Habilitation of Severe Craniofacial Anomalies—The Challenge of New Surgical Procedures: An NIDR Workshop

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Dramatic new surgical techniques have made habilitation of severe craniofacial anomalies possible. This remarkable accomplishment means that those afflicted with deformities of the face and head need no longer suffer the social stigma of grotesque deformities in isolation. Along with the recognition that treatment is possible comes the responsibility to provide the best possible care. On this basis, NIDR initiated a series of three one-day seminars to stimulate discussions of promising areas for research endeavors among experts in the relevant fields of (1) developmental biology, (2) neurosurgery, and (3) reconstructive craniofacial surgery. The workshops were held in Bethesda, Maryland on November 5, 13, and 21, 1973.

The workshops were planned by Drs. Seymour J. Kreshover, Director, NIDR, Jan Langman, Professor of Anatomy, University of Virginia, and Richard L. Christiansen, Chief, Craniofacial Anomalies Program, NIDR. The discussions were recorded verbatim by a stenographer and were summarized for this report.

Previously untreatable congenital craniofacial anomalies are now being habilitated as a result of recent innovative surgical procedures. The craniofacial anomalies of primary concern in this context are Crouzon syndrome (craniofacial dysostosis), Apert syndrome (acrocephalosyndactyly) orbital hypertelorism, facial clefts, hemifacial microsomia, and other rare defects. Now that a high level of surgical expertise and operative success has been achieved in the treatment of these highly complex deformities, there is a need to assure that afflicted individuals receive optimum correction and benefit from new techniques derived from etiological information through both basic and clinically oriented research. The NIDR presented the task of identifying the most urgent treatment and research needs in the area of craniofacial habilitation to a group of developmental biologists and to two groups of involved clinical specialists representing the

areas of craniofacial surgery (plastic and oral surgery) and neurosurgery. Their remarks and recommendations will help in planning future investigations and in reevaluating past efforts.

The Problem

The group of craniofacial malformations considered here presents an interesting complex of very difficult-to-treat problems. Both Apert syndrome and Crouzon syndrome are characterized by synostoses of cranial sutures and malformation of the cranial base. Along with the cranial pathology there are various facial deformities such as maxillary hypoplasia, hypertelorism, and exorbitism. Orbital hypertelorism usually is associated with other developmental malformations of the cranium or face such as frontal meningocele, encephalocele or facial clefting. In hemifacial microsomia, there are unilateral eye and ear abnormalities and hypoplasia of the mandible. The radical reconstruction of these deformities involves combinations of intracranial-extracranial surgical exposures, maxillary and mandibular osteotomies with block repositioning of deformed units permitting orbital repositioning and midfacial advancement, cranioplasty, and use of bone grafts and alloplastic material implants. Where intracranial access is indicated, a neurosurgeon performs a craniotomy which may involve removing frontal bone and exposing the base of the skull. In situations where facial malformation accompanies cranial stenosis, the facial deformity is reconstructed ideally at the time that the cranial sutures are released. In this respect, treatment of Crouzon and Apert syndromes may be managed similarly. This is not yet technically feasible in very young patients; in such cases cranial stenosis is released without correcting facial deformity.

The incidence and prevalence of the severe craniofacial defects is not known accurately. However, it is estimated that there are approximately 1200 new cases of these rare abnormalities born every year in the United States (or 20–25 cases per 5 million population base). The conditions are therefore quite rare. Yet there are many important benefits from studying the small number of affected individuals. The time and expense devoted to these people is justified for the following reasons:

1. Many of these people have normal intelligence or the potential for normal intelligence. New developments in habilitation can eliminate the need for lifelong institutional care.
2. Human data are obtained relating to growth and treatment prognosis. This knowledge is applicable to humans in other situations (other anomalies, trauma, and nutritional, metabolic and neoplastic disorders).
3. There is potential for new information in the fields of embryology and growth and development. New findings in dysmorphology and basic developmental mechanisms can be used as an additional means of following normal development and better understanding the large number of less severely deformed children.
4. This is the beginning of a new field of habilitation which has the

potential of much further development with necessary interspecialty cooperation.

Research into Etiology and Prevention

Although the recent advances in surgery provide new hope for the affected, habilitation is itself long and difficult. The only complete solution to the problem lies in finding preventive measures through etiological research. Several areas have been identified where efforts are most likely to result in understanding the mechanisms of malformation and where new information might lead to working hypotheses about why things go wrong in any of the skeletal dysplasias.

The primary area where knowledge is deficient is in the major processes of embryonic development. Areas in developmental biology that are not adequately understood are (1) problems in neural crest cell migration, aggregation, and synchrony during tissue development, (2) mechanical factors operating in forming the embryo, (3) problems of timing and biological clocks, including programmed cell death, (4) environment and cell expression, (5) innervation and vascularization, (6) basement membrane functions, (7) matrix and connective tissue synthesis, deposition, and degradation, (8) cell commitment and determination, and (9) cellular communication and interactions. Defects in any of these processes could result in deformity. There is potentially useful information to be gained from studying single gene defects to identify specific metabolic disorders, teratology and the phenomena of embryo protection, rescue and reversibility. Also certain aspects of limb bud research may have application to craniofacial developmental studies.

Epidemiological research could suggest *in vitro* and *in vivo* models that may later have clinical application. Further progress could be made in the areas of *in utero* diagnosis, genetic counseling and identifying and improving the favorable conditions for successful pregnancies.

Considerably more basic information is needed about normal and abnormal development before the clinical problems are understood and clinical applications instituted. This may require the development of new research techniques and model systems. The use of clinical entities such as cleft palate as a model for use in basic research may not be the most useful because the complexity of the malformation makes clear-cut answers difficult to obtain.

Clinical applications are not immediately forthcoming from basic science research in the field of developmental biology. Moreover, it is difficult to predict which investigative approaches will have ultimate clinical value. Exposing basic scientists to clinical problems and needs might be fruitful.

Treatment and Patient-Oriented Research

Clinicians faced with planning the surgical habilitation of severely deformed patients have only limited information available about the etiology of the deformity and the long term consequences of surgical procedures

because of the limited number of cases and the short history of many of the surgical methods. This difficult position would be eased by obtaining urgently needed information in applied research areas concerning postnatal interception and habilitation of craniofacial anomalies.

I. Timing of Surgery. There are many indications for operating on young children. Early surgery has psychological benefits both in permitting more normal personality development in the affected child and in reducing family stress. There is speculation that without treatment the skeletal defects are progressive with age, cranial deformity increases with time, and the secondary changes in the face are magnified. It is thought that normal growth would be promoted by surgically reducing distortions of anatomic structures adjacent to the defect. Also, certain biological phenomena such as regeneration of cranial bones from infant periosteum only take place very early. Early bone repositioning encourages normal physiological patterns such as eye movements, speech, breathing and feeding. Surgical repair is undertaken in infants with multiple suture stenosis to prevent mental retardation and increased intracranial pressure. As noted earlier, some facial corrective procedures can be performed at the same time.

Surgical techniques have been improved to deal with the problems of anesthesia, fluid balance, blood loss, heat loss, and the smaller anatomic parts encountered in infant and pediatric surgery. However, information on normal growth and growth after surgical procedures is needed to determine the optimal technique, time, and sequence of procedures for correcting deformities surgically.

II. Normal and Abnormal Development. Treatment planning for young, growing children depends on an understanding of normal development and the defects which occur in this process. This is in addition to etiological information from studies in genetics and embryology.

There are many aspects of the growth process that need further investigation. Studies are needed on the morphogenesis of cranial and facial sutures and whether fusion of bone at a suture line is a primary or secondary effect. It is not known what specific growth abnormalities account for the abnormal maxillary and orbital development in Crouzon syndrome. In addition, stimulus-response research on the effects of force on a suture represents a major area of need.

Another problem relates to the influence of muscle and periosteum on development. Are there biodynamic laws governing the structure and physiology of the soft tissues? Is bone growth of the skull influenced by attachment of the dura? What is the relationship between growth and development of brain, dura and skull tissues? Are there interactions between the dura and bone? How do craniofacial bones grow and remodel in the various malformations? Do cranial sutures behave differently from facial sutures?

III. The Effect of Surgery on Growth. The influence of surgery on subsequent craniofacial growth is generally not known. How the growth

processes are affected by denervation, muscle reattachment and changes in circulation is speculative at the present time. In children under 6 years who have had major resections for hypertelorism, there does not appear to be any progressive disproportion or any gross stunting of growth when growth areas and scar contractures are avoided. However, the extent of the impact of surgical manipulation, especially in procedures utilizing the intracranial approach, has not yet been determined.

A number of specific questions regarding osteotomies and bone grafting need to be investigated. Do bone cuts arrest facial growth? Does the effect of a cut placed in a suture differ from one placed adjacent to a suture? Is instrumentation a variable? Does bone grafting stimulate or inhibit sutural apposition? Does the position of the graft or the type of bone make a difference? Should bone grafts be placed under periosteum and should bone with intact periosteum be used? Will forward traction after an osteotomy reduce the amount of absorption of a bone graft placed in the osteotomy site? Does simple elevation of the periosteum affect development? How does cranial bone regenerate from elevated periosteum? Does the tightness of overlying soft tissues affect the success of a surgical procedure? What is the effect of surgical correction on dental development? Is tooth eruption affected by procedures reducing blood supply or nerve supply? How does denervation produce soft tissue hypertrophy resulting in macroglossia and compression of the eye? How does plexiform neurofibromatosis produce local giantism? What are the post-operative changes in muscle when bone segments are moved and muscles are detached, sectioned or repositioned? Can increased circulation affect growth in the same way that hemangiomas and atrioventricular fistulas promote growth in the size of bones and teeth and cause earlier eruption of teeth? What types of fixation of skeletal fragments are most satisfactory?

Another area with potential clinical relevance is the possibility that normal growth is released when abnormal restrictions are removed. There is some clinical evidence, for example, that if the synostosis in the cranial base is actually divided during the craniostenosis operation in infants, severe facial defects are avoided. It may also be possible that the peculiarities in the mandibular configuration in Crouzon syndrome are related to the interference in growth of the midfacial complex. It is noted that in cases of hemifacial microsomia, relatively normal maxillary growth is sometimes obtained when the entrapping effect of the mandible is removed. If growth can be released, the total amount of surgical management required will be decreased.

There is a great potential for biomechanical devices and techniques in the treatment of severely deformed children. It is possible that methods could be developed to apply forces to the growing cranium and thereby avoid such extensive surgery. One method already producing good results in cranial deformities is a combination of an orthopedic helmet and the manual molding of the skull by the child's mother after cranioplasty has

been performed. Another possible method would apply forward traction on the midface as a dynamic approach to pull the face into position. The growing brain itself applies natural expansile forces which can be used to help position comminuted bone during growth.

The safety of alloplastic materials in children needs to be evaluated. Tissue reactions, growth effects and the risks of infection should be considered for the various substances used, such as methyl methacrylate. Studies to develop methods of promoting wound healing around prostheses would be beneficial.

The amount of neurological disability in craniostenosis is generally correlated with the amount and duration of elevated intracranial pressure and may be related to the number of bony suture lines prematurely closed. It is usually thought that the increased pressure of the growing brain inside the non-expanding skull is responsible for producing brain damage. The justification for surgery in craniostenosis, therefore, is to allow more room for the growing brain, prevent brain damage, and enhance cosmesis. This must be done as soon as possible, preferably in infants. It is not known whether surgery done later has any influence on further mental development. If stenosis is allowed to persist, visual acuity may also suffer. A single closed suture probably has less effect on the total brain volume or mental status; corrections for isolated sagittal stenosis are mainly done for reasons of appearance.

Many questions are posed in relation to the neurosurgical procedures for craniostenosis and cranial reconstruction. How adaptable is the shape and volume of the brain in a reconstructed cranium? How is the ventricular system affected? Is there a potential danger of seizures postoperatively or future hydrocephalus from hemorrhage getting into the subarachnoid space? Are there risks of creating venous insufficiency or edema when emissary veins coming through the skull are excised? What procedures affect fluid balance in the brain? Will the duraplasty which is performed to shape brain contour alter intracranial pressure? Are techniques such as radiographic brain scan useful in monitoring changes in the size and shape of the brain after surgery?

Long-term follow-up studies on such procedures as surgical orthodontics, prosthodontics and reconstructive therapy instituted at different age levels will give insight into the optimal timing of treatment. The judgement of habilitative success must be made with periodic assessment of the patient generally over several years of observation. Such assessment has not previously been possible postoperatively because of the short history of such treatment.

IV. Other Effects of Surgery. Other questions needing answers are: What are the risks of infection from nasal and oral bacteria when the cranial cavity is opened during intracranial procedures? How are the sensory functions affected? There is evidence that hearing may be improved postoperatively in some instances. Also, postoperative ptosis has been observed. What will happen to taste, olfaction and speech? In cases

of hypertelorism, can fused vision be obtained if the operation is performed early enough? What can be learned from psychiatric and psychological evaluations of patients before and after correction of the deformity?

V. Animal Experimentation. Many of the above questions could be investigated in animal experiments especially those involving controlled applications of surgical techniques. Types of animal studies that could supplement clinical observation are: (1) pilot studies on limited surgical procedures, (2) more refined studies closely related to human surgery using larger primates, (3) experiments using naturally-occurring pathology such as rabbits with natural craniostenosis, or dogs with exorbitism. Animal experiments would be most useful in answering individual specific questions. Many of the shortcomings of human experimentation can be avoided by appropriately selected animal experiments. These shortcomings result from the fact that human surgery is aimed at the welfare of the patient. In humans, manipulations cannot be controlled for the sake of the experiment. Scientifically based observations are elusive because no two patients have the same problem with the same severity, and the number of patients is small. In addition, follow-up study is generally limited to non-invasive measurements.

Centers

Success in correcting craniofacial deformities is hampered by three major problems. First is the paucity of data available about the anomalies and results of reconstruction. The very small numbers of patients makes it difficult for any clinician to treat many of these patients. Second is that patients do not always receive the optimum care. There have been bad results when inexperienced or untrained personnel have tried to handle these cases. The team doing eventual radical reconstruction should see the patient from the start. A solution to this confusing situation may be found in centralizing data-gathering and treatment. The other problem is that relevant research needs to be encouraged.

A public central registry of biological data on craniofacial anomalies could provide clinicians with treatment records on large numbers of these patients. If a system of standardized data gathering could be developed, it would be possible to examine treatment results accurately. A great amount of usable information could be gained from patients with craniofacial deformities that is not now being obtained, if a uniform system of records were used in collecting data by all people in this field. A desirable system would (1) identify the deformities under study and (2) define parameters for study. It would include a quantitative assessment preoperatively and postoperatively based on techniques such as cephalometric radiography in both lateral views and posterior-anterior views. Implants might be a useful adjunct for cephalometric study. If the system were computerized, it could be easily and quickly available for clinicians in any location to add to or use the information.

The critical problem in providing the best care for the affected patients could be best handled by placing competent personnel in a central location. Identifying experienced treatment teams by a special designation would control to a great extent where patients receive treatment. This would help satisfy the need for leadership in this new field of habilitation.

This is the time to consider establishing craniofacial anomalies centers where data collection, treatment and research could be conducted. A similar decision was made in the cleft palate field several years ago and lead to the creation of cleft palate centers. Indeed, the hopes and expectations for centers for severe anomalies is based in part on the success of cleft palate centers.

The proposed centers for craniofacial anomalies would be scientific research centers with a broad perspective, considering the wide range of craniofacial problems from birth defects to developmental errors of post-adolescence. All major craniofacial deformities would be accepted including severe malocclusion. Based on the occurrence of severe anomalies, a center should serve a geographic area of no fewer than twenty-five million people.

The desired personnel and resources should be adequate to take care of all phases of habilitation. The clinical team would include such people as a reconstructive craniofacial surgeon, neurosurgeon, geneticist, pediatrician, orthodontist, pedodontist, social service worker, psychiatrist, speech therapist, etc. These specialists would be involved in treatment, epidemiology, genetics, and patient-oriented research. Another bonus of a center would be the potential for training clinical investigators.

A more controversial conception of a craniofacial anomalies center would include an extended interdisciplinary type of research environment where investigations in developmental biology could be conducted along with applied or clinically-related research. Would such centers be the best setting for developmental biology research? Would this encourage biologists to conduct basic research relevant to the anomalies?

There are strong feelings that justification for combining basic developmental biology within such centers does not exist. The clinical problems are very difficult and very complicated. At the present time, developmental biology does not have enough information to offer much clinical application. It is felt by some participants that when the state of science is developed adequately, communication will develop automatically. In the meantime, large organizational efforts that artificially impose direct interdisciplinary activities between clinical and basic scientists will likely fail. The basic science investment may be better spent on funding research fellows and supporting research needs in existing laboratories. This problem is also occasionally seen in clinical fields where multidisciplinary clinics are difficult to maintain. A craniofacial anomalies research program cannot be forced.

On the other hand, there should be communication between basic scientists and clinically-oriented people. The clinicians can help the basic scientist recognize the clinical relevance problem and the developmental biologist

can help the clinicians replace the empiric grounds for treatment with a biological foundation.

Recommendations

The following recommendations were supported by most of the workshop participants:

1. That the population of severe untreated craniofacially deformed individuals be identified as needing special attention from the health science community.
2. That craniofacial anomalies centers be considered for data collection, treatment and clinical research. The extent of direct basic science involvement in these centers is uncertain.
3. That basic science research into the etiology of craniofacial anomalies be encouraged.
4. That communications be developed to further the new field of habilitation. An international congress or symposium, publication, or newsletter could be considered.

Summary

Three NIDR-sponsored workshops were conducted with the goal of identifying research needs in treatment and basic sciences relating to a group of severe craniofacial anomalies that are now correctable by new radical surgical procedures. Experts in the fields of developmental biology, neurosurgery and reconstructive craniofacial surgery discussed areas of investigation dealing with etiology, prevention and treatment that are most likely to result in clinically-useful information. In addition the establishment of craniofacial anomalies centers for data collection, treatment and research was examined.

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