# Original Articles

# Interaction of Craniofacial Dysmorphology, Growth, and Prediction of Surgical Outcome

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**Craniofacial surgery is a multidisciplinary specialty that often uses the expertise of many specialists including surgeons, orthodontists, geneticists, and anthropologists. The clinical experience gained by their collaboration enables predictions to be made of the ultimate success of the reconstructive surgery. Various patterns among surgical outcomes are noted as greater experience is gained. These observations prompted the following questions: Is there a way to classify patients according to surgical results? What factors underlie a successful response to surgery? In a clinical setting, we are faced with a spectrum of presentations of craniofacial dysmorphology. We propose that the results of surgical correction may be based on the cause of the condition and not necessarily on the degree or character of the dysmorphology. Craniofacial dysmorphologies are often grouped under the terms *deformation, malformation, disruption, dysplasia,* or *syndrome.* Our hypothesis is that a categorization of craniofacial dysmorphology can be proposed on the basis of the response of the individual to surgery. We propose that such a classification reflects real differences in cause. A poor response to surgery reflects a condition that includes a growth disorder. Alternatively, cases that respond best to surgery are those in which the growth process is not affected. In the latter cases, a dysmorphic face is surgically transformed into an acceptable morphology, and normative growth vectors maintain or improve postoperative facial appearance. It is our belief that the physiological differences underlying our categorization scheme have to do with embryological timing of insults or specific components of the ontogenic process. The divergence in the response to surgery among patients relates directly to the role of the growth process in the various types of dysmorphologies.**

*Key Words:* Craniofacial dysmorphology, growth-based classification, morphotype, growth disorders

In an active craniofacial center, the spectrum of cases presented for reconstruction reflects myriad surgical challenges. Evaluation of the success of these complex corrections is based on the final aesthetic and functional results. Clinicians and surgeons will often evaluate each patient preoperatively and assess the potential success of the desired surgical reconstruction. This prediction is often based primarily on clinical experience. This article represents our attempt to answer the following questions that relate to these judgments: Is there a way of classifying patients to predict the likelihood of a successful functional outcome and a pleasing aesthetic result? What are the factors that underlie the ability to predict the response to surgery [1-6]? Can we use this information to improve patient treatment and further understand the conditions that we treat?

Craniofacial surgeons, orthodontists, geneticists, anthropologists, and other research scientists who work with clinical populations gain experience that allows both the characterization of morphotypes for diagnostic categories and the prediction of the success of reconstructive surgery for these morphotypes. Studies conducted by other scientists and centers [1, 3, 5] and the realization of our own intuitions of how children will progress postoperatively prompted the proposal of a new classification scheme for craniofacial dysmorphology. In this article, we present the foundation of this classification along with examples of its use in the management of craniofacial patients. Our initial ideas are presented in the hope that others will add their insights to our proposed scheme in future work.

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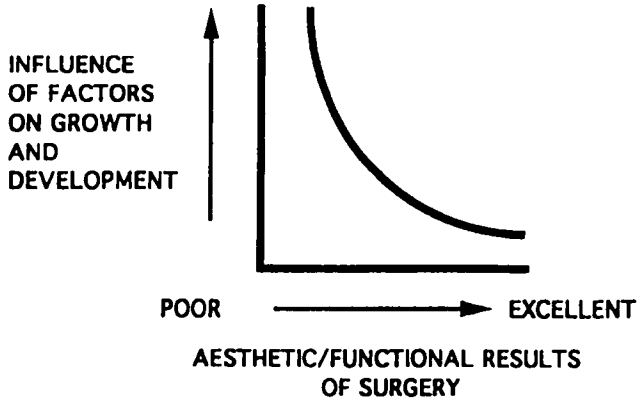



**Fig 1** The aesthetic and functional results of reconstructive surgery are inversely related to the number of factors affecting growth and development. The ultimate results of surgical intervention will be determined not only by whether the physiological components are the result of developmental insults during early embryological events, include the histogenic process, or affect organ development, but by whether or not the insult changes the postnatal craniofacial pattern of growth from normal to abnormal.

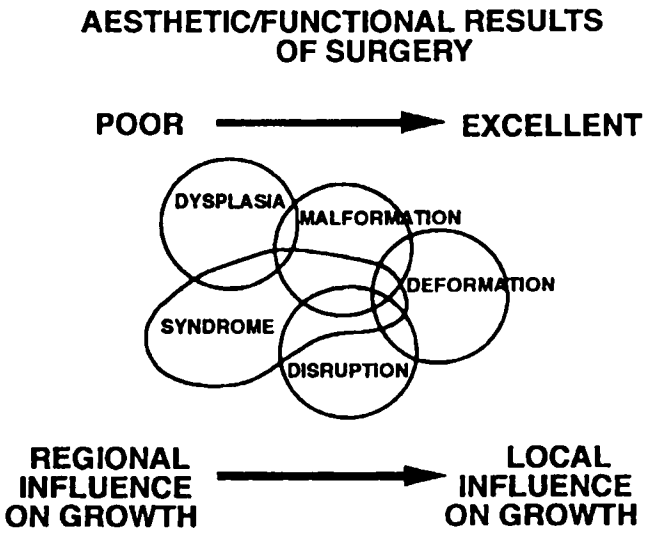



**Fig 2** Graphic representation of our emergent classification system. The greater the regional influence or intrinsic tissue abnormalities, the more severe is the influence and less acceptable is the result of surgical intervention. It should be understood that a syndrome can contain features of the other subgroups, as demonstrated by the overlapping into these conditions.

### Classification Based on Growth

In our view, just as there is a spectrum of severity of craniofacial dysmorphology, there exists a spectrum of responses to surgical manipulation and reconstruction [3]. The long-term results of each surgical procedure fall within two ends of the spectrum: those who present with an improved craniofacial morphology postoperatively and those who show little or no improvement (Fig 1) [1, 4–6]. Our hypothesis is that a categorization of cases on the basis of response to surgery reflects very real differences in the disease process underlying these conditions. In short, the response of a patient to reconstructive surgery may provide information about the cause of the condition.

According to this classification system, patients who do not respond well to surgery exhibit a condition that includes a fundamental disorder that directly involves the growth process [2, 3, 6]. Although the exact cause and pathophysiology of the condition may have to do with the way cells or tissues, or both, interact (or fail to do so), what we refer to as a "growth disorder" is not necessarily limited to those conditions identified by histological or other enduring properties. Instead, the initial error may lie in the organ-specific morphogenetic interactions of groups of cells according to specified processes and signals during morphogenesis [7]. This first error may initiate a cascade of events [8] that precludes normal growth patterns. Cellular activity may or may not be normal. In these children, surgery may improve the immediate postoperative appearance, but with time, continued patterns of maldevelopment result in a poor long-term response to surgery. On the other hand, patients who respond well to surgery present with conditions that do not involve a persistent growth disorder. In these cases, a primary insult may have involved the growth process, but the condition does not persist as a growth disorder. The surgeon can, therefore, contour the face and skull into an acceptable morphology and alignment in these patients. The "normalized" growth patterns should maintain or improve the postoperative form and appearance [1–3, 5, 6, 9–11].

We propose that those children who display an improved craniofacial appearance postoperatively exhibit a condition that does not involve the growth process, or the involvement is transient and extremely localized (i.e., the insult is targeted at a particular region for a finite period of time). The initial causes of the conditions may be consistent with the idea of a growth disorder because their initiation may have a direct effect on early development processes. However, the resulting anomalies are not defined by a generalized abnormal growth pattern. Those children whose appearance does not improve with surgery exhibit a morphological condition that directly involves the process of growth. These so-called growth disorders are initiated early, probably during embryogenesis, and the pattern of maldevelopment continues postnatally.

We have taken definitions of general classes of conditions given by several sources [7, 12–16] and arranged them to illustrate the principles of our emergent classification system (Fig 2). There are three types of anomalies: deformations, malformations, and disruptions [13–15]. A

deformation is defined as abnormal form, shape, or position of a body part caused by mechanical forces [7]. A malformation is a morphological defect resulting from an intrinsically abnormal developmental process [13]. A disruption is a morphological defect resulting from a breakdown of, or interference with, an originally normal developmental process [13]. Deformation, malformation, or disruption sequences are defined on the basis of the initial known (or presumed) structural defect that initiates a chain of subsequent defects. The concept of dysplasia is invoked in the study of craniofacial dysmorphology because of the important determinative function of neural crest cells [7, 17–19]. Opitz [7] defined dysplasias as abnormalities of cellular or tissue differentiation and malformations as abnormalities of organogenesis. This distinction may not always be clear-cut; hence, we show overlap between these categories in Figure 2. Finally, syndromes are causally homogeneous complexes of anomalies in one individual that cannot be explained on the basis of a single, initiating defect and its consequences but appear to be the consequence of multiple defects in one or more tissues. As shown in the diagram, syndromes can contain dysplasias and one or more of the other types of anomalies.

To present more thoroughly our ideas on this new classification scheme of craniofacial disorders, the following examples are presented.

## Clinical Presentations

***Deformations*** are conspicuous, extrinsic phenomena in which the surrounding tissues are relatively normal but are distorted and displaced. Surgical correction of localized deformations can result in a satisfactory immediate postoperative appearance. As time passes, acceptable facial appearance is maintained and continues to improve as a result of the contribution of normal growth vectors. The degree of postoperative improvement tends to increase if the patient is relatively young. This is due to an increased period of time for normal growth patterns to contribute to the eventual morphology. One example of a deformation is shown in Figure 3.

An additional example of a deformation occurring postnatally with regional instead of local consequences involves extensive multiple-suture secondary craniosynostosis (Fig 4). This child was born with severe congenital hydrocephaly. A low-pressure ventricular-peritoneal shunt was placed shortly after birth. After 18 hours, the cranium and ventricals were decompressed so dramatically and rapidly that the cranial bones settled in a position overlapping each other. The sutures eventually fused, resulting in an iatrogenic secondary craniosynostosis. Repair required release of these sutures, frontoparietal and occipital osteotomies with expansion, and replacement of the shunt for a higher intracranial pressure valve. This resulted in the eventual normal contouring of the skull. In this case, the hydrocephalus and secondary synostosis were severe and the morphological affects were global, involving multiple regions. However, because the conditions did not involve or affect craniofacial growth processes, the child responded favorably to reconstructive surgery. It appears that normal vectors of growth contribute to the long-term postoperative results. There has been no growth disorder in this case.

***Dysplasia*** is an abnormality of cellular or tissue differentiation [7, 12]. (Cohen [13] used the term *dyshistogenesis* to describe the same phenomenon.) Opitz [7] pointed out precisely that the properties of mature organ-specific cells may be histologically normal in cases of dysplasia and that the consequential abnormality has occurred earlier during the critical timing of morphogenetic interaction of tissues. As an example of a dysplasia we present a regional, intrinsic anomaly resulting from a frontal lobe teratoma in Figure 5. Associated features include orbital hypertelorism and duplicated metopic cranial sutures. The immediate postoperative appearance is good; however, as time progresses the facial morphological appearance worsens. We suggest that the degeneration in appearance is the result of abnormal regional growth patterns associated with the formation of the teratoma and duplication of related structures such as the metopic cranial sutures. This case also points to the inverse relationship between proximity of a craniofacial feature to the dysplasia and quality of long-term postoperative appearance of that feature (i.e., craniofacial features that are situated relatively close to the dysplasia show a greater degree of abnormality in tissue type and growth pattern).

***Malformations*** are abnormalities of organogenesis [7]. Opitz [7] divided malformation into primary and secondary forms. A primary malformation represents an intrinsic abnormality *of* a developmental field, whereas a secondary malformation (disruption) represents an extrinsic abnormality *in* a developmental field. The developmental fields are morphologically reactive units of the embryo that affect organogenesis in spatially and temporally coordinated ways and in an epimorphically hierarchal manner through processes of determination, induction, and differentiation [7]. As the extent of the disruption spreads from local to regional, surgical correction becomes less predictable and less attainable (see Fig 2).

Finally, a ***syndrome*** is a causally homogeneous complex of anomalies [7]. Because more than one anomaly is involved, syndromes present a number of challenges for the reconstructive surgeon. Many syndromes are defined as a group of anomalies that share a developmental history. Damage to an embryonic structure causes defects among those structures derived from the embryonic source. For example, patients with Treacher Collins syndrome exhibit similar maxillary and mandibular dysmorphology (Fig 6). This syndrome is a condition of

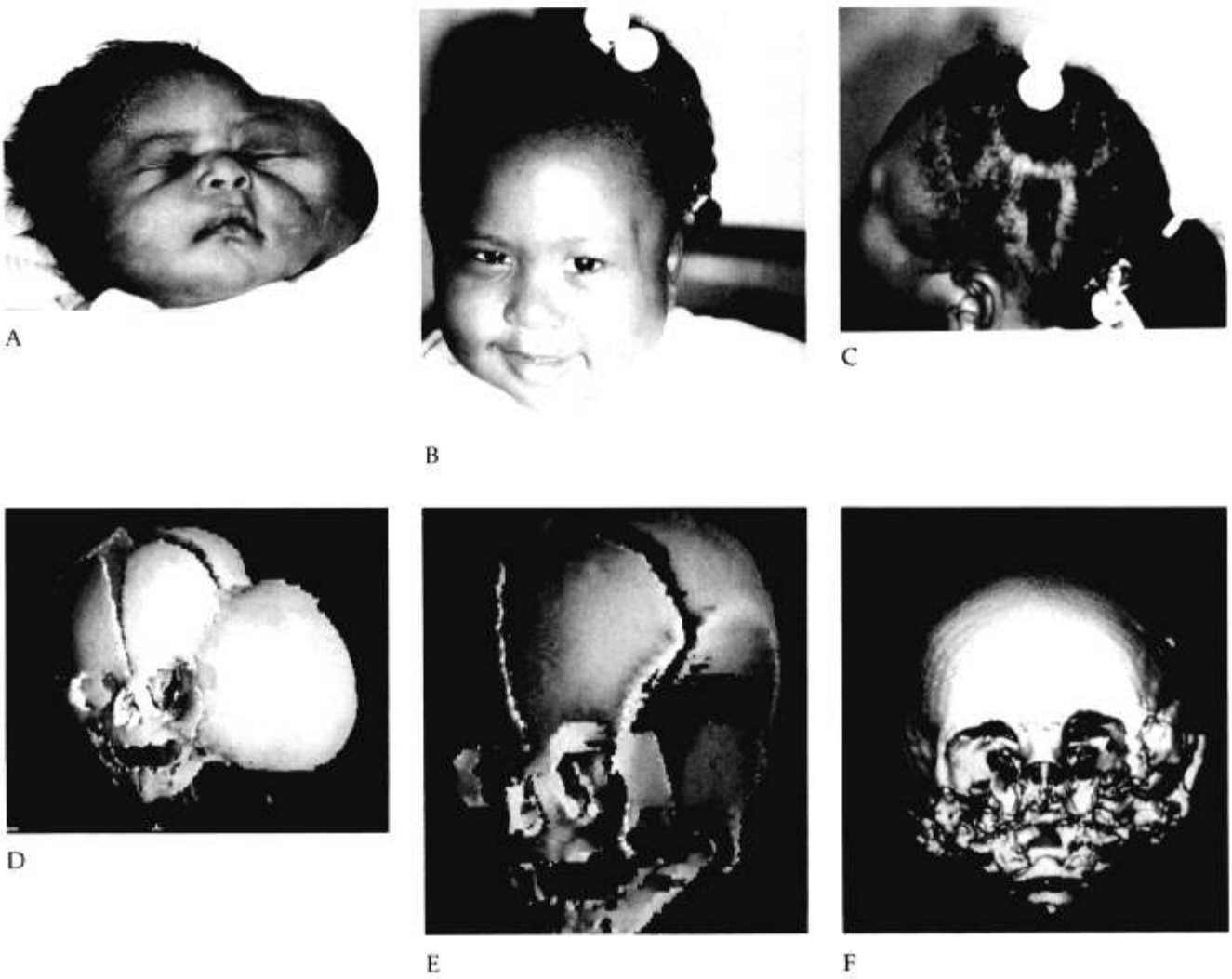



**Fig 3** This case demonstrates a deformation (i.e., an abnormal cranial shape resulting from mechanical force). The lateral meningocele in this patient greatly distorts the soft tissue (A) and craniofacial skeleton (D, E). This process is largely localized and extrinsic, with the surrounding tissues being relatively normal but displaced. Very satisfactory results are obtained by the removal of the meningocele and letting the normal growth and development take place as predicted, having been released from the extrinsic force (B, C, F).

bilateral craniofacial abnormalities of structures derived from the first and second branchial arches. For this reason, it is described as a disorder of craniofacial development [20–22]. Because the postoperative appearance of Treacher Collins syndrome patients is rarely satisfactory (and can degenerate with time secondary to surgical intervention and bone grafting), we believe that a developmental abnormality initiates the syndrome and abnormal growth patterns maintain the abnormal morphology. This is further supported by the application of bone distraction techniques to the Treacher Collins mandible in which existing bone tissue may be distracted and generate new bone; however, the growth pattern of that new bone will not be normal.

Children who exhibit craniosynostosis as part of a syndrome (e.g., Crouzon's syndrome and Apert's syndrome) rarely appear craniofacially normal postoperatively, and their appearance may degenerate or worsen with time. In these cases, the synostosis is part of a syndrome that incorporates a growth disorder, or the syndrome is the result of an insult so global that no amount of reconstructive surgery can ever establish a

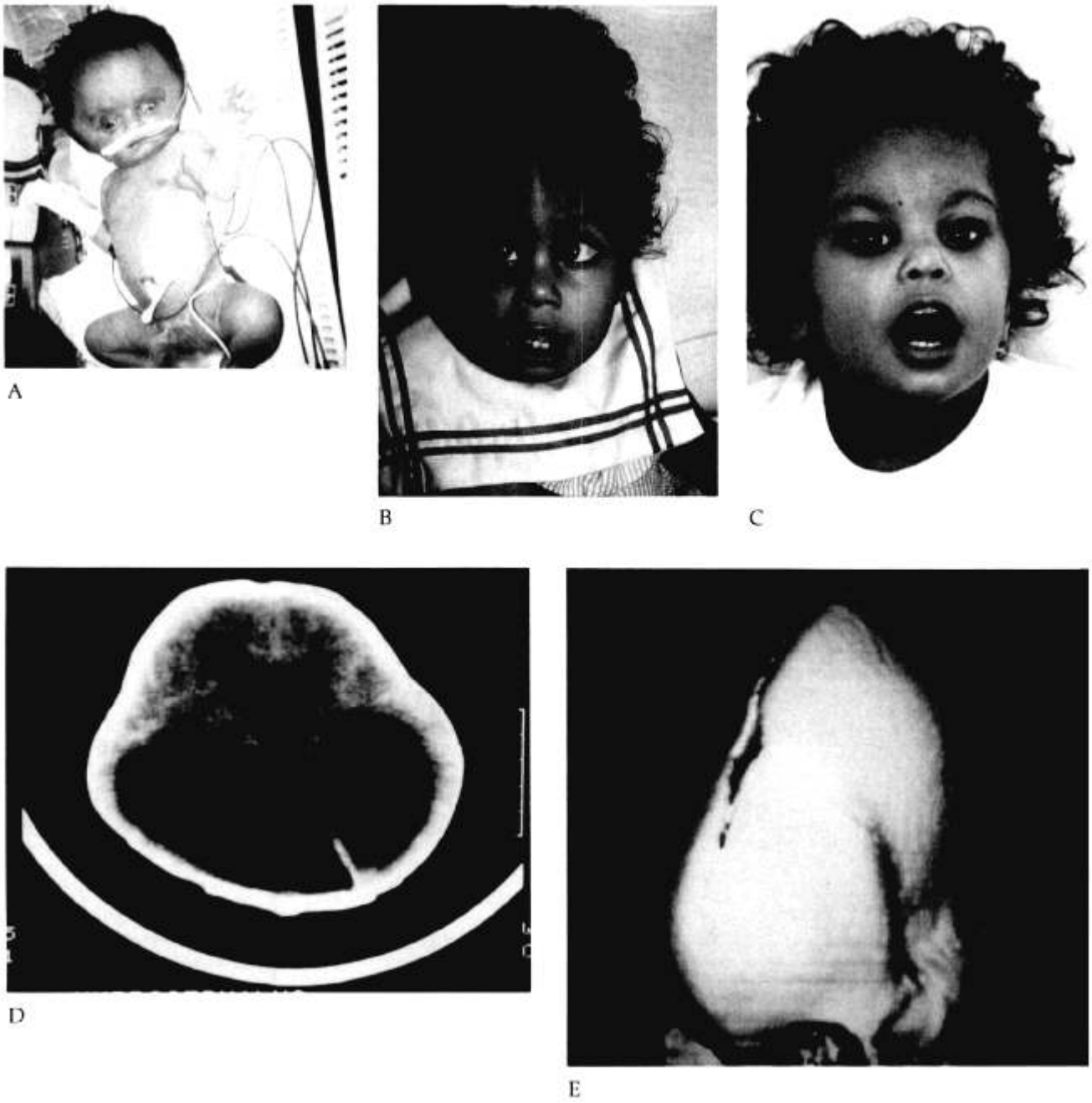



**Fig 4** This young infant was born with massive congenital hydrocephalus requiring emergency low-pressure ventricular-peritoneal (V-P) shunt placement shortly after birth (A). A computed tomographic (CT) scan performed at 1 day of age (D) reveals the greatly enlarged ventricles. Placement of the shunt improved the hydrocephaly; however, the collapse of the cranium resulted in the cranial bones overlying each at the site of the major sutures. The skull remained in this configuration; secondary craniosynostosis of multiple sutures developed by 18 months (B, E). Three-dimensional CT scans confirmed these findings and also revealed the unusual morphology of the cranium. Correction required total upper cranial vault expansion and replacement of the V-P shunt with a higher pressure valve. Photographs taken 6 months postoperatively revealed a more satisfactory shape and appearance of the entire craniofacial skeleton (C).

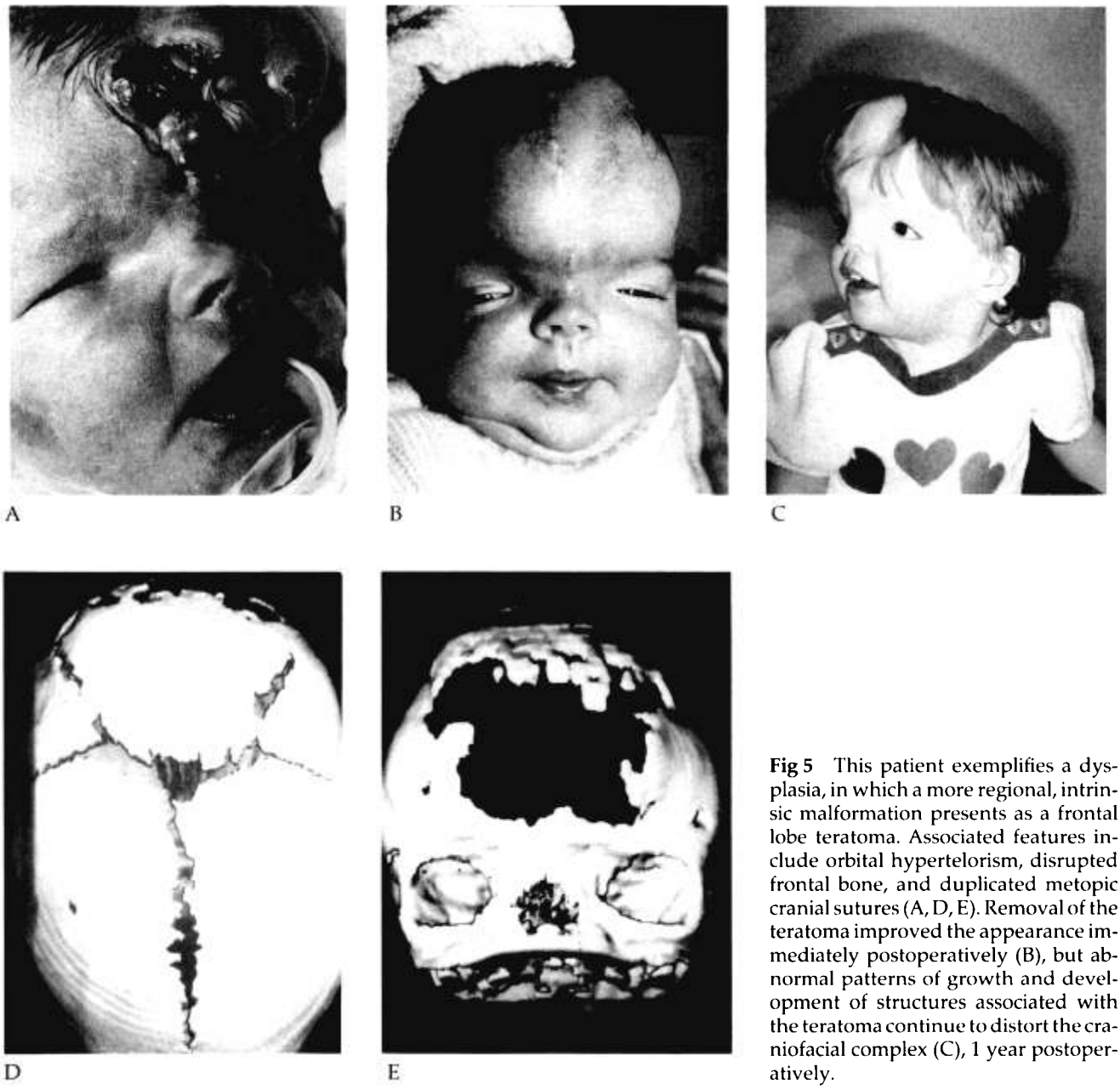



**Fig 5** This patient exemplifies a dysplasia, in which a more regional, intrinsic malformation presents as a frontal lobe teratoma. Associated features include orbital hypertelorism, disrupted frontal bone, and duplicated metopic cranial sutures (A, D, E). Removal of the teratoma improved the appearance immediately postoperatively (B), but abnormal patterns of growth and development of structures associated with the teratoma continue to distort the craniofacial complex (C), 1 year postoperatively.

normal face. A suture can be released in these cases, and faces can be contoured to a more normal appearance, but the growth disorder cannot be surgically or otherwise corrected. Although Apert's syndrome and Crouzon's syndrome both include craniosynostosis, the superior postoperative appearance of the Crouzon's syndrome patient relative to the Apert's syndrome patient may indicate the differing role of the growth process in the two syndromes [5, 6, 23–26].

Work by Kreiborg and colleagues [25] provides evidence for a differing role of growth in these two syndromes. Kreiborg and coworkers [25] used three-dimensional reconstructions of computed tomographic (CT) scans of the calvaria and cranial base to discuss growth in Crouzon's syndrome and Apert's syndrome. After examining the reconstructions and recording some characteristics of relative shape and size, the authors indicated that Apert's syndrome and Crouzon's syndrome are very different in cranial development, and their dysmorphology is highly age dependent. The authors concluded that the primary abnormality in Crouzon's syndrome is premature fusion of sutures and synchondroses and that these

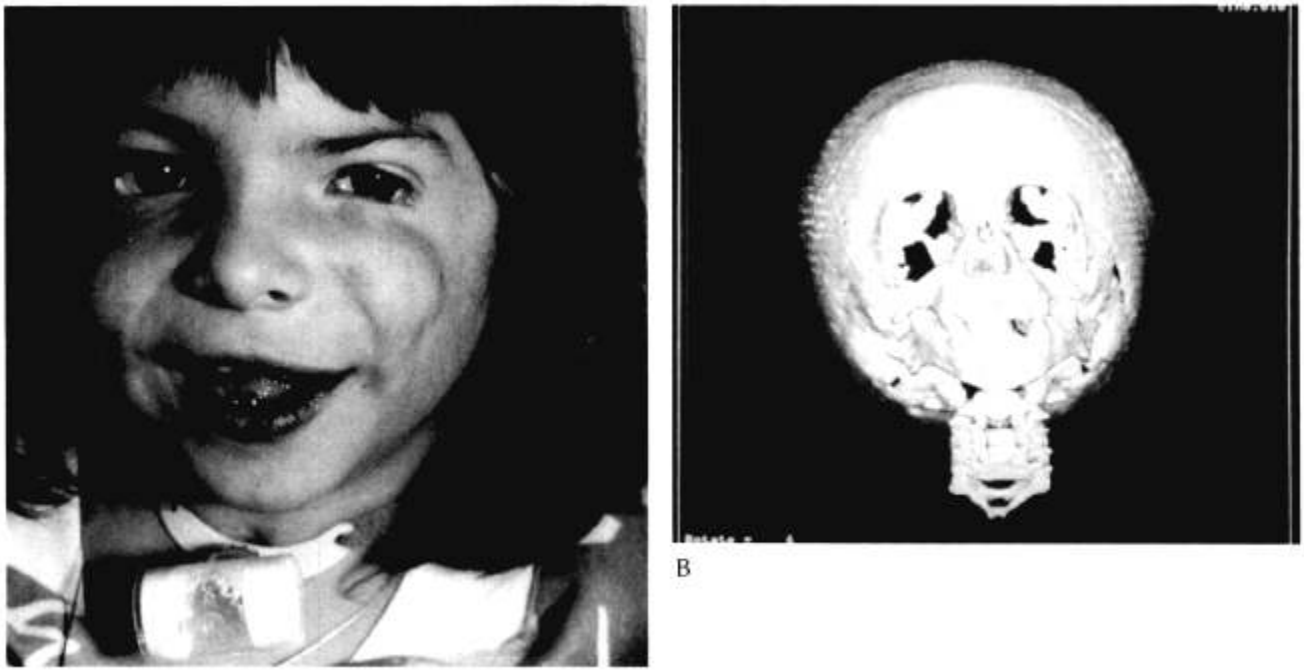


**Fig 6** (A, B) A patient with Treacher Collins syndrome. The typical features include hypoplastic zygomas, lateral orbital floors, downward-oriented orbital axis, and micrognathia, with hypoplastic mandibular condyles and rami. In general, the postoperative appearance of these patients is not satisfactory. This is because surgical intervention cannot alter the growth patterns.

fusions occur relatively late in fetal life. The form of the adult Crouzon's syndrome cranium is explained by resultant dysmorphic and compensatory growth changes. In contrast, the authors suggested that cartilage abnormalities play a primary role in cranial development in Apert's syndrome from early intrauterine life. Other cranial anomalies observed postnatally are caused by the resultant dysmorphic and compensatory growth in Apert's syndrome and are probably compounded by early cranial deformation [25].

A categorization like the one we propose will eventually cluster differing causes, genotypes, and diseases together, and this may offend certain scientists. However, evidence of the need for knowledge of the role of growth in the various craniofacial conditions is already apparent in the current literature. For example, the method used to separate Bruneteau and Mulliken's [1] sample of 60 patients with frontal plagiocephaly into subgroups or types involved evaluation of the role of growth in the production of structural defects. The authors [1] characterized one group (synostotic frontal plagiocephaly) as the result of intrinsically abnormal cranial development. Bruneteau and Mulliken [1] stated that accurate diagnosis of the type of frontal plagiocephaly is critical for proper management, and they suggested different treatment protocols for the various types of frontal plagiocephaly [1].

## Use of the Classification in a Clinical Setting

It is obvious that any child whose appearance prompts the parents to seek treatment by a craniofacial team has experienced some insult to the growth process. In the cases that are described as responding more positively to corrective surgery, the growth and development problems are viewed as being limited in space and time; that is, the insult is transient and localized. The condition affects the direction and magnitude of localized growth trajectories if it remains uncorrected, but tissues are histologically normal and are functioning and interacting in the expected way. In these cases, if one repairs the affected structures, normal growth of surrounding tissue will correct for local deformity [1, 2, 4-6].

The purpose of the classification system that we have introduced is to enable one to understand further the role of the growth process in craniofacial disorders so as to offer better prognostication and to improve treatment. The classification system will, therefore, be of most use to reconstructive surgeons performing the surgery by using what is known about growth to plan treatment [1].

When confronted with a clinical patient, the first step is to establish a diagnosis. If, for example, the clinical presentation is that of cranial asymmetry, the differential diagnosis will include (1) a unilateral craniosynostosis

(plagiocephaly); (2) a unilateral cerebral lesion arising from unilateral hydrocephalus from occlusion of the foramen of Monro, unilateral proencephalic cyst, unilateral macroencephaly, neoplasm, or hypoplastic or destructive lesion of one cerebral hemisphere; (3) unilateral meningeal lesion arising from a unilateral subdural fluid or unilateral leptomeningeal cyst; (4) postural molding; (5) unilateral inflammatory, traumatic, or destructive lesion to the suture; and (6) neuromuscular disorders and congenital cervical anomalies resulting in congenital torticollis [1, 2, 5, 9–11].

If the diagnosis is confined to an isolated craniosynostosis, it may be assumed that a direct surgical repair or reconstruction of the suture and surrounding bone will result in a very satisfactory result. This is because isolated craniosynostosis represents either a deformation or a malformation [1]. If it is a deformation and is corrected early in life, rearrangement of the deformed structures enables some of the malgrowth or maldevelopment already experienced by a pediatric patient to be "reversed" on the operating table. In the case of isolated craniosynostosis, the better the shape achieved on the operating table, the better is the eventual postoperative appearance. Young children will do better than older children because of the rapid expansion of the brain that occurs during the first 2 years of life. Although a reduced amount of craniofacial growth occurs after the first birthday relative to what occurs during the first year, brain growth that occurs postoperatively in a child younger than 2 years helps to "normalize" the shape of the surgically contoured skull. The thin, malleable cranial bones of young children (18 months of age and younger) will continue to change their form in accordance with the expanding brain, thereby improving their appearance as time passes [1, 5, 11].

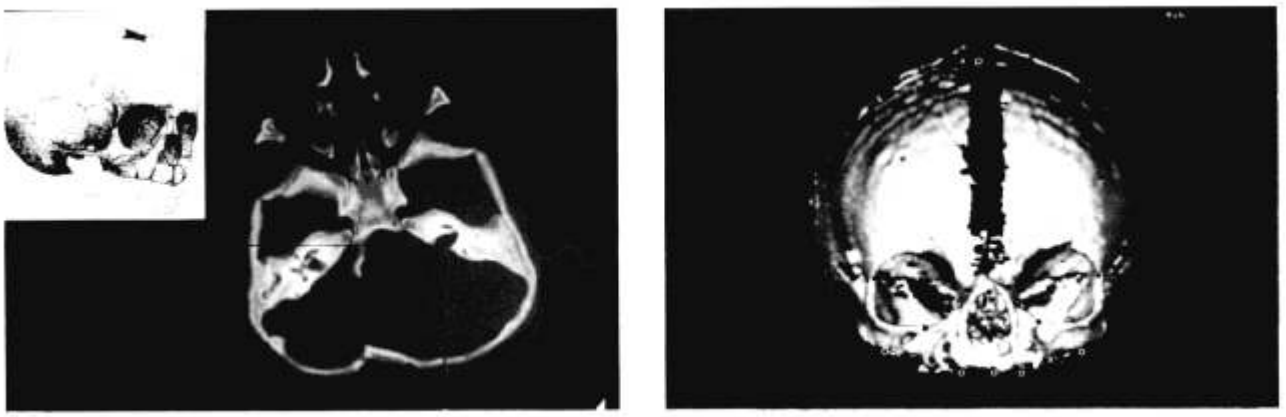
When the isolated craniosynostosis involves either unilateral coronal or unilateral lambdoidal synostosis, the postoperative appearance is often less satisfactory than that achieved when the synostosis is bilateral or involves the sagittal suture. In principal, unilateral synostosis should not be an exception in our classification scheme because we have no data to suggest that the involvement of the growth process differs according to which suture is involved or whether the involvement is unilateral or bilateral. However, craniofacial dysmorphologies that involve asymmetry appear very obviously different from normal to even the untrained eye. In the case of unicoronal synostosis, asymmetry of the forehead and orbits noted preoperatively is rarely totally corrected. There are probably several factors contributing to this perception. First is the simple human preference for symmetry. A nonprofessional can identify a deformity involving asymmetry more easily than a symmetric deformity. Consequently, postoperative aesthetic appearance of plagiocephaly may seem less successful than results for other types of isolated synostosis. Second, we may be treating these patients with an oversimplified understanding of the problem. In a three-dimensional analysis of growth in craniosynostosis, Richtsmeier and associates [27] found growth patterns of the cranial base to be more variable among patients with unilateral synostosis of the coronal suture than among other craniosynostosis patients (metopic, bicoronal, sagittal). The authors [27] suggested that the variability might be explained by the great variability in the degree of suture closure among these patients. Certain forms of unicoronal synostosis may involve the entire coronal ring, which includes sutures connecting the frontal, parietal, zygomatic, sphenoid, and ethmoidal bones. Because release of the entire sutural ring is not yet part of accepted surgical protocol, continued malgrowth resulting from the persisting synostosis of selected cranial base sutures may be contributing to a postoperative appearance that is less than perfect. The coronal ring could also be involved in severe cases of bicoronal synostosis, but because the involvement is bilateral the dysmorphology remains postoperatively and is not as obvious [27].

Delashaw and colleagues [28, 29] provided a novel and thoughtful hypothesis of calvarial growth in craniosynostosis, citing four principal rules of growth patterns. The rules stem from the idea that fused bones behave as single-bone plates and that the differential growth potential of sutures is determined on the basis of their relative distance from the site of synostosis. These rules were derived by critical examination of the clinical malformations observed with each form of craniosynostosis [28, 30–33]. The authors have made careful and significant observations, and at this time their hypothesis is the best information we have to explain the morphologies of various nonsyndromic forms of craniosynostosis from a growth perspective. However, the authors have not systematically and quantitatively analyzed the growth process. The authors acknowledge that their four guidelines may not apply to the cranial base abnormalities observed in craniosynostosis.

## Models for Quantifying Growth Patterns and Their Use in Patient Treatment

Establishing the role of growth in conditions commonly seen in craniofacial clinics may provide more realistic (i.e., quantifiable) expectations of postoperative results, helping parents and children to accept their appearance at an earlier stage in life. Predicting the outcome of surgery with a means for modeling growth and graphically displaying probable postoperative appearances could be a helpful tool for making decisions regarding whether or not surgery should be performed and the timing of reconstructive surgery. A major research focus of our laboratory is to learn more about the growth patterns of various anomalies using existing patient data.

Richtsmeier, Lele, and coworkers [34–39] presented theory, method, and models for the quantitative study of



A B

**Fig 7** Two ways to locate landmarks on computed tomographic (CT) scans. (A) Locating a landmark in X and Y spaces on a CT slice image is shown. X and Y coordinates are located according to pixel column and row. Z coordinates (in this case the superior-inferior dimension) are assigned according to the table position of the slice in which the landmark is located. (B) Locating landmarks on three-dimensional CT reconstruction is shown in which the landmark is located in a local coordinate space according to X, Y, and Z coordinates. (Adapted from Richtsmeier [58].)

growth patterns in three dimensions. The required data are three-dimensional coordinate locations of biological landmarks. If landmark coordinate data are collected from a form at one point in time and then collected from the same form later, the changes in the relative location of these landmarks produce a three-dimensional description of growth based on landmark data. We insist on using landmark data because they are required if the goal is to localize differences in growth patterns [34]. For our analyses of growth, the change of biologically meaningful locations (our landmarks) must be mapped exactly from one form to another. The change in relative distances among the landmarks serves as the backbone of the overall transformation quantified by the Euclidean distance matrix analysis (EDMA).

Landmark data can be obtained from facial surfaces captured by a surface scanner [40], from a three-dimensional digitizer [41], from CT scans of patients [27] (Fig 7), and from a specially designed series of linear measurements taken with more traditional anthropometric tools [42]. Because CT scans are routinely taken from craniofacial patients during their sometimes lengthy treatment period, and anthropometric data are taken directly from the patient's face in many clinics, data already exist that can be used to determine the growth pattern for classes of craniofacial patients. Validation studies done in our laboratory have shown that we can locate landmarks on CT slice images with a high degree of accuracy and precision and that these data are a valid representation of the three-dimensional volume of the skull [43].

Because the objective is to compare two images to determine the changes required to produce the image of the older form from the younger form, any method that compares the relative location of points in the two forms will give information on the transformation that has occurred. There are many morphometric techniques available when the raw data are landmark coordinates [42, 44–55]. Importantly, Lele [54] showed that EDMA [37, 55] provides a correct estimation of all the statistical parameters of interest and proper inference for statistical studies. Because our goal is to build a data base that enables the statistical study of growth using samples of images grouped on the basis of age, sex, race, and diagnosis, we use EDMA.

Using EDMA, all possible linear distances between the landmarks located on a patient are calculated from the original three-dimensional landmark coordinate data. The same landmark locations are collected from another scan of the same patient taken at a different point in time. All possible linear distances between the landmarks are calculated for this second scan. The two sets of data (one from the patient at time 1 and the other from the patient at time 2) are compared by computing a matrix of ratios of like linear distances from the two scans. The details of this method have been published elsewhere [34, 36, 37, 54, 55], but a simplified summary of the steps of the analytical procedure is given in Figure 8. The point we make here is that when the form of a young skull is compared with that of an older skull using this method, the result is a quantitative map of the growth pattern of the skull as defined by landmark coordinates. Moreover, once the three-dimensional growth pattern has been mathematically defined, it can be applied directly to the craniofacial form of another patient when that form is defined on the basis of the same landmark locations [38]. This technique has been described and applied in previous

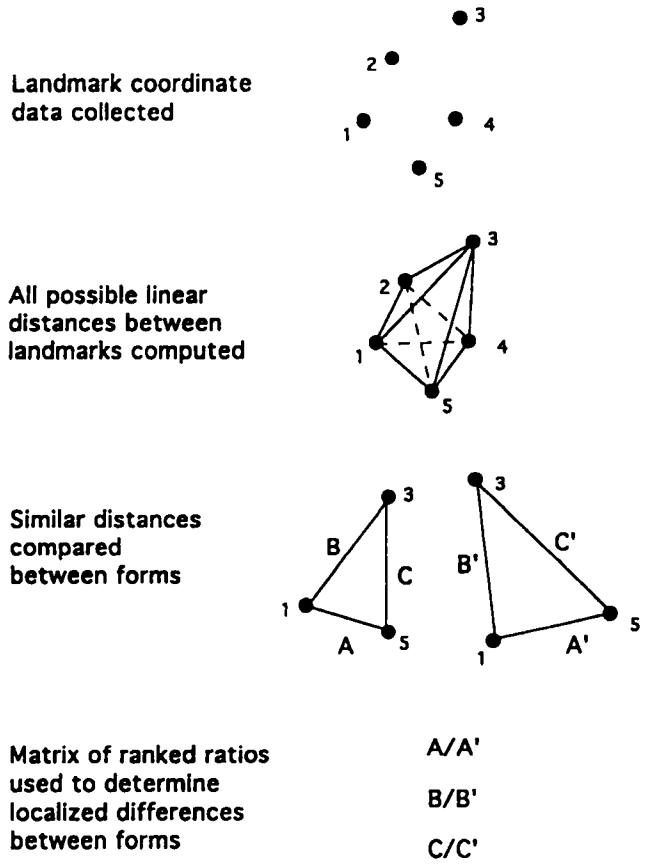



**Fig 8** Outline of how forms are compared using Euclidean distance matrix analysis (EDMA). Three-dimensional coordinate data are collected from all specimens to be compared. Then all linear distances among these landmarks are calculated. Homologous linear distances from two forms are compared by computing ratios of like linear distances. To keep this diagram simple, only 3 of the 10 possible linear distances are shown at the bottom half of this figure, but an EDMA analysis by definition uses all possible linear distances calculated from the landmarks used in analysis. (Adapted from Richtsmeier et al [59].)

articles [35, 56]. In one of these studies [56], growth patterns calculated from an age-graded set of normative skulls were applied to longitudinal series of patients with sagittal, bicoronal, and metopic synostosis. By "growing" the image of a patient with synostosis according to a normal growth pattern, we produced a hypothetical morphology for that patient, which can be compared with the actual cranial morphology of this patient after experiencing his or her own growth pattern over a specified interval.

More pertinent to this discussion is the application of a growth pattern (normal growth pattern calculated from normal cases, or Crouzon's syndrome growth pattern calculated from a series of Crouzon's syndrome patients) to the image of an infant with Crouzon's syndrome. If we quantified the growth pattern for Crouzon's syndrome, it can be applied directly to any Crouzon's syndrome patient to produce a form that represents the future morphology of a particular Crouzon's syndrome case. Additionally, if we can calculate a normative growth pattern from a relatively large sample of skeletally normal children, we can apply the normative growth pattern to the morphology of a Crouzon's syndrome infant to produce a hypothetical form representing what a Crouzon's syndrome patient would look like if the disease followed a normal growth trajectory. These morphologies, real and hypothetical, can be compared with one another to provide more information regarding the role of growth in the production of morphology.

We propose that these and related methods can be used in craniofacial clinics to improve patient treatment in the following way. Once the growth pattern of a sample of Crouzon's syndrome patients, for example, has been quantified, we will be able to produce a computer-generated model of what a particular Crouzon's syndrome patient's craniofacial form will look like in the future. We might also use these methods and computer simulations of surgical manipulations to produce hypothetical forms representing what the child will look like several years in the future, given the known growth pattern (that cannot be corrected) superimposed on the image of the Crouzon's syndrome patient that has undergone simulated reconstructive surgery using a computerized surgical tool. We believe that simulations like these will provide parents with more information for making a decision about surgery and also provide a more realistic expectation of the child's immediate postoperative and long-term future appearance. Matching expectations with reality can be beneficial to the patient, to the patient's parents, and to the surgeon. Ultimately, knowledge of growth patterns in differing craniofacial conditions may result in the design of new surgical approaches or changes in the timing of surgical procedures for particular conditions.

## Conclusion

The true test of the soundness of our classification system is whether or not it proves useful to the surgeon. Currently, the phrases "due to growth" and "growth disorder" are indiscriminately applied in the literature with little appreciation for the significance of the terms. We are beginning to test hypotheses regarding the role of growth in specific craniofacial cases. We believe that careful consideration of the role of growth in the production of craniofacial anomalies can bring a more thorough understanding of the morphology observed to the clinician, more realistic expectations of postoperative appearances to patients and their families, and perhaps improved surgical manipulations for patients on the basis of new knowledge of growth.

Our classification may coincide with ideas outlined by Hall [57]: The earlier the defect occurs during development, the more severe and the more clinically challenging it is. This is because of the cascading nature of developmental events [8]. Once a developmental process is set in motion, it can have profound effects on successive events. Early insults do not always produce an anomaly that affects the postnatal growth process, however.

We suspect that real and identifiable physiological components will ultimately define our categories. It may involve the embryological timing of the insults or teratogens, components of the histogenic process, or organ development. Our main hypothesis is that there are clear ways to categorize patients on the basis of their response to surgery. We believe that the divergence in response to surgery among patients relates directly to the role of the growth process in the various disorders. If the dysmorphology is produced in part or in whole by a growth disorder, good surgical results cannot be expected because the continuous maldevelopment will eventually undo what the surgeon has achieved in the operating room. If the growth process is not part of the disorder or is only operating locally, we expect a better response to surgical manipulation.

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