

## CHAPTER

# Nonsyndromic Craniosynostosis



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### INDICATIONS

*Craniosynostosis* refers to the premature fusion of one of the six major sutures of the craniofacial vault. Functionally, craniosynostosis may be defined as the premature conversion of a *dynamic* region of growth and resorption between two adjacent bones of the cranial vault into a *static* region of bony union. The final result is the formation of a single bony plate from two smaller segments. The term *craniostenosis* is used interchangeably but actually describes the consequences of craniosynostosis. The first description of the morphologic changes created by premature fusion was recorded by Hippocrates.<sup>60</sup> Galen<sup>91</sup> also described a patient with craniosynostosis and coined the term *oxycephaly*. Sommering<sup>86</sup> first recognized that skull growth occurred at the sutures and fusion of these "growth areas" would create a deformity. Subsequently, Virchow<sup>92</sup> initiated the use of the word *craniosynostosis* to describe the premature suture fusion and further established what is known as Virchow's law for compensatory cranial vault growth after suture fusion.

### CLASSIFICATION

Premature suture fusion may be characterized as described by Cohen.<sup>14</sup> Nonsyndromic, or isolated, craniosynostosis predominates and is defined as suture fusion that creates functional impairments related to local effects of the fusion, that is, intracranial hypertension or ophthalmoplegia. Occurrences are usually sporadic, but rare familial tendencies have been reported.<sup>32</sup> Furthermore, craniosynostosis in two members of the immediate family will increase the chance the next child will develop a premature suture fusion.<sup>70</sup> Craniosynostosis associated with craniofacial syndromes (e.g., Apert's syndrome, Crouzon's disease, Pfeiffer's syndrome) may be autosomal dominant or autosomal recessive and have second-

ary anomalies not directly associated with the suture fusion.<sup>15</sup> These may include the cardiovascular, genitourinary, or vertebral organs. Craniosynostosis may also be classified as simple (one suture) or complex (two or more sutures) and primary or secondary as a reflection of the underlying cause.

The most commonly affected nonsyndromic suture fusion usually involves the sagittal suture.<sup>63</sup> It is characterized by an increased anteroposterior position and decreased biparietal width (scaphocephaly). Presentation may be variable, but generally anterior sagittal fusion will present with significant frontal bossing; posterior sagittal fusion is characterized by an occipital bulge.

Coronal sutures may have unilateral (anterior plagiocephaly) or bilateral (brachiocephaly) involvement.<sup>70</sup> The primary dysmorphology involves the forehead and the supraorbital region, which includes the zygomatic process of the frontal bone (lateral orbital rims) and the temporal area. In unilateral coronal synostosis, the forehead is flattened and there is retrusion of the ipsilateral superior orbital rim. If both coronal sutures are involved, the lateral dimensions of the skull are widened and the superior orbital rim is displaced bilaterally. There may also be an associated increase in the height of the forehead (turriccephaly).

Trigonocephaly from metopic suture fusion is probably the most obvious deformity of the craniosynostoses. The occurrence is uncommon (7.9% to 10.0%),<sup>28,84</sup> and the presentation may range from a simple midline ridge to full expression, including a prominent keel-shaped forehead, bitemporal narrowing, and hypotelorism. Associated intracranial midline anomalies may also be seen in these patients.

Lambdoid sutures are paired and may be involved unilaterally or bilaterally. The subsequent deformity is often referred to as an occipital or posterior plagiocephaly and posterior brachiocephaly, respectively. The deformity usually occurs on the right side and may have compensatory bossing of the contralateral anterior skull. Bilateral involvement is characterized by a widened biparietal width and occipital flattening.

Vertex elongation is present in both unilateral and bilateral suture fusions. Lambdoid suture fusion must be differentiated from deformational plagiocephaly, which also presents with a flattened occiput. True lambdoid synostosis is extremely rare, with reports being 1% to 2% of all craniosynostoses.<sup>90</sup>

### Plagiocephaly without Synostosis

Craniosynostosis should be differentiated from plagiocephaly resulting from external forces on an otherwise normal cranial vault complex. Often called *deformational plagiocephaly*, or *plagiocephaly without synostosis* (PWS), shaping of the skull may come from intrauterine constraint and/or postnatal positioning.<sup>43</sup> The incidence has been cited as being as low as one in 300 births<sup>11</sup> to as high as 48% of otherwise healthy newborns.<sup>6</sup> Postnatal forces may come from supine positioning favoring one side or mild flattening of the occiput during birth, which is accentuated in the supine position from head turning by force of gravity.<sup>79</sup> Muscular torticollis, a fixed head position from vertebral malformations,<sup>49,101</sup> and extraocular motor dysfunction<sup>35</sup> have also been related to plagiocephaly.

Deformational plagiocephaly is uniquely different from craniosynostosis-induced plagiocephaly and may be determined by the physical examination. Frontal examination of the patient with deformational plagiocephaly reveals retrusion of the ipsilateral frontal bone and superior orbit with a narrow palpebral fissure, lower eyebrows, angulation of the nasal root, and a slightly inferior position of the ipsilateral ear. There is bossing of the contralateral frontal area. The vertex view demonstrates a "pushed" posterior position of the ipsilateral chin and ear associated with a parallelogram shape of the skull.

Unilateral coronal craniosynostosis is characterized by a widened palpebral fissure and a superiorly placed eyebrow and supraorbital rim. The ipsilateral ear may be higher, and the nasal root is deviated to the flattened side. The vertex view demonstrates a trapezoid shape to the skull and an anterior displacement of the chin and ear.

### NORMAL DEVELOPMENT AND ANATOMY

Sites of suture formation in the neurocranium are thought to be determined by dural reflections.<sup>85</sup> Cranial bone expands from intramembranous ossification centers within a fibrous membrane called the *ectomeninx*. The leading edge of these bone plates, referred to as osteogenic fronts, contains a wedge-shaped proliferation of osteoprogenitor cells.<sup>22</sup> A syndesmosis (no interposing cartilage) is formed through apposition of these bony plates. In contrast, a synchondrosis, which contains a cartilage interposition, is seen in cranial base sutures.<sup>21</sup>

A suture contains the leading edge of the bony plates and the intervening radiolucent fibrous tissue. Five distinct layers of the cranial suture were identified by Pritchard<sup>74</sup> and include two cambial and two capsular layers of the periosteum with a middle vascular layer. The interposed fibrous tissue between the bony fronts has been shown to contain collagen types I, III, and V,<sup>13</sup> fibronectin, osteoprogenitor cells, and osteonectin.<sup>33</sup>

The bony edges may approximate in an end-to-end relationship, as seen in the midline sagittal and metopic sutures, or overlap, as seen in the coronal, lambdoid, sphenozygomatic, and squamosal sutures. Initially all the bone edges are smooth,<sup>42</sup> but as the time of suture patency increases, the number of interdigitations also increases.<sup>46</sup> Studies have not demonstrated an association between the number of interdigitations and the onset of suture fusion. Facial sutures formed in the absence of dura have different developmental and growth patterns from those seen in sutures of the cranial vault.<sup>68,74</sup>

Cranial vault sutures usually close in early adult life, with the exception of the metopic suture, which begins to close at age 2.<sup>13</sup> Initial bone bridging is usually seen on the endocranial surface, although it can also begin on the ectocranium.<sup>58</sup> There is a single focus of suture fusion that may occur anywhere along the course of the suture and is especially true for the sagittal suture.<sup>1</sup> In contrast, metopic suture fusion progresses from inferior to superior.<sup>50</sup> During suture fusion, there is a zone of osseous obliteration characterized by nonlamellar bone across the preexisting suture. As one progresses away from the site of fusion, an area of both connective tissue and osseous union exists, followed by areas of thinned connective tissue (impending suture fusion) and, eventually, an area of uninvolved sutures with normal-appearing connective tissue.<sup>45</sup>

### PATHOGENESIS

The specific cause of premature suture fusion is unclear and may be multifactorial. Nonsyndromic suture fusion may be related to extrinsic causes, such as metabolic disorders (e.g., vitamin D deficiency, hyperthyroidism) or brain malformations (e.g., microcephaly, encephalocele, corrected hydrocephalus). Chromosomal abnormalities and exposure to teratogens (e.g., aminopterin, diphenylhydantoin, retinoic acid, valproic acid) are usually associated with syndromic fusion (Box 47-1).<sup>16</sup>

Three general theories of the pathogenesis of craniosynostosis have been described. Virchow<sup>92</sup> suggested that the primary abnormality was localized to the affected suture and translated to the cranial base. Moss<sup>61</sup> theorized that the cranial base was the source of the pathogenesis. Tension translated from the cranial base to the cranial vault sutures (presumably by the dura) cause a premature fusion of the suture. Finally, Park and Powers<sup>66</sup> suggested that the defect was secondary to an abnormality in the local mesenchymal blastema. It is important to understand that the latter theory of mesenchymal cell dysfunction does not stand in conflict with the initial two theories. The pathology, as proposed by Moss and Virchow, reflects the initial *site* of abnormal growth, not the primary *cause* of the abnormality.

The biochemical activities at the cellular and molecular levels are not well understood, but some possible mechanisms have been suggested. The predominant cell type in fused sutures has been found to be osteoprogenitor cells.<sup>27</sup> The dura in proximity to the suture is necessary to maintain pa-

### Box 47-1. Known Causes of Craniosynostosis

Monogenic conditions  
 Chromosomal syndromes  
 Metabolic disorders  
   Hyperthyroidism  
   Rickets  
 Mucopolysaccharidoses  
   Hurler's syndrome  
   Morquio's syndrome  
    $\beta$ -Glucuronidase deficiency  
 Mucopolipidoses  
   Mucopolipidosis III  
 Hematologic disorders  
   Thalassemias  
   Sickle cell anemia  
   Congenital hemolytic icterus  
   Polycythemia vera  
 Teratogens  
   Aminopterin  
   Diphenylhydantoin  
   Retinoic acid  
   Valproic acid  
 Malformations  
   Microcephaly  
   Encephalocele  
   Shunted hydrocephalus  
   Holoprosencephaly

From Cohen MM: *Craniosynostosis: diagnosis, evaluation and management*, New York, 1986, Raven Press.

teny.<sup>36,64</sup> Growth factors have been suggested as a regulator of osteogenesis and may be temporally and spatially specific to this task.<sup>53,80</sup> Recently, cells at sites of active suture fusion have demonstrated "programmed" cell death, or apoptosis.<sup>29,87</sup> Controlled cell death may be an avenue of normal suture fusion that is misregulated at a gene level in craniosynostosis. Finally, Cohen<sup>13</sup> has suggested that a migration of osteoprecursor cells may occur at suture sites, causing a fusion to occur prematurely.

### MORPHOGENESIS

In 1851, Virchow<sup>92</sup> described the principle that growth is restricted in the plane parallel to the prematurely fused suture. This explanation was challenged by Moss<sup>61</sup> based on observations that abnormal skull shapes occur in the absence of suture fusion and that cranial vault suture fusion was often associated with a cranial base deformity. He concluded that the initiating event for premature suture fusion was an abnormality in the cranial base. He also expanded the concept that the approximating soft tissue plays an active role in the shape and size of the associated bone. In light of these principles, Delashaw et al<sup>23</sup> outlined four components of compensatory cranial

vault growth that more fully explain morphologic findings seen clinically.

With the assumption that sutural edges may have asymmetric growth activities, they proposed the following:

1. Cranial vault bones that are prematurely fused act as a single bone plate with decreased growth potential.
2. Abnormal asymmetric bone deposition occurs at perimeter sutures with increased bone deposition directed away from the bone plate.
3. Perimeter sutures adjacent to the prematurely fused suture compensate in growth more than perimeter sutures distant to the sutural stenosis.
4. A nonperimeter suture that is contiguous to the prematurely fused suture undergoes enhanced symmetric bone deposition along both edges.

These four principles of cranial vault restriction and compensation have been supported by clinical findings in nonsyndromic craniosynostosis.

### POTENTIAL FUNCTIONAL COMPLICATIONS

Functional disability is an ill-fitting term in plastic surgery, especially in the area of craniofacial abnormalities. It not only includes anatomically related disabilities but should also incorporate psychologic and developmental issues. In isolated craniosynostosis, concerns related to exorbitism; speech; and associated neurologic anomalies, such as hydrocephalus and Chiari's malformations, may be minimal.

### Intracranial Hypertension

The primary concern with premature suture fusion relates to brain growth. The brain volume of the infant increases twofold by age 1 and threefold by age 3. This rapid brain growth is paralleled by an equally rapid accommodating increase in the size of the cranial vault (Table 47-1). The major functional problem associated with restrictive craniostenosis is the development of increased intracranial pressure (ICP). Elevated ICP may manifest in two forms. The first is the well-recognized global increase in ICP subsequent to a restrictive cranium. Late radiographic signs may include "fingerprinting" or "copper beating" of the endocranial surface or loss of the cisternae on two-dimensional CT scans. If severe and untreated, intracranial hypertension can translate to the optic nerve with development of papilledema; nerve ischemia; and, eventually, optic atrophy.

Elevated ICP may also occur transiently and be limited to a region of the brain near the fused suture. Focal regions of pressure and ischemia associated with areas of suture fusion have been identified using technetium 99 cerebral flow studies.<sup>82</sup> Focal hypertension probably has less dramatic consequences than are seen with overt elevations in ICP, but the effects may correlate more with long-term brain function, such as mental development, learning disabilities, and intelligence quotients.

Aside from the potential for optic atrophy, some forms of craniosynostosis may lead to other ocular disturbances. A

**Table 47-1.**  
**Cranial and Brain Growth during the First**  
**20 Years of Life**

AGE	VOLUME OF BRAIN (cm <sup>3</sup> )	CRANIAL CAPACITY (cm <sup>3</sup> )
Newborn	330	350
3 mo	550	600
6 mo	575	775
9 mo	675	925
1 yr	750	1000
2 yr	900	1100
3 yr	960	1225
4 yr	1000	1300
6 yr	1060	1350
9 yr	1100	1400
12 yr	1150	1450
20 yr	1200	1500

From Blinkov SM, Glezer II: *The human brain in figures and tables: a quantitative handbook*, New York, 1968, Plenum Press and Basic Books.

significant decrease in the volume of the orbit may cause exorbitism and subsequent corneal abrasions from exposure. Likewise, suture fusion associated with orbital hypertelorism may cause restricted binocular vision. The most common intrinsic ophthalmoplegia associated with coronal synostosis is either a divergent or convergent nonparalytic strabismus or exotropia. This is related to the misshapen orbital roof and subsequent malalignment of the extraocular muscles.

## CONSENT

The importance of informed consent for any procedure has been well established (Figure 47-1). It does not relieve any physician of responsibility, but it does provide a format for discussing aspects of the procedure, including potential complications and the magnitude of the surgery. Specific complications related to corrective surgery are discussed in this chapter. The parents or legal guardians should be aware of the potential for blood transfusions and provide donor-directed blood, if possible. Complications associated with the intracranial components of the procedure should also be discussed in conjunction with the neurosurgeon. A lumbar drain may be necessary if there is potential for dural compromise (for instance, during a reoperation) or evidence of elevated ICP and should be included in the preoperative review. Finally, the

expected scar, postoperative course (including recovery period in the intensive care unit), and potential donor sites should be discussed.

## OPERATIONS

The first recorded surgical approach for craniosynostosis was performed by Lannelongue<sup>48</sup> in 1890 and Lane<sup>47</sup> in 1892, who completed strip craniectomies of fused sutures. The classic neurosurgical techniques developed over the ensuing decades were geared toward resecting the synostotic suture. It was thought that a new suture line would be created that would permit normalization of the cranial vault as further growth occurred. With the realization that this goal was rarely achieved, attempts were made to further fragment the cranial vault surgically, replacing the bone as autogenous grafts that would improve preoperative cranial shape. Uncontrolled postoperative skull molding during the healing process often resulted in skull distortions. Skull reossification by the technique of calvarectomy and morcellation was found to be unpredictable and associated with substantial residual cranial vault deformity.<sup>71</sup> In 1967, Tessier<sup>88</sup> described a new approach to the management of Crouzon's disease and Apert's syndrome. His landmark presentation and publications were the beginning of modern craniofacial surgery. Tessier combines an intracranial-extracranial approach with the use of a coronal incision, extensive periorbital subperiosteal dissection, autogenous bone grafting, and ingenious osteotomies. The concept of calvarial suture resection combined with skull reshaping in infancy was later pioneered by Hoffman,<sup>37</sup> Whitaker,<sup>98</sup> and Marchac.<sup>51</sup> Hoffman<sup>37</sup> reported lateral canthal advancement of the supraorbital margin as a new corrective technique in the treatment of coronal synostosis in 1976. This heralded reports by Whitaker<sup>98</sup> in 1977 and the classic article by Marchac and Renier,<sup>51</sup> which presented the floating forehead technique combined with frontoorbital advancement.

It has become accepted clinical practice with patients with nonsyndromic and single-suture craniosynostosis for clinicians to perform the primary operative procedure—frontoorbital advancement with cranial vault remodeling—at an early age to improve craniofacial form and function and lead to satisfactory long-term growth and development of the calvaria. Our current approach to single-suture and nonsyndromic craniosynostosis varies with the underlying sutural fusion. In general, once a diagnosis has been established by physical examination and appropriate radiologic studies, a surgical treatment plan is recommended. It is critical that children undergo multidisciplinary evaluation by a craniofacial team. The team geneticist rules out associated abnormalities that can occur to a greater or lesser proportion in a number of craniosynostosis patients. In children with bicoronal synostosis, it is especially important to rule out syndromic involvement because this will not always be

