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Controversies in the Management of Craniofacial Malformations

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The controversies in the management of patients with craniofacial malformations originate from a lack of knowledge of the etiology, the pathogenesis, and the long-term effects of the currently accepted treatments. The craniofacial malformations found most commonly, excluding cleft lip and/or palate, are malformations of the upper face and the cranial vault (craniosynostosis) and the mandible (hemifacial microsomia). The classification and etiology of these conditions are subject to controversies. The use and effectiveness of new imaging methods is debated, but they have had a major impact on diagnosis, treatment planning, and the evaluation of the treatment outcome. Currently, orthodontic treatment is delivered in preparation for surgical procedures and this is the current state of the art. The use of distraction osteogenesis is a new trend in surgery, often misused because of inexperience. Unfortunately, evidence-based care is lacking and treatment decisions are based on empirical experience of the individual professional or on anecdotal reports of success of a specific treatment modality. The role of the orthodontist in a craniofacial team is somewhat unclear and an important goal is to maintain well-defined protocols for the management of the different malformations. This is critical in light of the pressing need for proper clinical trials involving large samples of patients. There is an urgent need to create collaboration between craniofacial teams with a history of high volume and with an excellent track record for care of patients with craniofacial malformations. This approach will ensure a successful delivery of evidence-based care in the future.
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Well-established craniofacial teams have widened the scope and visibility of care provided by their specialists. They also have generated numerous new controversies in addition to the classic discussions on appearance improvement, function, and psychology of patients with craniofacial malformations. Every major surgical advance impinges unexpectedly on other branches of medicine and dentistry. The use of implants, bone transplantation, and distraction osteogenesis has a vast impact on the indication for treatment as well as timing of treatments, although the evidence for long-term stability of treatment outcomes has not been demonstrated. Also a renewed dialogue with genetics, embryology, and anatomy has been taking place and again new ethical questions have or should be raised. Slavkin stated that "new results have led to the new biology, a biological revolution in which traditional concepts and methods now merge within a new intellectual and methodological synthesis in cellular, molecular and developmental biology."[1] But for the clinician, this brave new world gives no direct answers to the successful management of the craniofacial malformations.

A World Health Organization (WHO) report[2] in 2002 identified three interrelated research issues related to the care for patients with craniofacial malformations including evidence-based care, quality improvement, and access and availability. Three other major themes are gene/environment interaction, genetics, and prevention. It is of major importance that progress is made on gaining more insight on these issues and themes. However, the simple reality on a macroscopic level is that an understanding of the normal craniofacial development is a prerequisite to better comprehend changes resulting in craniofacial malformations.

As advanced by Bjork,[3] abnormal craniofacial development is a demonstration of the importance of certain growth centers in the head. Certainly, a new classification of craniofacial malformations is needed because the current terminology used in syndromology has always been far from satisfactory,[4,5] as some syndromes have ceased to exist as separate entities with the additional knowledge gained in this field. The dualism between

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morphological and morphogenetic types of classification may be solved when the pure genetic description of the malformation can be given. The best description of the craniofacial malformations can be found in the fourth edition of *Syndromes of the Head and Neck*.[6]

Controversies in the General Management of Craniofacial Malformations

Children with craniofacial malformations present a wide spectrum of problems and should therefore be treated by an interdisciplinary team.[2] To be able to cover all possible problems, the following disciplines should be represented on the craniofacial team: surgeon, orthodontist, oral surgeon, neurosurgeon, ophthalmologist, ear nose and throat specialist, psychologist, pediatrician, and social worker.

For such a team to be cost-effective, a certain volume of patients must be seen. A quality assurance program needs to be in place to respond to the requirement of developing quality care. For the management of children with cleft lip and palate, mission statements or guidelines have been formulated[7] and agreed on by an international working group. Similar mission statements could be formulated and adopted for the management of craniofacial malformations. From a medico-ethical standpoint, the danger for a team is to overtreat and not to consider the risks/benefits ratio for the child under treatment. If, during the course of therapy, treatment is harmful to the child, it is always done unintentionally, and a more realistic approach to treatment must take into account the wishes of the patients and the parents.[8]

Data collection is different for quality control assessment in children with craniofacial malformations than for traditional medical technology assessment or randomized clinical trials. Randomized clinical trials are important for the creation of evidence-based care. Quality control assessments are important for monitoring improvements of the care and guaranteeing a state-of-the-art quality of care. The most important differences are illustrated in Table 1.

The health care of children with craniofacial malformations should be improved by applying methods of evidence-based medicine and utilizing the results of medical technology assessment in decision making regarding the treatment of these children.

The main characteristic feature of children with craniofa-

Table 1 Main Differences in the Design and Philosophy of Data Collection for the Purpose of Information Management and Evidence-Based Clinical Care

	Clinical Database	Clinical Trial/RCT
Number of patients	Big	Small
Amount of variables	Small	Big
Basic principles	Management information	Scientific information
Duration	Indefinite	Short
Environment	Variable	Controlled
Connection with others	Close	Remote
Purpose	Quality development	Evidence

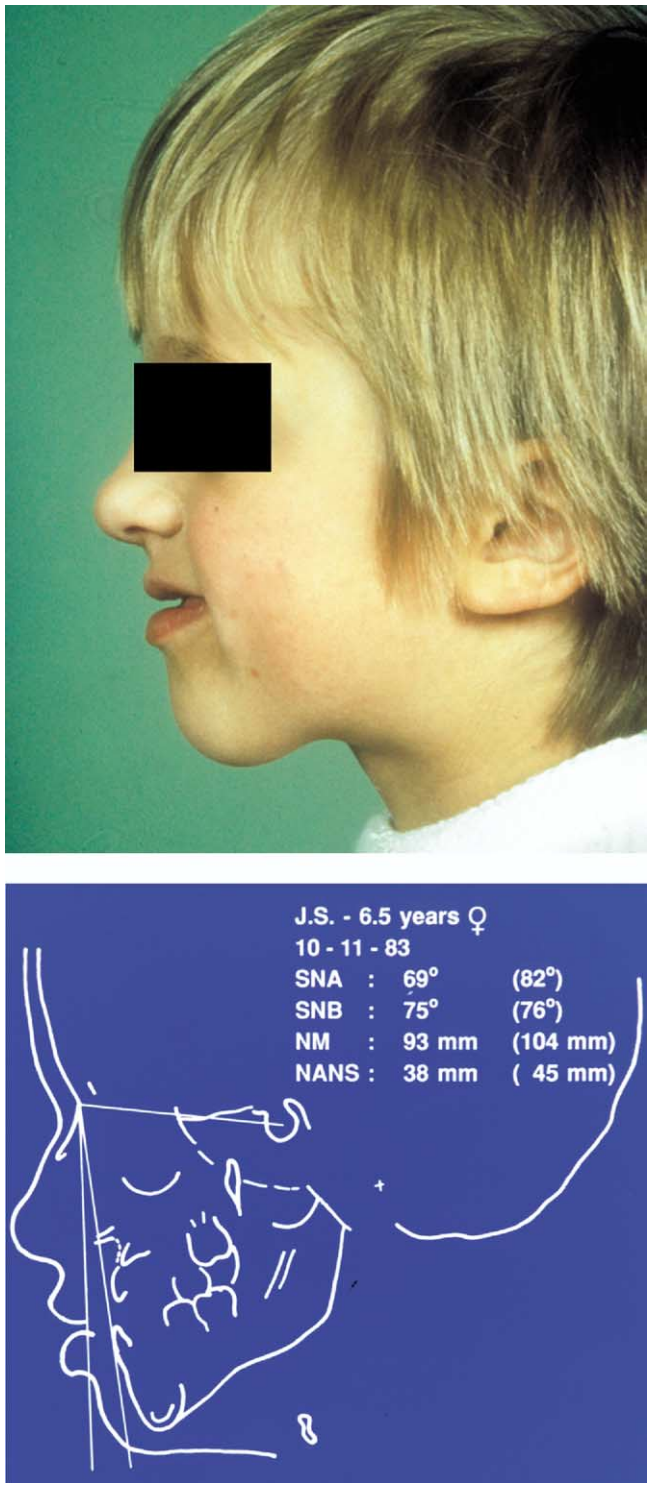

Figure 1 Photograph of a girl with Crouzon syndrome and cephalometric measurements with standards for children with normal growth between brackets (NM, nasion-menton; NANS, nasion-ANS). (Color version of figure is available online.)

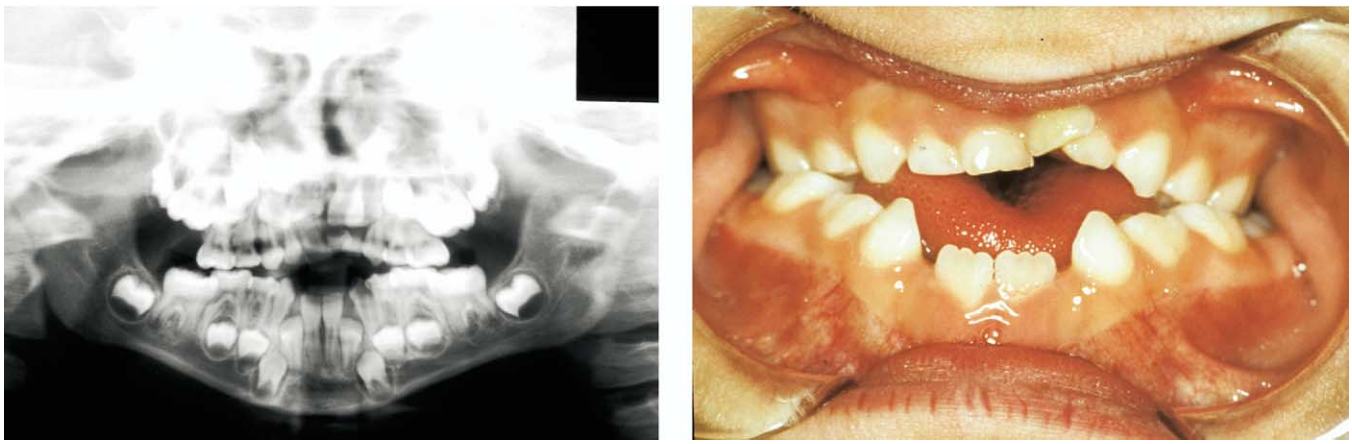

Figure 2 Dental situation in a girl with Crouzon syndrome (same patient as in Fig 1). (Color version of figure is available online.)

cial malformations is the variation in the structures involved, in the degree of malformation, in the etiology of the malformation and in the individual reaction to intervention or treatment.

The role of the orthodontist in a craniofacial team is generally considered to be:

- Data collection for monitoring craniofacial growth.
- Assistance in decision making on treatment modality with obligation to inform the patient.
- Orthodontic treatment in agreement with the surgeon's requirements.
- Evaluation of treatment results.

No real consensus on the evaluation of treatment results has been reached internationally.

As guidelines for the practice of orthodontics within the craniofacial team, the following aspects of the care should be considered: Development of a standard of care of treatment and information to educate the patient, procedures for documentation of both the treatment choice and the treatment outcomes, documentation of the overall treatment plan and treatment outcomes by standardized records, participation in intercenter comparisons of treatment outcome, and implementation of a quality control system.

The orthodontic protocol for monitoring the development of

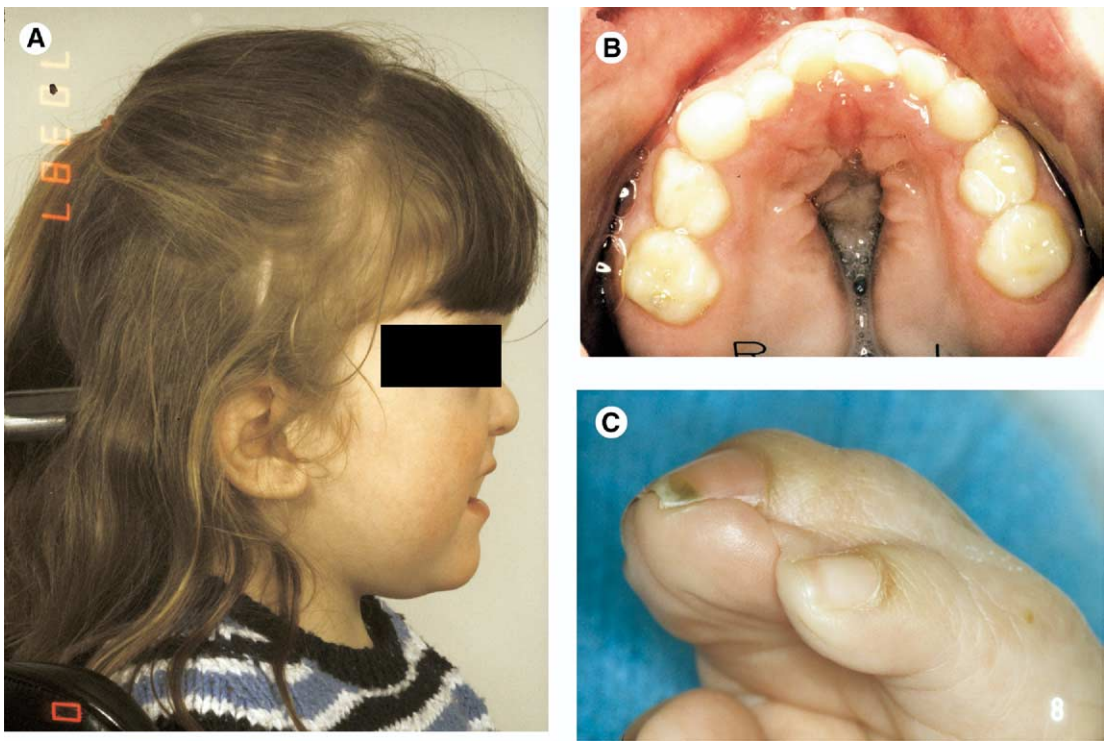

Figure 3 Illustration of a girl with Apert syndrome: (A) profile, (B) upper jaw, and (C) malformation of hand. (Color version of figure is available online.)

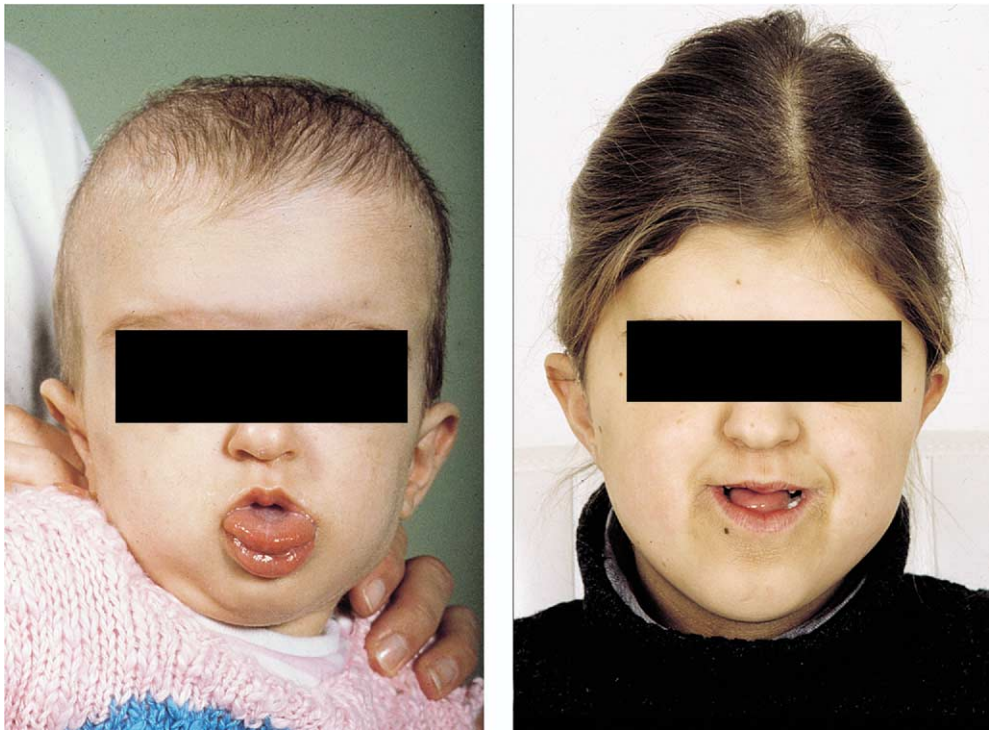

Figure 4 Facial development of a girl with Apert syndrome. (Color version of figure is available online.)

a child with moderate malformation (without a life-threatening condition) could be on the following schedule as an example: at 4 years of age introduction to the craniofacial team, at 6 years an extensive examination with the necessary x-rays, dental models, and photographs (problems in the early mixed dentition can be detected and long-term planning for surgery can be discussed with the parents of the child), and at 9 years of age either evaluation of early surgery and/or control on the dental development should be undertaken. In both cases an extensive examination should be performed. A similar checkup must be performed at 12 years of age (end of the late mixed dentition) and will include decision making for definitive orthodontic treatment. At 15 years of age, the decision must be made for the final surgery and the pre/postsurgical orthodontic treatment. Finally, at age 18, the patient who is now a young adult should be released from the craniofacial team.

Midface Deficiency

Midface deficiency is usually caused by craniosynostosis and deficient growth of the sutures including most facial sutures. For most craniosynostosis syndromes, an autosomal dominant inheritance pattern has been found. Mutations in the gene encoding the fibroblast growth factor receptor 2 (FGFR) located on chromosome 10 were first described in patients with the Crouzon syndrome.[9] Later other mutations were detected. Although these growth factors have a distinct pattern of expression during development, little is known with respect to their expression during skull development. It was shown in animal models[10] that the mutated receptor forced the expressing cells within the developing suture to undergo bone differentiation prematurely at the expense of proliferation. The ossification of the suture was enhanced and the growth was restricted. This may be an explanation also for syndromic craniosynostosis in humans.[3] However, the potential of genetic mutation analysis as basis for a new classification system of craniofacial malformations is still far from being implemented.[9]

Early closure of cranial sutures result in an abnormal cranial vault and retrusion of the midface (Figs 1 and 2). Ninety different syndromes have been described with craniosynostosis of some form: The Apert syndrome (Fig 3), the Pfeiffer syndrome, the Jackson-Weis syndrome, and the Saethre-Cotsen syndrome are the best known apart from the Crouzon syndrome. Today, many syndromes have been mapped to specific chromosomal locations, and the genes and the molecular mutations involved have been identified. It is not unusual that an old diagnosis based on the craniofacial morphology of an individual child has to be revised due to this new information.

One in 2500 births may be a child with a craniosynostosis. Not all malformations have to be treated because they may not present aesthetic or functional problems. On the other hand, some cases may have an absolute indication for early surgery because the intracranial pressure may increase if the cranial vault does not give way to the growth of the brain. If not treated, blindness due to damage to the optical nerve may occur or respiratory problems may result from a too narrow upper airway.

Two syndromes are very well described,[11,12] the Crouzon syndrome (Figs 1 and 2) and the Apert syndrome (Figs 4 and 5). They present a challenge to the orthodontist and to the craniofacial surgeon. The symptoms are exophthalmus, a small, retrognathic and backward inclined maxilla with

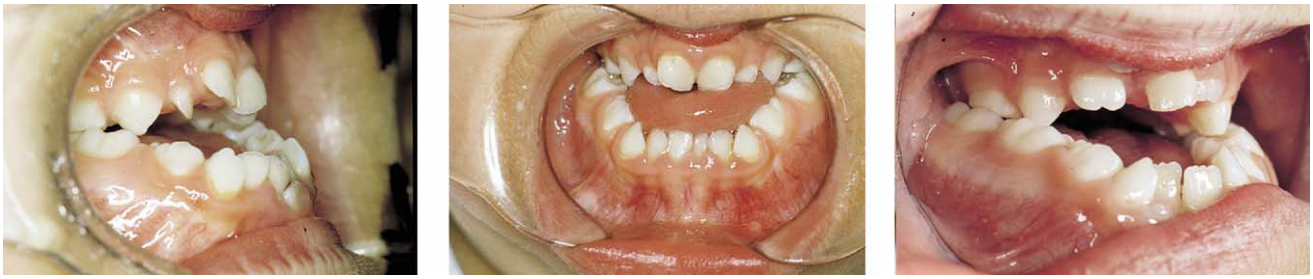

Figure 5 Dental development of a girl with Apert syndrome (same patient as in Fig 4). (Color version of figure is available online.)

crowded teeth. In addition, children with Apert syndrome have a cleft palate and abnormal hands and feet. The appearance of children with craniosynostosis is very variable and the availability of age-dependent data is therefore very important so it can serve as a baseline for comparison (Fig 7).

The dental development in these children is nearly always abnormal because of an underdevelopment of the upper jaw or damage to the permanent tooth buds in the case of an early surgical intervention. Also, the dental age has a tendency to be delayed. As early as in the early mixed dentition, impaction of the upper front teeth and of the second deciduous molars can be observed because of a small upper jaw and this may result in impinging on the upper first molars eruption (Fig 2). This explains the need for an evaluation by the craniofacial team when the child is 6 years of age. It is very difficult to accommodate all the front teeth in the upper jaw without expanding the upper jaw. Unfortunately, the transverse distraction of the upper jaw cannot be performed before the eruption of the canines to avoid damage to the tooth bud. One of the consequences of leaving a child with delayed eruption in the anterior portion of the maxilla is the impaction of the teeth involved if there is no orthodontic intervention (Fig 6).

In recent years, an extensive synopsis of the management of craniosynostosis has been published.[14] Since then, the use of distraction osteogenesis has increased significantly. The use of three-dimensional (3D) images and models made from scans has made it possible to plan the reconstructive operations with more precision. The use of gradual traction on the soft tissues is believed to decrease the amount of the postsurgical relapse. However, until proper prospective randomized clinical trials evaluate the outcome of the different treatment options, there is no real evidence supporting this clinical practice. Also, the effectiveness and efficiency of this new technique has not been demonstrated yet.[15,16]

At the age of 9 or a little later, distraction of the upper jaw in the transverse direction can be performed in conjunction with orthodontic treatment as a preparation phase for future distraction osteogenesis in the sagittal plane (potentially for a Le Fort I or III, depending on the amount of exophthalmus). The choice of either an intra- or an extraoral device is left to the surgeon performing the surgery.

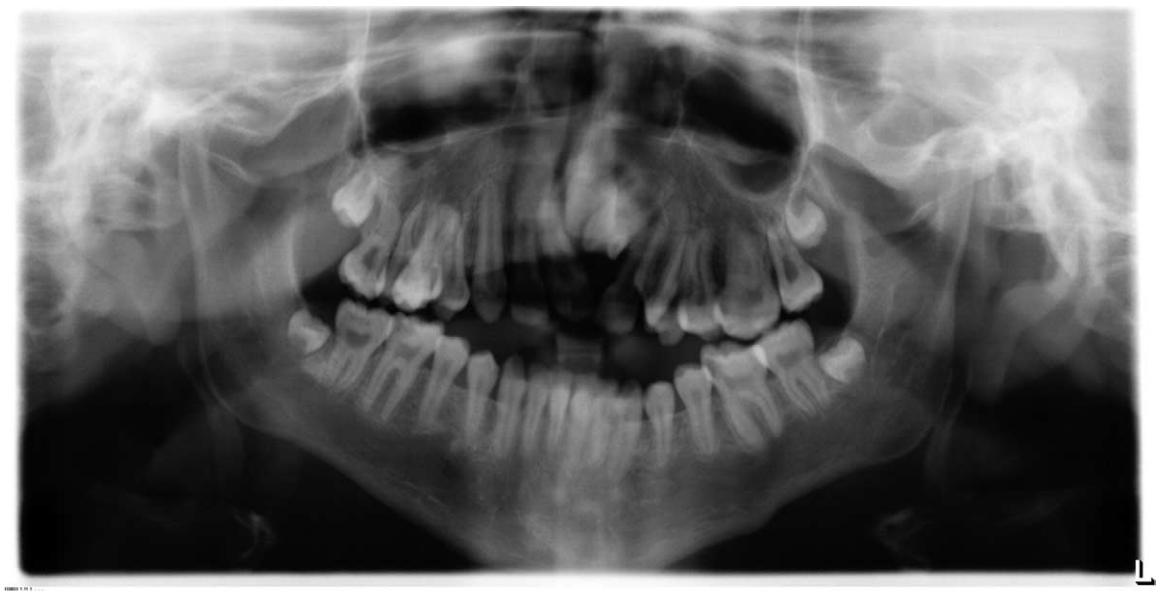

Figure 6 Orthopantomogram showing the neglected dental situation of a 15-year-old boy with Crouzon syndrome. Note the impaction of the teeth.

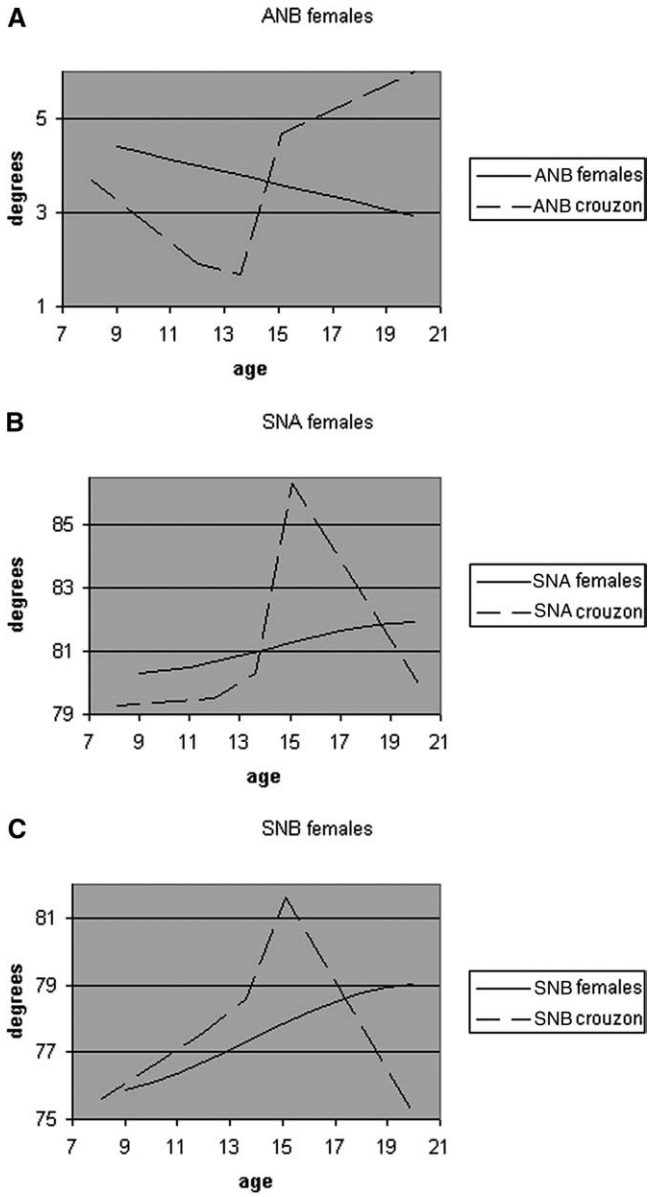

Figure 7 Cephalometric measurements (A) ANB, (B) SNA, and (C) SNB of a patient with Crouzon syndrome. Note the effect of operation at 13 to 14 years of age and the relapse, plotted on normal growth curves based on data from the Nijmegen growth study, the Fells growth study, and the Michigan growth study.

Before the introduction of distraction osteogenesis, children with Crouzon or Apert syndrome were operated on with a Le Fort I, II, or III at the age of 17 to 18 years, depending on their gender, generally earlier in girls than in boys (Fig 7A, B, and C). This philosophy was based on the premise that the growth capacity of the bone would not be further restricted because of the surgical intervention and the scar formation.[17] Early intervention resulted in scar formation and often required additional surgery. A secondary procedure was technically challenging with a higher complication rate. On the other hand, the late surgery often showed relapse of the surgical result. It remains to be seen if new techniques will produce more stable results in the long term. Timing of the procedure is still open to discussion as is the instrumentation.

Mandibular Deficiency

The etiology of malformations of the lower jaws such as hemifacial microsomia is not very clearly understood. Neither are the genetic or the pathogenetic backgrounds of these syndromes.[18] The underdevelopment of the lower jaw is also called dysostosis otomandibularis, oculo-auriculo-vertebral spectrum, temporo-auromandibular dysplasia, or the first and second branchial arch syndrome. Mandibular dysostosis, (Treacher-Collins syndrome) has an autosomal dominant inheritance and a birth prevalence of 1 in 25,000 births. In one form or another, asymmetrical growth of the mandible occurs in 1 in 5000 births. The anomaly often extends beyond the mandible and defects are observed in the form of variation in the outer and middle ear, in the malar and frontal region, in the orbit, with involvement of both bone and soft tissue.

The degree of muscular underdevelopment of the different muscles of mastication in these patients has been shown to vary widely[19] and the severity of the muscular involvement cannot be predicted from the severity of the bone involvement. This is important to realize because expectations of

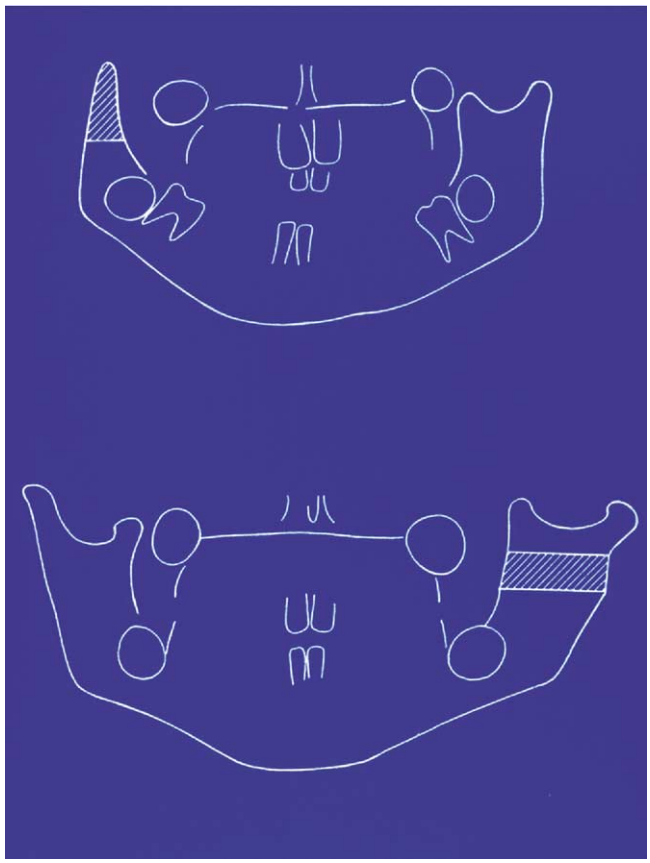

Figure 8 Illustrations of the possible surgical solutions to unilateral deficiency of the mandible (rib transplantation or distraction indicated by the crosshatched area left side. (Color version of figure is available online.)

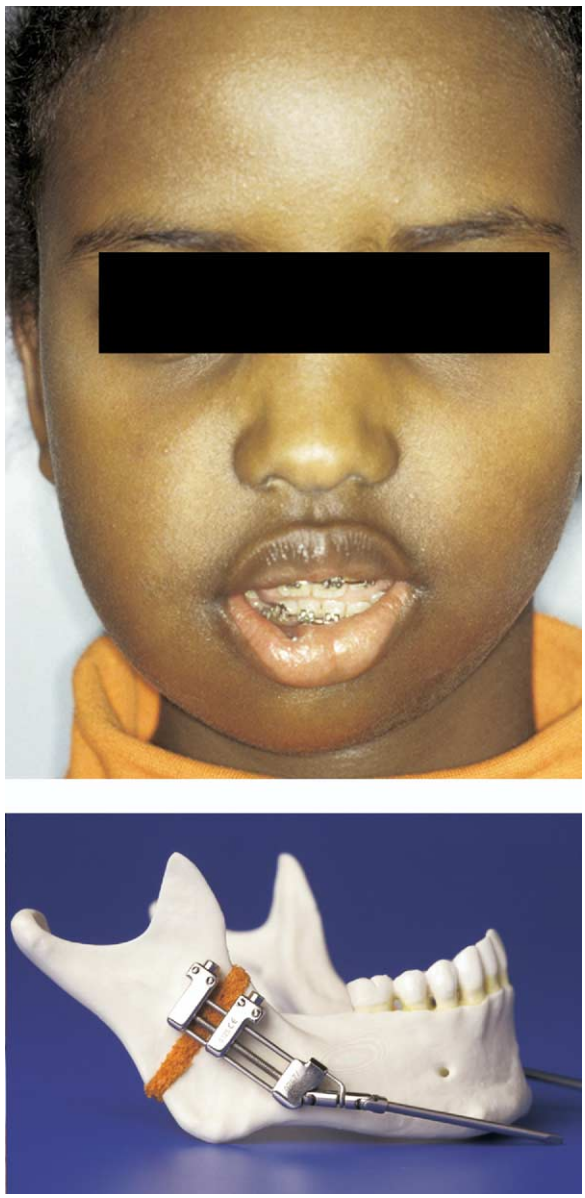

Figure 9 Illustration of intraoral distraction device in a patient with unilateral mandibular deficiency after ankylosis and rib transplantation. (Color version of figure is available online.)

treatment results will depend to a certain degree on the soft tissue deficiency.

At least seven classifications of mandibular deficiencies have been proposed in the literature.[20] The number of proposals calls for agreement on an international guideline, because literature search or meta-analysis cannot easily be performed.

The dental development is usually normal in children with hemifacial microsomia. The aggressiveness of the orthodontic intervention is debatable, but prevention and correction of dentoalveolar adaptation to the asymmetric position of the maxilla and the mandible is recommended to avoid extensive surgery of the maxilla.[21]

The surgical treatment of the bony asymmetry of the mandible can be addressed in two ways. Bone can be added by a bone transplant—usually a rib graft or the deficient part of the mandible is split in two and bone added in between the two bony surfaces (Fig 8). The latter can be performed by distraction osteogenesis or by a sliding osteotomy. In case of

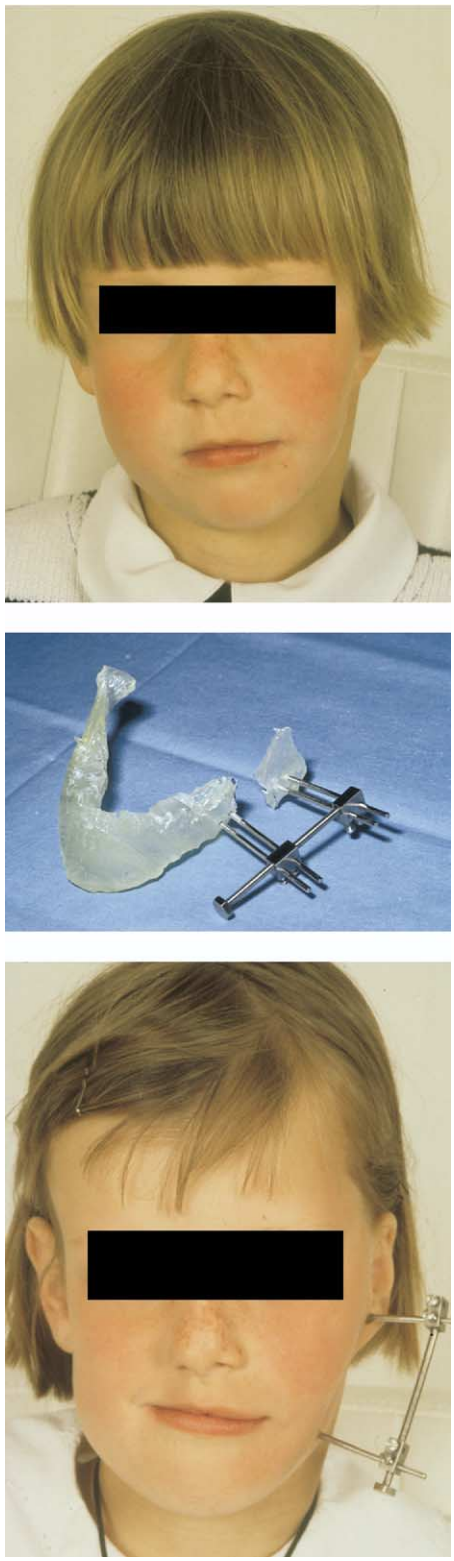

Figure 10 Illustration of an appliance based on computed tomographic scan modeling of the mandible. (Color version of figure is available online.)

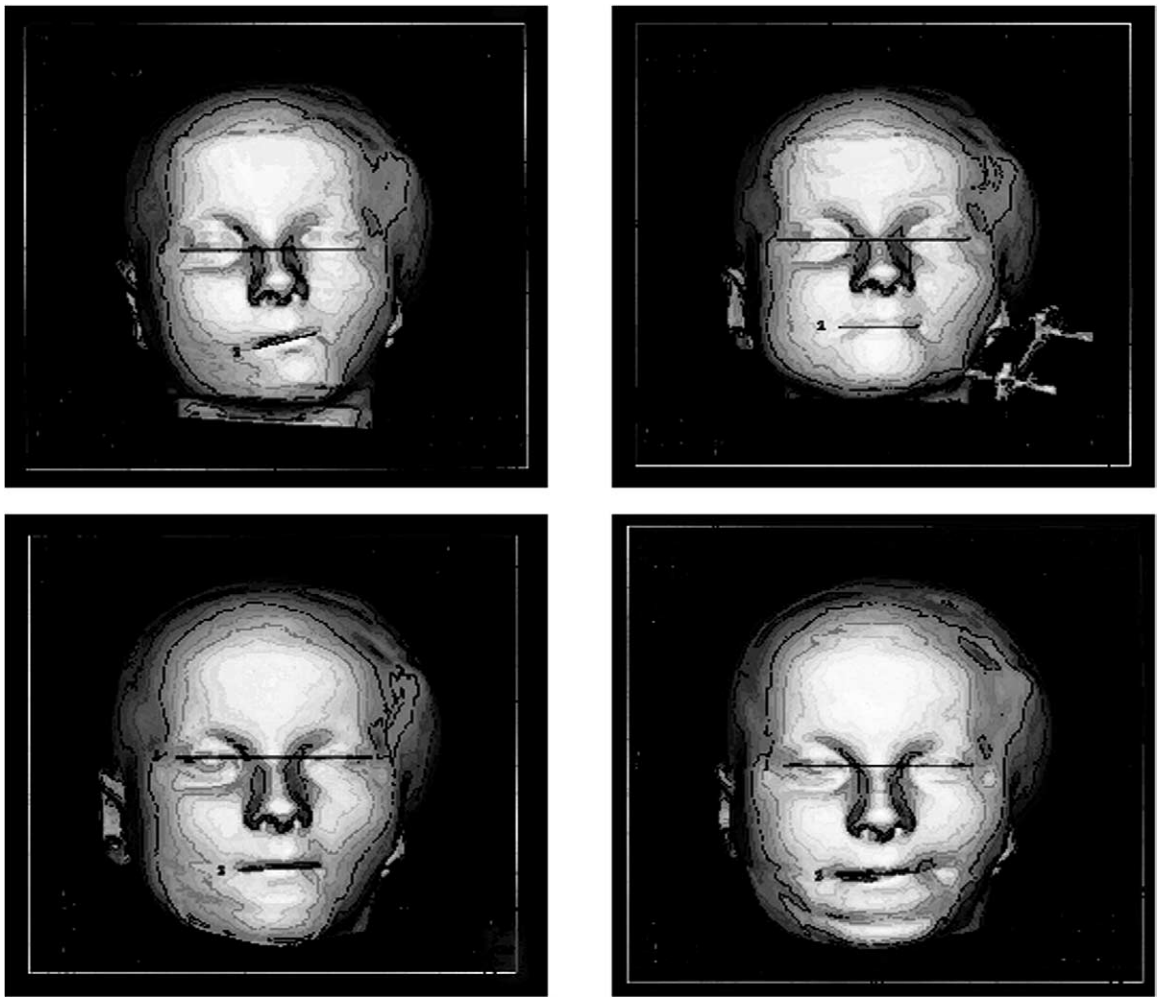

Figure 11 Evaluation of the outcome of distraction osteogenesis using computed tomography, 3D imaging.

a serious asymmetry of the lower jaw, with hardly any ramus present, it is advisable to delay the distraction procedure until the lower molars at the affected site are present. It may mean postponing the time of operation until after the age of 9 years and until the last deciduous molars have exfoliated before distraction or transplantation of a rib graft is performed. This allows for a better bony support for the distraction device.

The optimal time for the intervention in cases with hemifacial microsomia is debatable, depending on the size of the defect, the impact on the general health of the child, functional factors, and psychological factors.[22-26] Some of the unknown factors in managing distraction osteogenesis cases are the optimal age for the procedure, the possible amount of distraction per day, the optimal duration of retention, the optimal distraction device (Figs 9 and 10), and whether or not the procedure is more cost-effective and successful than the more traditional methods of managing these patients. An early distraction osteogenesis procedure will help the patient overcome possible psychosocial problems with an abnormal appearance, but it very often means that a second reconstruction will have to be performed at a later age.

A relapse has been reported in approximately 50% of the cases 1 year after distraction osteogenesis[19] and it is debatable whether or not the muscle volume increases. Probably an increase can be expected in the length of the muscle fibers, but it does not add to the bulk of the muscles. Evaluation of the effect of distraction osteogenesis is done best with 3D computed tomographic imaging[27] (Fig 11). Having experienced professionals on the team is important. Newer methods of treatment are rapidly being developed. Many practitioners who treat patients with craniofacial malformations often do so while still maintaining their regular orthodontic practices. Knowledge of the general principles of orthodontics and experience in this area are prerequisites to an optimal partnership in a craniofacial team.

Conclusions

Three areas of controversies in the treatment of craniofacial malformations are emerging and becoming more distinguishable: evidence-based care, need for treatment, and cost of treatment. In 2000, the WHO started a 5-year project with one of the objectives being to develop an international network for consensus building and planning of international

studies of craniofacial research. Fragmentation of care or treatment needs are most problematic at the present time.

Up to the present time, new methods of care have not been adequately tested for effectiveness and no evidence for effectiveness is actually available for the care that children with craniofacial malformations are routinely receiving. For example, the "new" method of distraction osteogenesis has been adopted for many years without adequate evidence. In the ideal circumstances the professional rendering the care should determine the need for treatment in concert and consultation with the patient or the parents. However, often patients, parents, and professionals have different perceptions of treatment needs. Guidelines for the treatment need should be developed and consensus reached between all involved.

The cost of treatment is a significant factor in the quality of the care. The quality of care should always be taken into account whenever strategies are developed to reduce the health care burden of craniofacial anomalies treatment. It should be a beneficial situation for the patient, the professional, and society at large. To improve the quality of care for children with craniofacial malformations, a general acknowledgment of the need for outcomes assessment is the real challenge.[13,27]

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