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# Prenatal Imaging of Craniosynostosis Syndromes

Pamela Deaver Ketwaroo, MD,* Caroline D. Robson, MB, ChB,*
and Judy A. Estroff, MD*,†

**This article reviews the prenatal diagnosis of those syndromes in which craniosynostosis is a key feature. Although not an exhaustive list, the authors highlight conditions that may be encountered with some regularity, especially in a higher volume fetal imaging center. Rare conditions are also discussed. Normal sutural anatomy and development are first reviewed, followed by a discussion of specific syndromes, the salient imaging findings, and pathologic as well as postnatal correlations when possible.**
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## Introduction

First described by Virchow[1] in 1851, craniosynostosis is defined as the premature fusion of the cranial sutures, which often leads to characteristic abnormal morphologies of the pediatric cranium. Though craniosynostosis is a feature of many syndromes, single sutural synostosis is most commonly an isolated, nonsyndromic finding.[2] Some of these nonsyndromic patients may have an underlying genetic etiology for their phenotype.[3] There may be overlap in the appearance of multisutural synsotosis among different syndromes, though characteristic associated hand dysmorphology may help distinguish one from the other. When distinctive features are present, an eponymous syndromic diagnosis may be possible even prenatally, though this is not always the case.

Craniosynostosis syndromes can be evaluated in fetal life by both sonography and magnetic resonance imaging (MRI). MRI provides complementary information to fetal sonography and is of great value for fetuses with syndromic craniosynostosis. Fetal MRI in such patients may reveal concomitant structural abnormalities of the face and brain that affect prenatal counseling. Though sonography has the advantage of being dynamic, it may be hindered by maternal body habitus, operator experience, oligohydramnios, fetal head position, or shadowing from the fetal skull. Prenatal diagnosis of craniosynostosis syndromes is especially important given the risk for perinatal distress in a newborn with multisutural synostosis, including feeding intolerance, airway compromise, lack of eye protection in patients with exorbitism, and elevated intracranial pressure.

## Normal Sutural Anatomy and Embryology

Cranial sutures are interruptions of calvarial bone by undifferentiated mesenchyme, which is composed of proliferative osteoprogenitor cells.[4] These osteoprogenitor cells transform into osteoblasts and lay down osteoid, allowing the sutures to eventually fuse at the appropriate developmental time. Depending on the circumstances, the normal suture edges may slightly overlap one another without the development of suture fusion. This process of growth, suture overlap, and ultimately fusion is tightly regulated by a variety of genes, including several in the fibroblast growth factor receptor (FGFR) family.

The "major" calvarial sutures can be loosely defined as inclusive of the sagittal, coronal, and lambdoid sutures (Fig. 1). Some authors would also include the metopic suture in this list of "major" sutures. The maintenance of open sutures allows for normal growth and development of the skull and face, with premature fusion resulting not only in cosmetic deformity but also restricted brain growth.[5]

The calvarial and craniofacial sutures vary greatly in appearance over the span of one's life, many of them not

*Department of Radiology, Boston Children's Hospital, Harvard Medical School, Boston, MA.
†Advanced Fetal Care Center, Boston Children's Hospital, Harvard Medical School, Boston, MA.
Address reprint requests to Pamela Deaver Ketwaroo, MD, Department of Radiology, Boston Children's Hospital, 300 Longwood Ave Boston, MA 02115. E-mail: pamela.ketwaroo@gmail.com

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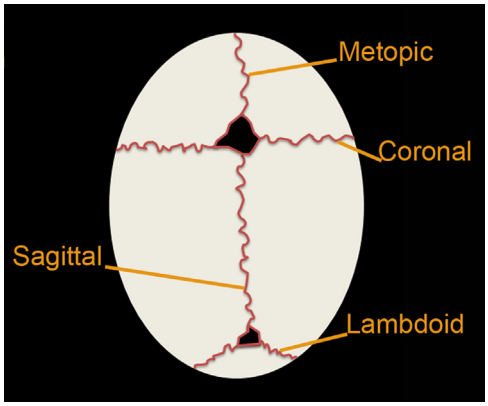


**Figure 1** Axial rendition of the normally occurring major calvarial sutures. (Color version of figure is available online.)

normally fusing until well into adulthood. The notable exception to this fusion in adulthood is the metopic suture, which typically fuses between 3 and 9 months of age.[6] Premature fusion of the metopic suture produces a characteristic narrowed and pointed forehead, known as trigonocephaly, which can be readily detected on prenatal imaging (Figs. 2D and 3).

## Syndromic vs Nonsyndromic Craniosynostosis

Approximately 85% of patients with craniosynostosis do not have other organ system malformations and tend to involve a single suture. Thus, they are categorized as "nonsyndromic" craniosynostosis.[2] By contrast, the less common "syndromic" craniosynostoses, which have a propensity for multisutural involvement and therefore often more severe phenotypic manifestations, are more likely to be diagnosed prenatally than those with isolated nonsyndromic synostosis. Despite the fact that most of the craniosynotosis syndromes have autosomal dominant inheritance, sporadic mutations account for many of the unsuspected de novo prenatal cases.

Genes that most commonly play a role in the pathogenesis of both syndromic and nonsyndromic craniosynostosis are *FGFR-2* (32%), *FGFR-3* (25%), *TWIST* (19%), and *EFNB-1* (7%), though less common mutations are increasingly being recognized as well.[4,7,8] Not surprisingly, these are the same genes responsible for regulation of normal sutural fusion. It should also be noted that there is a familial propensity, even for single sutural (nonsyndromic) craniosynostosis, with siblings of an affected child having approximately double the estimated

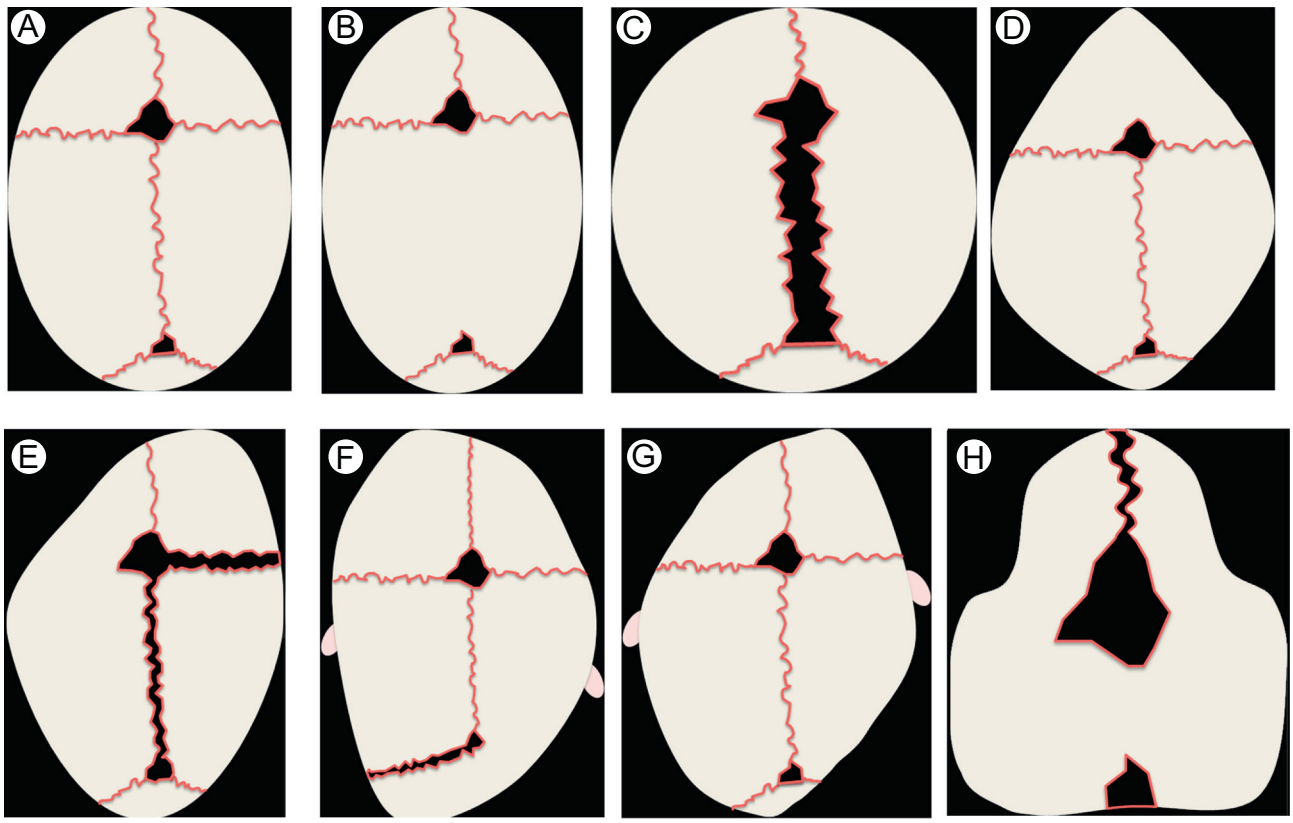


**Figure 2** Characteristic calvarial morphologies as viewed from above, as would be seen in the course of a typical fetal ultrasound or MRI. With the exception of positional plagiocephaly, detection of one of these calvarial morphologies in the fetus is always abnormal and should raise suspicion for craniosynostosis. (A) Normocephalic, no synostosis present. (B) Scaphocephaly or Dolichocephaly, sagittal synostosis. (C) Brachycephaly, bicoronal synostosis. (D) Trigonocephaly, metopic synostosis. (E) Anterior plagiocephaly, unicoronal synostosis. (F) Posterior plagiocephaly, unilambdoid synostosis. (G) Positional plagiocephaly, no synostosis present. (H) Kleeblattschädel, multisutural synostosis. (Color version of figure is available online.)