Abnormal craniofacial growth

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Treatment of patients with craniofacial (CF) anomalies necessitates knowledge about normal CF growth and how it deviates in the abnormal state. There are different basic types of CF anomalies and various kinds of aberrations that influence CF development. These factors might help to explain why patients display growth variations. The effect of surgery on subsequent development is significant, but the heterogeneity among patients with regard to the morphology, etiology, and pathogenesis of the anomalies could also explain certain growth results. Roentgencephalometric findings related to CF growth in three different groups of anomalies are discussed. □ *Cephalometry; cleft lip; cleft palate; craniosynostosis; mandibulofacial dysostosis*

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Craniofacial (CF) structures are unique in many ways. It has been said that the face of man is his window to the world and, as such, reflects his health, emotion, and character (1). The growth and development of the CF skeleton have always interested orthodontists because they have a great influence on dental occlusion. Comprehension of how normal CF growth occurs is essential to our decision-making in treatment of malocclusion. It is also important to study CF growth in patients with anomalies, because it not only gives direction in treatment but might also deepen our understanding of the normal growth process. This knowledge can further be enhanced by studying the effect of the treatment on the abnormal state, sometimes called 'the experiment on nature's experiment' (2).

In 1982 Spranger et al. (3) and Cohen (4) drew attention to the different types of anomalies: malformations, deformations, and disruptions. A *malformation* means a defect resulting from an intrinsically abnormal development. If a nondisruptive mechanical force causes a body part to assume an abnormal form or shape, a *deformation* has developed. Finally, a *disruption* is an interference or breakdown of an originally normal developmental process. This classification system can be used for CF as well as general anomalies of the body. Pathogenetic knowledge is helpful for better understanding of growth results in a specific anomaly.

In a similar attempt to better comprehend the vast variability in facial growth results in one specific anomaly, cleft lip and palate, Dahl (5) suggested three categories of aberrations: intrinsic, adaptive, and induced. The *intrinsic* factors are primarily related to the cleft formation process but might also influence later development. As an example of *adaptive* growth, Dahl mentioned the premaxillary protrusion seen in bilateral clefts. The position and growth of the premaxilla influence treatment considerably, not only in infancy but also in later development. The third category, the *induced* aberration, is especially related to the surgical management of the cleft. Traditionally, this factor has been given most attention, since it is responsible for the midfacial growth attenuation seen in many cleft patients.

CF growth can be studied in several ways, but roentgencephalometry is undoubtedly the principal clinical method. When the technique was introduced by Broadbent in 1931 (6), it was adapted for serial studies of facial growth in children. Most of the concepts and knowledge reviewed in this paper are based on investigations using roentgencephalometric records. To exemplify abnormal CF growth, this presentation will discuss three different anomalies: cleft lip and palate (CLP); craniosynostosis (CS); and mandibulofacial dysostosis (MFD).

Cleft lip and palate

In an early growth study of CLP patients, Graber (7) investigated facial morphology in 45 patients of different ages and with various types of clefts. He concluded that the cleft patients studied as a group showed severe maxillary deficiency in all dimensions. These characteristics were evident especially in those children who had been operated on at an early age. Although the author's general conclusions were correct, certain criticisms can be raised against how he studied his heterogeneous sample. Not only were all ages included, but all different types of clefts were also combined into one group. If the general growth influence from the operations had been less, then he would probably have reached a more differentiated answer—for example, he would have noticed the need to report the morphologic outcome related to type of cleft.

Simultaneously with the work of Graber a growth

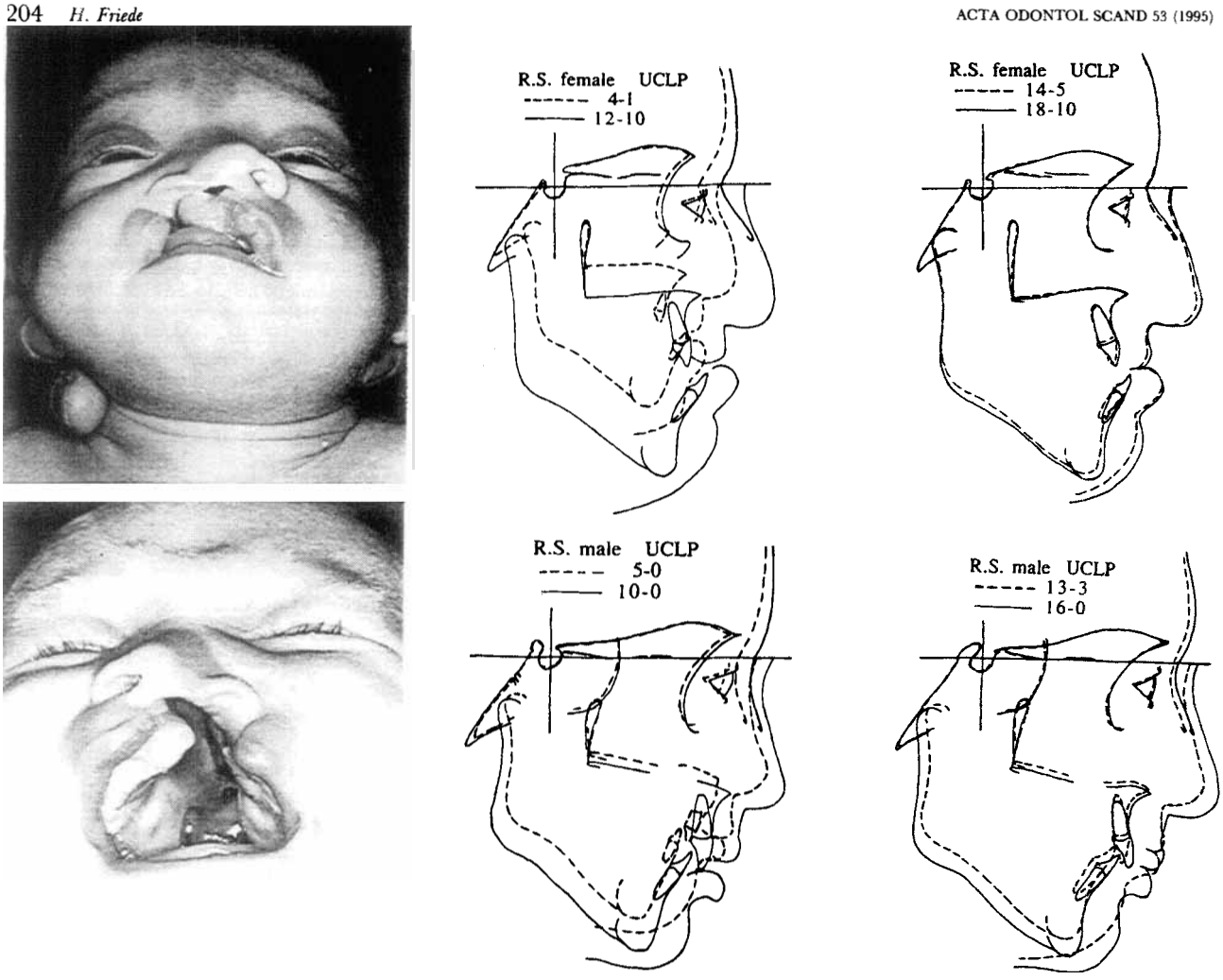

Fig. 1. Two patients with complete unilateral cleft lip and palate (UCLP). (Upper row) Treatment has included early bone grafting. The follow-up tracings show progressive midfacial growth retardation both horizontally and vertically. (Lower row) Surgery in this patient has been performed in accordance with the concept of delayed closure of the hard palate. Note satisfactory midfacial development.

study with a new approach was initiated at the University of Illinois in Chicago (8). The new aspect was that the records began in infancy before any surgery had been performed. The study was then repeated at regular intervals for as long as possible. The heterogeneity within the CLP diagnoses was recognized, and each cleft category was therefore analyzed separately. By starting with the unoperated state, new data were obtained. This information could in part resolve why growth results after repair differed between different patients. For instance, in some cases of unilateral CLP the postoperative position of the palatal segments resulted in arch collapse (9). In others, however, there was only approximation of the segments. These different responses to treatment were ascribed not only to surgical factors but also to the anatomy of the nasal septum and inferior turbinate, the bulk of the alveolar process close to the cleft, and so forth.

Another longitudinal follow-up investigation studied bilateral CLP patients (10). It also showed great variation in infant cleft morphology, especially with regard to the position of the premaxilla. Surprisingly, this variability did not reflect subsequent surgical treatment approaches. For example, the regimen that included so-called surgical setback of the premaxilla was performed not only in patients with extreme premaxillary protrusion but also in babies with moderate protrusion. As a result, patients treated with early premaxillary setback had straight or most often concave facial skeletal profile in adulthood (11). Thus, not only diagnostic and morphologic heterogeneities but also variations in surgical treatment can influence later midfacial growth of cleft patients.

Many cleft centers have imitated the longitudinal follow-up approach initiated by Pruzansky, although most of them have no roentgencephalometric records from the infant stage. The Oslo Cleft Lip and Palate Archive is a prime example of how a sequential collection of plaster casts and cephalometric radiographs can produce reliable information about CF growth effects of one treatment regimen (12). The surgical method used in Oslo was conservative and careful, especially with regard to treatment of the hard palate and the alveolar process (13). Consequently, the reported growth results were very satisfactory for both unilateral (14) and bilateral (15) CLP patients.

In our center in Göteborg we have also followed up our patients longitudinally, but the surgical treatment routines have changed over the years. The present regimen is characterized by palatal surgery in two stages, the repair of the hard palate being delayed to the age of 8–10 years. The new regimen has led to an improvement in the results with regard to midfacial growth, especially since the method of early bone grafting was excluded from our treatment (16) (Fig. 1).

Which growth mechanisms might then be influenced by surgery in the CLP patients? Both displacement growth and the cortical drift mechanism may be affected. In normal development of the midface, displacement of the two maxillae occurs mainly in the midline and also in relation to the palatal bones, the pterygoid processes, and the nasal septum (17–19). This sliding of the maxilla is particularly important for proper development of basal maxillary bone. Simultaneous with the maxillary displacement periosteal growth activities occur. The bony surfaces of the maxilla are selectively resorptive or depository to maintain the general shape of the midface. The periosteal growth is also very important for proper development of, for example, the alveolar processes.

In subjects with severe midfacial deficiency, the displacement type of growth is the mechanism most likely to be disturbed. During palatal surgery mucoperiosteal flaps are raised and pushed both medially and posteriorly, resulting in denuded bony areas. These defects will heal with formation of scar tissue bands which, with variable extent and strength, connect the maxillae, the palatal bones, and possibly the pterygoid plates, thus compromising midfacial displacement growth. Ross (20) described the scar tissue effect as a maxillary ankylosis. Another possible negative effect of palatal surgery is the collapse of the maxillary segments and distortion of the alveolar processes. This is also caused by scar tissue, which contracts the dental arch in both the sagittal and the transverse planes. If the scars run close to the teeth, the effects are especially severe (21).

When bone grafting to the cleft area is done early, the adverse effect on maxillary growth can be dramatic (22). Under these circumstances maxillary dimensions may be variably reduced in all three planes of space. However, Ross (20) expressed the view that it is difficult to comprehend how a bone graft, if placed in the anterior cleft area, where no sutural growth occurs, can cause maxillary retrognathia. Although this view might be correct in certain cases, it is evident that in subjects displaying severe growth impairment the poor midfacial development is the result of a more comprehensive grafting procedure than just adding bone to the cleft in the alveolar process. For instance, with the method developed in Göteborg the whole cleft space in both primary and secondary palate was filled with bone chips at surgery already at about 1 year of age. When the graft healed to the bone bordering the cleft, it blocked the displacement growth mechanism, with negative consequences for later development of the size of the maxilla.

The maxillary dimensions do not constitute the only important factor responsible for a correct intermaxillary relation. Proper position of the upper and lower jaws relative to the cranial base is also essential for correct CF development. According to growth concepts originating from studies of CLP cases, the maxilla is displaced forwards and downwards relative to the nasal septum (23). This sliding growth has been documented to occur between the premaxilla and vomer in both unilateral (23) and bilateral clefts (24). A bone graft joining these bones inhibits the growth movements between them, with a resultant midfacial deficiency in both sagittal and vertical dimensions. It is very likely that similar displacement occurs in normal cases, as has been suggested by Björk (17), who based his speculation on circumstantial evidence. Björk was unable to test his hypothesis because in a noncleft subject it is impossible, from a practical point of view, to place metallic implants in the vomer for later roentgencephalometric follow-up. This exemplifies nicely the concept mentioned in the introduction of this paper that study of the abnormal state, 'nature's experiment', might give important information about normal development.

Craniosynostosis

Craniosynostosis (CS) is another condition in which cranial, and possibly facial, growth is affected. The heterogeneity within this group of anomalies is great, with differences in the complexity of the malformation, the location and extent of the suture fusion, and, consequently, also in the treatment protocols.

In 1980 Cohen (25) introduced three types of dichotomies of CS in an effort to improve the diagnostic nosology of these anomalies. According to the first pair, patients were classified as having either *simple* (one affected suture) or *compound* synostosis (two or more synostotic skull sutures). The second dichotomy was *primary* (most common) as opposed to *secondary* CS (caused by known diseases such as hematologic or metabolic disorders). Finally, CS could occur in an *isolated*

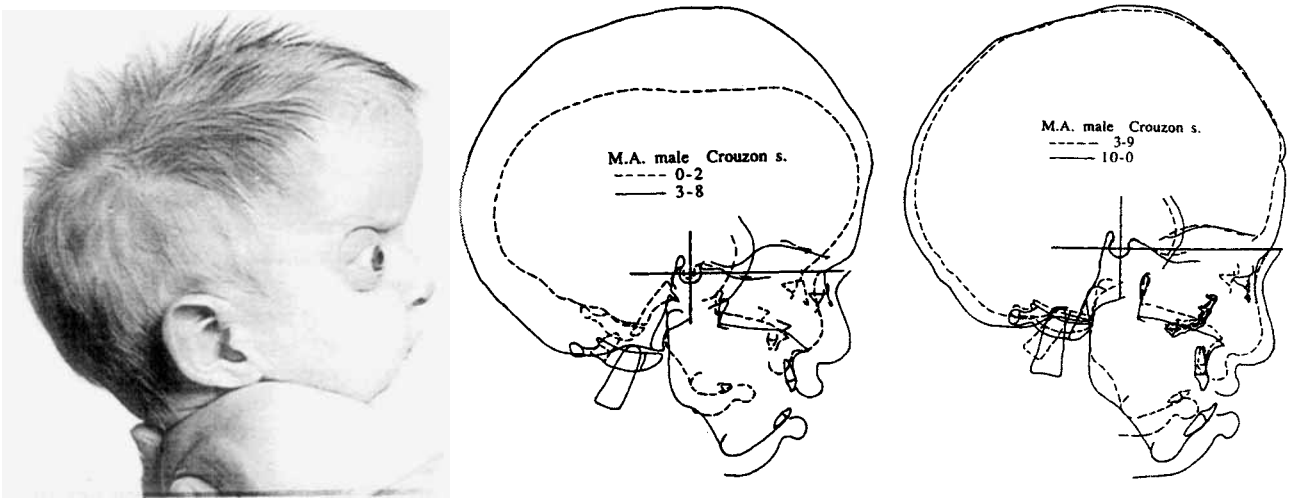

Fig. 2. Patient with Crouzon syndrome with unusual, elongated skull. Improved calvarial shape after three craniotomy operations during the 1st year of life. A LeFort III procedure was performed at age 3 years 8 months to improve the patient's breathing. Note the insufficient growth of the maxilla as compared with the mandible at age 10 years.

form (no other abnormalities) or be part of a *syndrome* such as in Apert or Crouzon. It is quite obvious that craniofacial growth is affected differently in these different types. Cohen (25) adviced particularly to distinguish between primary and secondary CS because surgical intervention may be very effective in the former provided no concomitant malformation of the central nervous system exists. In most cases of the latter, however, the result of surgery usually is poor. The commonest type of *simple* CS is fusion of the sagittal suture, and it occurs in about 50–60% of the cases in which only one suture is affected (26). As an example of the diagnostic heterogeneity in CS it can be mentioned that even within a single category, such as sagittal synostosis, four different subtypes have been identified (27). Similarly, Apert syndrome is no longer regarded as the only anomaly in which CS is combined with malformation of the hands and feet. At present, the Saetre-Chotzen, Pfeiffer, Carpenter, and Jackson-Weiss syndromes are also found to be conditions with similar malformation profile (28). These new concepts underscore the need for differential diagnosis when discussing craniofacial growth in CS.

Other heterogeneities important to understand when considering growth aspects are the etiologic and pathogenetic differences between CS patients (29). Over the years many different etiologic theories for CS have been suggested (30). Virchow (31) believed that the fusion of the skull sutures was the primary defect and the associated cranial base deformity was a secondary phenomenon. Moss (32) postulated the opposite: the cranial base anomaly was the primary event, resulting in secondary fusion of the skull sutures. A third theory was advanced by Park & Powers (33), who proposed that CS was caused by a primary defect in the mesenchymal blastema of the skull, resulting in both lacking sutures and malformation of the cranial base. All three theories could very well be correct, and there are probably also others. Each of them might explain some, but not all, cases of CS.

The heterogeneity in etiology suggests heterogeneity in pathogenesis, which might explain various growth results in different patients. According to the theory of Moss (32), the dural bands attached to malpositioned parts of the cranial base transmit aberrant tensile forces to the dura during growth, which in turn might lead to synostosis of the overlying suture(s). After surgical craniotomies the dural attachments to the cranial base are generally unchanged, and synostosis is therefore likely to recur, resulting in poor long-term growth. Similarly, if a Crouzon or Apert syndrome patient undergoes craniotomies, the etiologic factors remain. In these cases the pathogenetic mechanism is thought to be a biochemical defect leading to, among other things, progressive calcification and fusion of not only sutures and synchondroses but also bones of the hands, feet, and cervical spine (34). Therefore, despite the immediate improvement in the shape of the skull obtained through the surgical procedure, the potential for long-term sutural growth adjustments is usually very limited (Fig. 2).

A further pathogenetic pathway should be mentioned, but in contrast to the previous examples the surgical release of the synostotic suture(s) in this case is likely to restore possibilities for growth. The mechanism to consider is intrauterine mechanical factors, which have been suggested to cause different types of isolated CS, both in humans (35) and in experimental animals (36). After birth the adverse mechanical factors no longer operate, which explains the prospects for satisfactory growth after release of the suture fusions.

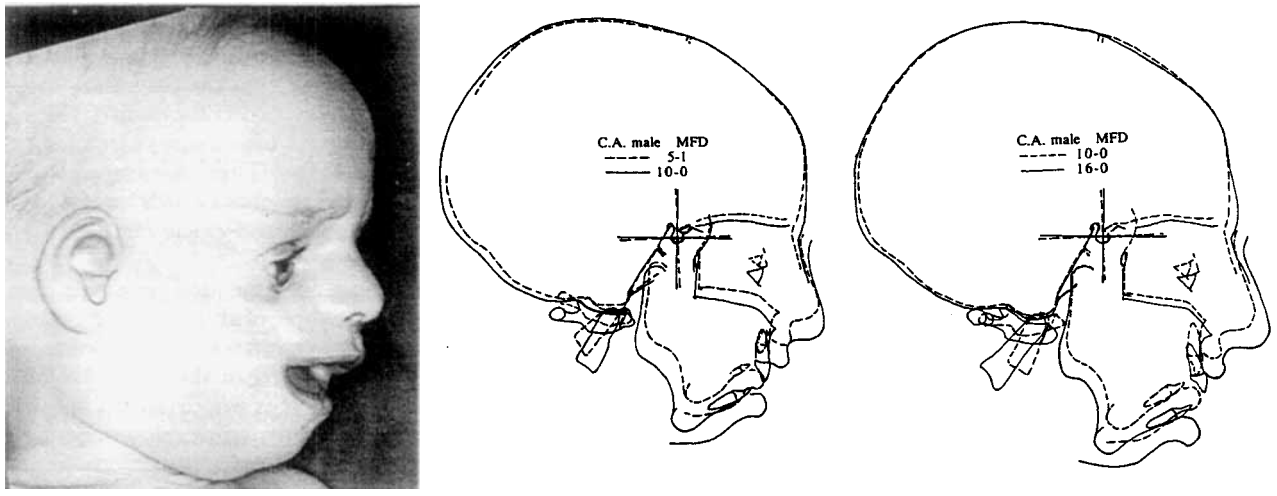

Fig. 3. Patient with mandibulofacial dysostosis (MFD). Growth tracings are superimposed on sella and posterior cranial base. Note the downward bending of the anterior cranial base and the downward growth of the facial skeleton between 5 and 16 years of age.

CS is associated with facial malformations in many syndromes, and Crouzon and Apert are probably the best-known examples. In these cases the suture fusion is not limited to the skull and cranial base but may also involve facial sutures and cartilages (34, 37). It should be remembered, however, that other growth sites (= other sutures) and mechanisms (=especially periosteal growth) might compensate for lacking bone displacement related to fusion of one particular suture.

Kreiborg (34) described in detail how facial growth was affected in Crouzon syndrome subjects, but only a few points will be mentioned here. The premature arrest of maxillary sutural growth usually occurred already during the 1st years of life. This resulted in reduced bone deposition at the maxillary tuberosities and a short maxillary dental arch, with crowding of the teeth. The lowering of the nasal floor, caused by remodeling, was pronounced, as was the development in height of the alveolar process. The orbital floor was resorptive, in contrast to the bone deposition normally seen on this surface. All of these processes attempted to compensate for the lacking displacement of the bones of the maxillary complex. The mandible displayed a relatively normal growth pattern. There was progressingly increased occurrence of mesial occlusion, open bite, and crossbite as a result of the midfacial growth deficiency. This development is very different from what is seen in subjects with simple craniosynostosis (such as scaphocephaly), in which facial growth is essentially normal (38).

Mandibulofacial dysostosis

Patients with MFD, a malformation also called Treacher Collins syndrome, display typical CF features. Important characteristics include downward-slanting palpebral fissures of the eyes and colobomas of the lower eyelids, hypoplastic zygomatic bones and arches, malformed auricles of the ears, and also mandibular hypoplasia with a syndrome-specific shape of the lower jaw (for other, less frequent traits, see the review by Gorlin et al. (28)).

MFD is usually considered to be an autosomal dominant malformation syndrome with variable expressivity but with essentially complete penetrance (39). MFD might also occur as a less frequent autosomal recessive type (40). The gene has recently been mapped to the 5th chromosome (41). With regard to the pathogenesis, it is usually considered that the defect occurs some time during the 2nd month of pregnancy (42). The mechanism responsible for the development of the malformations in MFD is under discussion. According to one theory, the reason is destruction of neural crest cells that are migrating to the first and second branchial arches (43). Since especially derivatives from the dorsal parts of the arches appear to be affected in the malformation, it was suggested that neural crest cells, with a short distance to travel and therefore starting relatively late, are damaged during their migration. An alternative hypothesis has been presented by Sulik et al. (44), as they had difficulties understanding how only the late starters and not all neural crest cells were influenced by the defective gene(s). In their view cells from the ectodermal placodes rather than the neural crest cells are the ones primarily affected. In MFD the gene(s) directing development of the ectodermal placode might function improperly, resulting in markedly excessive cell death in regions where programed cell death normally occurs. Therefore, the deficiencies of the branchial

arches might result not only from localized tissue damage but also secondarily from effects caused by inadequate promotion of growth of neural crest cells from the cells of the ectodermal placodes. According to this latter theory, the defect is initiated already during the end of the 1st postfertilization month.

In MFD growth of the neurocranium including the cranial base has been found to deviate from the norm. With regard to the cranial base, it was reported that MFD patients as a group show increasing flexure of the cranial base angle (45). This trait is especially expressed in males. Kreiborg & Dahl (40) made an interesting suggestion that the observed reduction in the cranial base angle with age was not caused by a growth process in the posterior part of the cranial base but rather by a bending downwards of its anterior component. In this area especially the sphenoid bone is deficient, which together with zygomatic arch defects might reduce the strength of the anterior cranial base to withstand functional forces from, for example, facial soft tissues, including the masticatory muscles.

The size of the anterior and posterior cranial base has also been found to be smaller than the norm, as have the height and length of the anterior neurocranium (46). On the other hand, the posterior length and particularly the posterior lower height of the neurocranium appear to be increased. The latter variable seems to be negatively correlated with the cranial base angle. The different shape of the neurocranium might be associated with variations in the cranial base morphology, as suggested by Moss (32) and discussed above for craniosynostosis patients. Interestingly, Granström & Kullaa-Mikkonen (47) found reduced cranial base size and the same elongated head shape already at the fetal stage in rats treated with retinoic acid, a teratogen considered to produce MFD phenotypic malformations.

Both the maxilla and mandible are hypoplastic in MFD, but the latter is particularly affected, resulting in a convex facial profile that generally remains unchanged throughout life (48) (Fig. 3). The mandibular body and the rami with their condyles are severely reduced in size, and the gonial angles are obtuse (49). The mandibular plane angle is steep, and the symphysis is distorted in shape (50). The lower border of the mandible displays a typical 'broad' curvature, which is obvious already in infancy (51). The mandible grows with posterior rotation, as displayed clearly by Björk & Skieller (52), using their metallic implant method. The intramatrix rotation was especially pronounced in their case used for illustration. To maintain the shape of the mandible during rotation, extreme periosteal remodeling took place in the ramus and gonial areas. The symphysis and alveolar process were also exposed to comprehensive bone remodeling.

The dysmorphology of the mandible and cranial base is likely to cause airway reductions in some MFD patients (50). These problems may develop, according to the suggestion of Kreiborg & Dahl (40) with regard to changes of the cranial base angle, as discussed above. The functionally caused downward bending of the anterior cranial base closes the cranial base angle, thereby reducing the airway. To compensate, the patient then extends his head, which causes stretching of the facial soft-tissue envelope. This, in turn, will pull the mandible downwards and backwards, which also might impinge on the airway and cause further extension of the head (53).

This presentation was not intended to cover completely the comprehensive topic of abnormal CF growth. Rather, the objective has been to review some concepts related to growth, as illustrated in the literature on a few selected CF anomalies. It is important to know as much as possible about growth and development of the skull and face to provide good care for these patients.

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