneurysms. **AJNR Am J Neuroradiol** 23:953–957, 2002
- Britz GW, Newell DW, West GA, et al: The ISAT trial. **Lancet** 361:431–432, 2003
- Buckingham MJ, Crone KR, Ball WS, et al: Traumatic intracranial aneurysms in childhood: two cases and a review of the literature. **Neurosurgery** 22:398–408, 1988
- Bullock R, van Dellen JR, van den Heever CM: Intracranial mycotic aneurysms. A review of 9 cases. **S Afr Med J** 60:970–973, 1981
- Cekirge HS, Saatci I, Firat MM, et al: Interlocking detachable coil occlusion in the endovascular treatment of intracranial aneurysms: preliminary results. **AJNR Am J Neuroradiol** 17:1651–1657, 1996
- Chun JY, Smith W, Halbach VV, et al: Current multimodality management of infectious intracranial aneurysms. **Neurosurgery** 48:1203–1214, 2001
- Cushing H: Arteriovenous aneurysm of the occipital vessels. **N Y Med J** 82:1305–1310, 1905
- Cushing H: Hydrocephalus, in WO (ed): **Medicine**, ed 3., 1928, Vol 6, pp 255–266
- Cushing H, Bailey P: Medulloblastoma cerebelli: a common type of mid-cerebellar glioma of childhood. **Trans Am Neurol Assoc** 14:89–121, 1924
- Cushing H, Bailey P: **Tumors Arising from the Blood Vessels of the Brain: Angiomatous Malformations and Hemangioblastomas**. Springfield, IL: Charles C Thomas, 1928
- Diringer MN: To clip or to coil acutely ruptured intracranial aneurysms: update on the debate. **Curr Opin Crit Care** 11:121–125, 2005
- Donaghy RMP, Yaşargil MG: **Microvascular Surgery**. St. Louis: CV Mosby, 1967
- Dott NM: Intracranial aneurysms: cerebral arteroradiography: surgical treatment. **Edinburgh Med J** 40:219–234, 1932/1933
- Eppinger H: Stenosis aortae congenita seu isthmus persistens. **Vrtljschr Prakt Heilk** 112:31–67, 1871
- Fulmer BB, Dillard SC, Musulman EM, et al: Two cases of cerebral aneurysms in HIV+ children. **Pediatr Neurosurg** 28:31–34, 1998
- Gnanalingham KK, Apostolopoulos V, Barazi S, et al: The impact of the international subarachnoid aneurysm trial (ISAT) on the management of aneurysmal subarachnoid haemorrhage in a neurosurgical unit in the UK. **Clin Neurol Neurosurg** 108:117–123, 2006
- Harbaugh RE, Heros RC, Hadley MN: More on ISAT. **Lancet** 361:783–784, 2003
- Herman JM, Rekatte HL, Spetzler RF: Pediatric intracranial aneurysms: simple and complex cases. **Pediatr Neurosurg** 17:66–73, 1991/1992
- Humphreys RP, Hendrick EB, Hoffman HJ: Cerebrovascular diseases in children. **Can Med Assoc J** 107:774–781, 1972
- Husson RN, Saini R, Lewis LL, et al: Cerebral artery aneurysms in children infected with human immunodeficiency virus. **J Pediatr** 121:927–930, 1992
- Jane JA: A large aneurysm of the posterior inferior cerebellar artery in a 1-year-old child. **J Neurosurg** 18:245–247, 1961
- Jones RK, Shearburn EW: Intracranial aneurysm in a four-week-old infant. Diagnosis by angiography and successful operation. **J Neurosurg** 18:122–124, 1961
- Kanaan I, Lasjaunias P, Coates R: The spectrum of intracranial aneurysms in pediatrics. **Minim Invasive Neurosurg** 38:1–9, 1995
- Kimbell FD Jr, Llewellyn RC, Kirgis HD: Surgical treatment of ruptured aneurysm with intracerebral and subarachnoid hemorrhage in a 16-month-old infant. **J Neurosurg** 17:331–332, 1960
- Kovoor JM, Jayakumar PN, Srikanth SG, et al: Intracranial infective aneurysms: angiographic evaluation with treatment. **Neurol India** 49:262–266, 2001
- Kure K, Park YD, Kim TS, et al: Immunohistochemical localization of an HIV epitope in cerebral aneurysmal arteriopathy in pediatric acquired immunodeficiency syndrome (AIDS). **Pediatr Pathol** 9:655–667, 1989
- Laitinen L: Arteriella aneurysm med subarachnoidal-blodning hos barn. **Nord Med** 71:329–333, 1964
- Lam CH, Montes J, Farmer JP, et al: Traumatic aneurysm from shaken baby syndrome: case report. **Neurosurgery** 39:1252–1255, 1996
- Lang C, Jacobi G, Kreuz W, et al: Rapid development of giant aneurysm at the base of the brain in an 8-year-old boy with perinatal HIV infection. **Acta Histochem Suppl** 42:83–90, 1992
- Lasjaunias P, Wuppalapati S, Alvarez H, et al: Intracranial aneurysms in children aged under 15 years: review of 59 consecutive children with 75 aneurysms. **Childs Nerv Syst** 21:437–450, 2005
- Lee KS, Liu SS, Spetzler RF, et al: Intracranial mycotic aneurysm in an infant: report of a case. **Neurosurgery** 26:129–133, 1990
- Leung CH, Poon WS, Yu LM: The ISAT trial. **Lancet** 361:430–431, 2003
- Locksley HB, Sahs AL, Knowler L: Report on the cooperative study of intracranial aneurysms and subarachnoid hemorrhage. Section II. General survey of cases in the central registry and characteristics of the sample population. **J Neurosurg** 24:922–932, 1966
- Matson DD: Intracranial arterial aneurysms in childhood. **J Neurosurg** 23:578–583, 1965
- McDonald C, Korb M: Intracranial aneurysms. **Arch Neurol Psychiatry** 42:298–328, 1939
- Meyer FB, Sundt TM Jr, Fode NC, et al: Cerebral aneurysms in childhood and adolescence. **J Neurosurg** 70:420–425, 1989
- Mohr JP: The ISAT trial. **Lancet** 361:431, 2003

47. Molyneux A, Kerr R, Stratton I, et al: International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. **Lancet** **360**: 1267–1274, 2002
48. Molyneux AJ, Kerr RS, Yu LM, et al: International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. **Lancet** **366**:809–817, 2005
49. Moniz E: Anevrysme intra-cranien de la carotide inferne droite rendu visible par l'arteriographie cerebrale. **Rev Oto-Neuro-Ophthalmol** **11**:746–748, 1933
50. Noonan JA, Wilson CB, Spencer FC, et al: Cerebral and cardiac complications from bacterial endocarditis. A successfully managed case with unusual complications. **Am J Dis Child** **116**: 666–674, 1968
51. North-Coombes D, Schonland MM: Cerebral mycotic aneurysm. A case report. **S Afr Med J** **48**:1808–1810, 1974
52. Olivecrona H, Ladenheim J: **Congenital Arteriovenous Aneurysms of the Carotid and Vertebral Arterial Systems**. Berlin: Springer-Verlag, 1957
53. Ostergaard JR, Voldby B: Intracranial arterial aneurysms in children and adolescents. **J Neurosurg** **58**:832–837, 1983
54. Pasqualin A, Mazza C, Cavazzani P, et al: Intracranial aneurysms and subarachnoid hemorrhage in children and adolescents. **Childs Nerv Syst** **2**:185–190, 1986
55. Patel AN, Richardson AE: Ruptured intracranial aneurysms in the first two decades of life. A study of 58 patients. **J Neurosurg** **35**:571–576, 1971
56. Piastra M, Chiaretti A, Tortorolo L: Ruptured intracranial mycotic aneurysm presenting as cerebral haemorrhage in an infant: case report and review of the literature. **Childs Nerv Syst** **16**:190–193, 2000
57. Piatt JH Jr, Clunie DA: Intracranial arterial aneurysm due to birth trauma. Case report. **J Neurosurg** **77**:799–803, 1992
58. Pool J, Colton RP: The dissecting microscope for intracranial vascular surgery. **J Neurosurg** **25**:315–318, 1966
59. Quincke H: Ueber Lumbalpunktion. **Berl Klin Wochenschr** **32**:889–891, 1895
60. Ringertz HG, Brasch RC, Brody A, et al: Magnetic resonance imaging of vascular lesions in children. Assessment of flow patterns. **Acta Radiol Diagn (Stockh)** **25**:449–456, 1984
61. Rufenacht DA, Mandai S, Levrier O: Endovascular treatment of intracranial aneurysms. **AJNR Am J Neuroradiol** **17**: 1658–1660, 1996
62. Sade B, Mohr G: Critical appraisal of the International Subarachnoid Aneurysm Trial (ISAT). **Neurol India** **52**: 32–35, 2004
63. Sanai N, Quinones-Hinojosa A, Gupta NM, et al: Pediatric intracranial aneurysms: durability of treatment following microsurgical and endovascular management. **J Neurosurg** **104 (2 Suppl Pediatrics)**:82–89, 2006
64. Scialfa G, Valsecchi F, Scotti G: Treatment of vascular lesions with balloon catheters. **AJNR Am J Neuroradiol** **4**:395–398, 1983
65. Stehbens WE: Intracranial berry aneurysms in infancy. **Surg Neurol** **18**:58–60, 1982
66. Storrs BB, Humphreys RP, Hendrick EB, et al: Intracranial aneurysms in the pediatric age-group. **Childs Brain** **9**: 358–361, 1982
67. Strassman: Der plotzliche Tod bei Stenose des Isthmus Aortae. **Beitr gerichtl Med** **5**:91–97, 1922
68. Sugita K: **Microneurosurgical Atlas**. Berlin: Springer-Verlag, 1985
69. Sundt TM Jr: Neurovascular microsurgery. **World J Surg** **3**: 53–65, 127, 1979
70. terBrugge KG: Neurointerventional procedures in the pediatric age group. **Childs Nerv Syst** **15**:751–754, 1999
71. Tomsick TA, Tew JM Jr, Lukin RR, et al: Balloon catheters for aneurysms and fistulae. **Clin Neurosurg** **31**:135–164, 1983
72. Uzan M, Cantasdemir M, Seckin MS, et al: Traumatic intracranial carotid tree aneurysms. **Neurosurgery** **43**:1314–1320, 1998
73. Ventureyra EC, Higgins MJ: Traumatic intracranial aneurysms in childhood and adolescence. Case reports and review of the literature. **Childs Nerv Syst** **10**:361–379, 1994
74. Whitfield PC, Bullock R: Infected intracranial aneurysm in an infant: case report. **Neurosurgery** **28**:623–625, 1991
75. Yaşargil MG: **AVM of the Brain**. Stuttgart: Thieme, 1987, Vol IIIA
76. Yaşargil MG: **Microneurosurgery. Clinical Considerations, Surgery of the Intracranial Aneurysms and Results**. Stuttgart: Thieme, 1984, Vol II
77. Yazbak PA, McComb JG, Raffel C: Pediatric traumatic intracranial aneurysms. **Pediatr Neurosurg** **22**:15–19, 1995
78. Zee CS, Segall HD, McComb JG, et al: Intracranial arterial aneurysms in childhood: more recent considerations. **J Child Neurol** **1**:99–114, 1986
79. Zimmerman RA, Grossman RI, Goldberg HI, et al: Comparison of digital subtraction arteriography and conventional film screen subtraction arteriography for neuroradiology. **Neuroradiology** **26**:457–462, 1984

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