

Clinical Research In Cleft Lip and Cleft Palate: The State of the Art*

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I. INTRODUCTION

This report has been prepared at the request and through the support of the National Institute of Dental Research. A contract was awarded to the American Speech and Hearing Association for the following purposes: (1) To review in depth the present status of clinical research on cleft lip and palate and to explore the gaps in knowledge. (2) To discuss approaches to filling the research gaps. (3) To identify areas that need no special research emphasis. (4) To recommend specifically those research areas that need development and to stimulate research activity in these areas.

K. Kenneth Hisaoka, Deputy Associate Director for Extramural Programs, NIDR, initiated the State-of-the-Art review. Richard F. Curlee, Associate Secretary for Research and Scientific Affairs, American Speech and Hearing Association, was the Project Director for ASHA. Zora J. Griffo, Chief Developmental Biology and Orofacial Anomalies, Extra-

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The Committee Chairman was D. C. Spriestersbach, Ph.D., Vice President and Dean, Graduate College, University of Iowa, Iowa City, Iowa. Chairmen of the Sub-Committees were: Aspects of Etiology and Pathogenesis, F. Clarke Fraser, Department of Biology, McGill University, Montreal, Quebec, Canada; Anatomical and Physiological Aspects, David R. Dickson, Ph.D., Cleft Palate Center, University of Pittsburgh, Pittsburgh, Pennsylvania; Pediatric and Otologic Aspects, Jack L. Paradise, M.D., Department of Pediatrics, University of Pittsburgh, Pittsburgh, Pennsylvania; Orofacial Growth and Dental Aspects, Sidney L. Horowitz, D.D.S., School of Dental and Oral Surgery, Columbia University, New York, N.Y.; Surgical Aspects, Peter Randall, M.D., Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania; Speech and Psychosocial Aspects, Betty Jane McWilliams, Ph.D., Cleft Palate Center, University of Pittsburgh, Pittsburgh, Pennsylvania.

mural Programs, was the Project Officer for NIDR. Richard L. Christian-sen, Program Officer, was an NIDR observer.

This report summarizes the current state of knowledge among the major clinical and research disciplines involved in the study and management of cleft lip and palate. In addition, it suggests some fruitful areas for future research, findings from which may help to reduce the prevalence of the disorder, achieve more effective functional results, ameliorate the psychological problems of affected persons and their families, and lower the financial cost of treatment.

The clinical management of patients with cleft lip and palate has improved remarkably in the past 20 years. In large part this favorable trend is attributable to support of research and training in the field of orofacial development and function by the National Institute of Dental Research and other concerned federal agencies. In addition, the development of interdisciplinary teams has improved the quality of therapy and has been a significant factor in attracting to the cleft palate field many research workers and clinicians. Despite the advances of the last two decades, however, large gaps still exist in our understanding of how persons with cleft lip and palate should be treated. For example, it has become increasingly evident that the masticatory-respiratory-phonatory-articulatory-auditory system is tightly coupled both developmentally and functionally. Consequently, changing the parameters in any part of the system is likely to change the function of the entire system. Yet many aspects of these parameters and the restraints within which they operate remain to be delineated. It is clear, therefore, that much more research, both fundamental and applied, will be required before many of the problems related to the management of individuals with cleft lip and palate can be solved.

To accomplish an assessment of this complex field the Planning Committee established subcommittees to evaluate the following: etiology and pathogenesis aspects, anatomical and physiological aspects, pediatric and otologic aspects, orofacial growth and dental aspects, surgical aspects, and speech and psychosocial aspects. Each subcommittee prepared a preliminary assessment of its assigned area. These drafts were circulated to the chairmen and two chosen representatives from each area. A two-day face-to-face review by the chairmen and representatives from all subcommittees provided the chairmen critical evaluations of their preliminary reports. The subcommittee chairmen then returned to their subcommittees and prepared a final report. It is anticipated that each of these reports will find its way into the literature. This report being presented to the readers of the *Cleft Palate Journal* is organized according to the topics assigned to the subcommittees followed by general conclusions and recommendations. And, the report presents the essence of the findings and recommendations of all of the subcommittees. The roster of participants may be found at the end of the report.

II. ASPECTS OF ETIOLOGY AND PATHOGENESIS

A. ETIOLOGICAL STUDIES IN MAN

Perhaps the greatest drawback to genetical and epidemiological research on clefts of the lip and of the palate has been the unfortunate tendency to lump them together. There is good embryological and genetical evidence that isolated cleft palate is developmentally and genetically different from cleft lip (4, 14), which may or may not have an associated cleft of the palate. Conclusions based on data in which the two types were combined have led to considerable confusion.

1. Epidemiology

There is no evidence from population studies of incidence that important environmental factors influence the frequency of cleft lip (with or without palate, but without other defects), and further epidemiological studies directed to the detection of such factors are not likely to be fruitful, unless they are designed to detect far more subtle influences than could previous studies (11a). Clinical and family investigations directed to the question of etiological heterogeneity could be useful.

For isolated cleft palate, on the other hand, and for clefts combined with other defects, there is a little evidence for nonrandom environmental influences (11a). Further studies, particularly looking for differences between familial and non-familial cases of cleft palate, and between clefts with and without other major defects, might be informative. For such enquiries, as for twin studies, data on a much larger population would be needed than are now being assembled in any one place in the United States.

There is need for data on prenatal events associated with cleft lip. Retrospective studies are likely to be biased, and prospective studies expensive and tedious. A compromise approach would be to study the physiology and metabolism of mothers who had given birth to an affected child. Such mothers could also be followed through subsequent pregnancies, about 5% of which would result in affected children. This would probably require a collaborative study.

ANALYTIC STUDIES. Analytic studies, comparing other characteristics of individuals with and without defects, have suggested association between clefts and (a) nausea and vomiting in pregnancy (1, 13); (b) miscellaneous drugs, including anti emetics (13); (c) maternal bleeding (1, 4); (d) toxemia (4); (e) increased maternal antagonism to insulin (15); and (f) toxoplasmosis antibodies (2). Folic acid deficiency and abnormalities of serum proteins have both been reported in abnormally high proportions of mothers of malformed children generally (8, 10). Several preliminary reports suggest that anti-epileptic drugs may, occasionally, cause cleft lip and palate (12), and this is a question that should be thoroughly investigated.

If these findings are not fortuitous, some (such as the association with maternal bleeding) may be due to the malformation producing the other findings, rather than the reverse; and others (such as the positive nutritional and biochemical findings) may indicate genetically determined abnormalities which predispose to clefts, interacting with environmental factors. In either case, further study of the possible relationship of nutrition and biochemistry to clefts (especially during pregnancies of women who have already had affected children) could well be rewarding, since if it were found that, for example, a genetically determined low level of tissue folate could cause clefts, it might be possible to override this effect by massive doses of this vitamin in high-risk cases.

2. Genetics of Cleft Lip and Cleft Palate

There are now several extensive bodies of data on families of probands with cleft lip, with or without cleft palate, providing frequencies of recurrence in various categories of relatives. These are, in general, reliable and are useful for genetic counseling (4).

In an unselected series of children with cleft lip or cleft palate, a small proportion (about 5%) would be caused by major mutant genes (these children often have associated defects which constitute a syndrome), a small proportion by chromosomal aberrations (these also are likely to result in syndromes), a few by nonrecurrent environmental factors and the majority by the interaction of many genetic and environmental factors, individually indistinguishable—the multifactorial group.

The existence of an environmental component to the etiology raises the possibility of reduction in frequency by environmental means.

It would be useful to identify measurable indications of genetic susceptibility. Data from teratological studies on mice suggested that shape of the embryonic face might be such an indication (14). Preliminary studies in man support the hypothesis both on the basis of surface topography (4), and cephalograms (11b). The most efficient indication of genetic predisposition would be the unaffected monozygotic twin of a child with cleft lip, since such a twin would presumably be near the threshold. A small series of twins does show some of the expected features (9), but many more monozygotic discordant pairs are needed.

Another indication of genetic susceptibility would be the occurrence of "microforms," or minor degrees of the major defect. There are many uncritical studies and unjustified claims in this area (4). To be a microform, the anomaly must occur more frequently in the near relatives of persons with the major defect than in the general population. This appears to be true for cleft uvula and submucous cleft palate in the families of patients with cleft palate. It does not seem to be true for nostril asymmetry or missing lateral incisors in relation to cleft lip. Further critical studies would be useful.

3. Genetics of Cleft Palate

Because isolated cleft palate is less frequent than cleft lip (with or without cleft palate), there is much less genetic data available. Cases of cleft palate probably fall into the same four categories—major mutant genes, chromosomal, environmental, and multifactorial, but the proportion of multifactorial cases may be smaller than for cleft lip. There is a need for the collection of more information on frequencies in relatives, on twins, and on the physical characteristics of unaffected near relatives.

4. Syndromes

Cleft lip and/or cleft palate may be part of a syndrome of defects, in which case its cause and mechanisms will be related to that of the syndrome. Over 100 syndromes are known (7) that involve clefts of the lip or palate, of which about a third are caused by major mutant genes, a few result from recognized chromosomal aberrations, and many have no recognized cause.

The study of syndromes may provide useful information on the causes of clefts, but syndromology is a field that still presents some difficulties. For one thing, there is a great need for normative standards. Many syndromes are characterized by various subjectively determined features, such as low-set ears, wide-spaced eyes, low-set thumbs, or micrognathia. It is necessary to develop criteria for such features that are both objective and easily determined at the bedside. We need to be able to assess objectively whether an ear is low-set, or a mandible small, without radiologic cephalometry, for example.

Furthermore, not all features of a syndrome occur in every case, and some features occur in some normal individuals. There is a need for data on the frequencies of features such as confluent eyebrows and hypertelorism in the general population, and for extensive data on the frequencies with which the features of a syndrome occur in cases of the syndrome.

B. EXPERIMENTAL STUDIES ON MECHANISMS AND CAUSES

Observations on normal palate closure and experimental analysis of mechanisms by the use of teratogens and genetic differences have contributed greatly to our understanding of the process and how it may fail, but there is much to learn (5). Knowledge of lip formation and its failure is much less advanced than that of palate closure, but similar concepts and strategies apply (6).

The methods of modern molecular biology are just beginning to be applied to the problem (16). Although analysis is difficult—being complicated by the fact that the process is proceeding in utero, in an amnion, in an embryo in which many things are happening at once—progress is being made. There is need for further research along the following lines.

1. Continuing Study of the Normal Process in Human Embryos

Understanding the normal increases the probability of understanding the abnormal, and developing preventive measures. Conclusions based on experimental material must be confirmed in man by study of therapeutically or spontaneously aborted embryos. Much valuable material is being wasted, either through being discarded or being stored in inaccessible places, or being inadequately processed. There is a need for an organized system for collecting embryos in a state suitable for analysis (e.g., karyotyping, biochemistry, gross and microscopic anatomy), with proper antecedent histories, and a system for making them available to interested scientists.

2. Further Study of How Teratogens Cause Cleft Palate

Further study will

(a) improve understanding of the mechanisms by which cleft palate can occur;

(b) elucidate possible synergisms between factors—for example, possible interactions between a susceptible genotype, a transient maternal nutritional deficiency, and oligohydramnios resulting from pernicious vomiting;

(c) warn of possible teratogenic hazards in man, such as drugs, pesticides, herbicides, food additives, or chelating agents. Demonstration of teratogenicity in experimental animals does not necessarily mean teratogenicity in man, however, and failure to demonstrate teratogenicity of an agent in animals does not mean it will be harmless to the human embryo (3). Experimental testing is a guide, not a safeguard;

(d) allow a search for possible preventive measures—e.g., ways of making the palatal shelves move earlier (without having disruptive effects elsewhere) would increase the resistance of the embryo to all cleft-palate-producing factors.

3. Utilization of Present Methods of Organ Culture and Development of Better Ones, to Aid in the Objectives Stated Above**C. RECOMMENDATIONS (NOT IN ORDER OF PRIORITY)**

1. The techniques of molecular biology are beginning to be applied to mammalian teratology. Careful, critical work in this field should be encouraged with a view to a better understanding of normal and abnormal developmental mechanisms, environmental predisposing factors and possible preventive measures.

2. Systems should be developed, on a regional or national basis, for preserving and making available for morphologic, genetic and biochemical study, embryos obtained from spontaneous and therapeutic abortions. A workshop should be organized to develop such a system.

3. Further epidemiological studies should be done only to test specific hypotheses. Studies based on information from birth certificates will be untrustworthy until there is a marked improvement in reporting.

4. Twins, and particularly discordant monozygotic twins, should be exploited more fully both to identify predisposing features and to evaluate the effect of the malformation on the total phenotype. This would require collaboration (since no one center sees enough twins) and perhaps a data bank.

5. Prospective studies should be organized, on a collaborative basis, on the prenatal biology of each mother who had given birth to an affected child to follow subsequent pregnancies in an attempt to identify predisposing environmental factors.

III. ANATOMICAL AND PHYSIOLOGICAL ASPECTS

Today there is a critical need to develop more efficient and effective methods of diagnosis and treatment of persons with cleft palate. However, the palate is but one part of the developmentally, acoustically and physiologically coupled aural-oral-facial-pharyngeal-laryngeal-respiratory system subsuming oral communication, mastication, deglutition, and respiration. Thus all parts of the system are of immediate relevance to a study of the cleft palate.

In all areas of research on clinical problems, prime requisites are an adequate body of information on the exact nature of the disorders in all of its forms, and the necessary normative data to act as points of reference. Unfortunately, the structure and function of this system in the normal is not well understood. It is natural, then, that data on the abnormal is grossly lacking. The literature on this subject has been reviewed and documented in detail (19, 22). Some of the most imperative needs for research will be highlighted here.

THE PALATE AND PHARYNX

The need for further anatomical and physiological research in the areas of normal and cleft palate is apparent. With regard to normal patterns of movement, the specific nature of the lateral pharyngeal wall involvement needs to be further delineated (33). The site of maximum movement relative to the torus tubarius needs particular attention (23). Detailed electromyographic investigation of all the muscles of this area is still necessary to resolve the conflicts apparent in the available literature (21, 26). However, this work must be either preceded by or coincident with more detailed anatomical study of the normal mechanism. There is little specific information on the developmental morphology of this musculature. Detailed studies of the palatopharyngeus, palatoglossus, and uvular muscles are almost nonexistent. With regard to nerve supply there is still a need to sort out the pharyngeal plexus and the origins of

the vagus nerve. This may be possible through embryologic and fetal studies. Studies of the anatomy and physiology of the palate and pharynx of the person with cleft palate are not nearly as advanced as studies of the normal structure and function. Radiographic and motion picture studies of these movement patterns and their degree of variability needs to be pursued in a manner similar to that in studies of the normal. The field of electromyography of the cleft palate is practically virgin territory. While some good information is available on the musculature of the cleft palate (25, 35), more detailed information is necessary to indicate the degree of variability which should be expected with various types of cleft palate. Nerve supply and blood supply in cleft palate have received very little attention.

THE EUSTACHIAN TUBE

Middle ear disease associated with cleft palate has a high incidence and has been related to malfunction of the Eustachian tube (20). However, normal Eustachian tube function is still not agreed upon (30), and information on its structure and function in cleft palate is extremely sparse.

THE TONGUE

With regard to the tongue, the most urgent need in terms of the normal mechanism is for better information on the anatomical structure of the human tongue. There is ample evidence of the fact that the structure of the human tongue is unlike that of lower animals in many important ways. Thus animal studies will not suffice. Yet, only fragmentary human research on tongue anatomy has been reported (17). Physiological studies of the normal tongue and anatomical and physiological studies of the tongue of cleft palate persons should be planned.

THE LARYNX

The anatomy of the normal larynx has been the subject of intensive investigation (28, 34). However, much work remains to be done on the musculature, blood supply and innervation (18). Electromyographic studies of laryngeal function (24, 27, 29, 31, 32) have been numerous. However, there is still a lack of agreement on specific muscle function. No information has been found on the anatomy or physiology of the larynx in cleft palate.

THE FACE

With regard to facial anatomy, one of the areas of chief concern in the management of cleft palate about which we have only fragmentary information is the anatomy and developmental morphology of the nasal

and alar cartilages and the nasal septum. These structures need to be further delineated in the adult and in the child. From information which is available, it is apparent that there are distinct racial and ethnic differences in the morphology of these structures. Yet, little has been done to delineate the nature of these differences or the range of variability. Thus, within the human species, we need much more comparative anatomical information.

COMPARATIVE ANATOMY

As in the case of necessity for comparative studies within the human species, studies comparing and contrasting human and subhuman form and function is necessary in order to improve understanding and derive basic biomechanical concepts of function. By contrasting the form and function of one adaptive arrangement with that of another, the workings of these different structural complexes may be, in part, deciphered. There are many instances in which light has been shed on problems of human function such as the overlapping innervation of the middle ear and mandibular musculature by such comparative studies.

DEVELOPMENTAL ANATOMY AND PHYSIOLOGY

A most obvious area of important information is how anatomical and physiological parameters change with growth. With regard to the structures referred to above, such information is almost totally lacking. In addition, further delineation of the differences between the processes of synchondrosis and syndesmosis and the implications that these differences suggest for surgical management is necessary. Also, more complete understanding of the embryogenesis of peripheral structures will aid us in understanding the embryogenesis of the central nervous system. This may help us to understand certain enigmas such as that related to the development of the mesencephalic nucleus within the brain stem rather than external to it.

CONCLUSIONS

Basic knowledge of the structure and function of the normal mechanism, differences in structure and function associated with clefting, degree of variability in the normal and abnormal, and parameters of developmental morphology are all basic to (1) the development of more efficient and effective methods of diagnosis and treatment, and (2) evaluation of treatment methods. However, not only is such basic knowledge lacking, but the rate at which information is being accumulated is retarded by several factors. First, there is a need for more investigators well trained in anatomical and physiological research who are also trained in an interdisciplinary atmosphere with extensive exposure to speech, dental, and surgical management problems. Second, more opportunities for joint

research among current investigators must be encouraged. Third, there is need to integrate studies of structure, muscle function, growth and development, air flow and pressure, acoustics, and movement patterns. Fourth, there is urgent need for translation of foreign research. Our progress is impeded in part by our lack of familiarity with the work currently being reported in languages not spoken by the majority of investigators in this country. For example, work on the anatomy of the tongue has been reported in the Portuguese literature. No translation of this work is available. Adequate translations of scientific articles are extremely expensive. Yet no means is currently available for routine translation of this type of work. Thus, much of it goes unrecognized.

IV. PEDIATRIC AND OTOLOGIC ASPECTS

The cleft palate patient poses major and continuing problems from birth onward. His parents must be supported through their initial reactions to the deformity, and their questions about prognosis must be faced even though complete answers are not available. Other congenital anomalies which may be present sometimes require more extensive care than does the cleft itself.

Pediatric concern with the physical well-being of infants and young children with cleft palate tends to be directed toward three general areas discussed below.

FEEDING, NUTRITION, AND GROWTH

From the beginning, infants with cleft palate are likely to encounter difficulty with feeding, characterized by inefficient suction, nasal regurgitation, and choking episodes. Individual feedings are often laborious, time-consuming, and of lesser volume than in normal infants.

Although standard pediatric textbooks (91, 98) tend to minimize these feeding problems, various authors (109, 102, 56) have provided valuable descriptive accounts; in one study (56), 73% of 124 infants with cleft palate had moderate or severe feeding difficulty. Palatal prostheses have been considered helpful by some authors (109, 56, 74, 46, 105, 78), but supporting data are lacking.

In several studies the height and weight of children with cleft palate have been found to be lower than those of siblings or other controls (56, 61, 65), and in one of these studies (56) there appeared to be a correlation between severe feeding difficulties in infancy and below average weight in later childhood. However, prenatal factors, rather than post-natal nutrition, might have been mainly responsible.

Information is inadequate concerning the prevalence and severity of feeding difficulties in infants with cleft palate; their possible relationship to the type of cleft, or type of care; the degree of their impact on the infant, mother, and other family members; and the degree of success in

compensation, either through intrinsic mechanisms, or with the help of introduced maneuvers or devices. Unfortunately moreover, the published studies concerning feeding are not prospective, and do not provide data on rates of growth.

Recently, work in both experimental animals (104, 39, 80, 103, 81, 107, 47, 57, 68, 49, 73) and humans (45, 100, 55, 86, 72, 93, 85, 48, 50, 63, 53, 66, 52, 106, 108, 97) has suggested, but by no means established, that restricted nutrition during early infancy may leave permanent, adverse effects on both somatic and brain growth, and mental or psychological development. The extent to which infants with cleft palate are at nutritional risk therefore takes on added importance. As a first step, there is need to document the anthropometric growth of cleft palate infants by organizing existing data, or by collecting new data prospectively, concerning (a) increments in height, weight, and head circumference, and (b) basic laboratory parameters of nutrition, such as hemoglobin, serum albumin, amino acid, and alkaline phosphatase levels. Studies of monozygotic twins discordant for clefting might provide useful comparative data.

THE PIERRE ROBIN SYNDROME

Cleft palate infants who also have retrognathia and glossoptosis often have more serious symptomatology, and are at greater risk, than infants without these associated abnormalities. Specifically, more severe feeding and nutritional problems (56), glossoptotic hypoxia, aspiration pneumonia, and even cor pulmonale with congestive heart failure and pulmonary edema (70) may occur. Although most patients can be managed adequately if kept in a prone position, glossopexy (87), tracheostomy (94, 92), gastrostomy (59), or combinations of these procedures are sometimes undertaken in an effort to avoid or overcome respiratory obstruction. Most patients weather the early months of life, during which spontaneous mandibular growth eventually results in sufficient forward movement of the base of the tongue (94), but some patients fail to survive despite vigorous medical and surgical therapy, and some who survive continue to have retrognathia.

That periods of hypoxia can cause brain damage is well documented (96, 51). Moreover, the hypoxia and hypercapnia resulting from respiratory obstruction tend to generate a vicious pathophysiologic circle, characterized by acidemia, intracellular acidosis, massive catecholamine release, and pulmonary vasoconstriction, hypertension, and parenchymal changes (60, 54, 67) which enhances the risk of further hypoxia, hypercapnia, etc.

Insufficient information is available on the prevalence and severity of such hypoxic episodes in patients with the Pierre Robin syndrome. Hypercapnia is an early indication of respiratory obstruction, and its presence can be readily established by determination of the P_{CO_2} . Data

concerning both P_{O_2} and P_{CO_2} would provide an improved basis for assessment of risk in this syndrome and for further study of its pathophysiology and of methods of management. Neurologic, psychometric, and psychologic studies in later childhood of patients with Pierre Robin syndrome who had experienced hypoxia during infancy have not been reported, but would be of interest.

OTOLOGIC AND AUDIOLOGIC PROBLEMS

The literature concerning middle ear disease and hearing loss in patients with cleft palate is extensive (40). Only recently, however, has it been established (101, 89, 88) that middle ear disease is a universal and persistent problem in infants with unrepaired clefts. Sterile, inflammatory effusions of varying viscosity (77) are the rule, although suppuration occasionally occurs.

Roentgenographic studies, employing image-intensification fluoroscopy, of the nasopharynx, Eustachian tube, and middle ear-mastoid area in patients with unrepaired cleft palates, have demonstrated obstruction to the normal retrograde flow of instilled radiopaque contrast media from the nasopharynx into the nasopharyngeal end of the Eustachian tube (40, 41). This suggests that functional impairment of the opening mechanism of the tube, with consequent hypoaeration of the middle ear, may be important in the pathogenesis of the otitis media of these patients. Certain changes in these X-ray findings occur in some patients following palatal repair (42), but their significance remains uncertain.

Other, simpler studies of Eustachian-tube function both before and after repair might provide useful information in patients with cleft palate. Thus, if tympanostomy tubes are in place, ventilatory function studies (62) can measure the ability of the Eustachian tube to equilibrate positive or negative middle ear pressure. If the eardrum is intact, both middle ear pressure and acoustic impedance can be measured by means of an electroacoustic impedance bridge,¹ and indirect information concerning Eustachian-tube function can thereby be obtained (36, 71). Efforts to correlate the results of Eustachian-tube-function tests with roentgenographic findings would probably be worthwhile. It is not at present clear whether factors other than abnormal Eustachian-tube function (or structure) are involved in the pathogenesis of otitis media in patients with cleft palate.

It seems reasonable to assume, on the basis of both the physics of sound and experience in older children and adults with similar middle ear effusions (79), that infants with unrepaired cleft palates and serous otitis media experience conductive hearing losses of variable degree. Additional work is necessary to clarify whether correlations exist between viscosity, or other properties of middle ear effusions (64), and degrees of

¹ This apparatus also may make possible objective assessment of the presence of middle ear effusions (44), even in infants; uncertainty concerning the significance of otoscopic findings can thus be minimized.

hearing loss. In patients too young to be tested by standard audiometry, new techniques such as those utilizing auditory-evoked responses (95) will be necessary.

To the extent that sustained hearing loss of significant degree might be present in infants with cleft palate, interference with important aspects of learning, speech, and emotional development is to be expected. Thus, problems in these areas which have seemed unusually prevalent in older children with cleft palate (84, 99, 83) might be traceable, at least in part, to hearing loss in infancy. Limited evidence suggests that mild, sustained hearing loss, or fluctuating hearing losses during infancy and early childhood—such as are probably the rule in patients with cleft palate whose otitis media is not treated—also can affect adversely the acquisition of language skills (69, 75, 90). Whether they can also result in sensory deprivation or distortion sufficient to affect emotional development is entirely speculative. Further study of these possible relationships is urgently needed.

Since the permanent otologic and audiologic handicaps prevalent in older patients with cleft palate probably have their origin during infancy, it is important to consider whether they can be prevented or appreciably lessened by early intervention. Limited experience to date (88) suggests that otitis media in cleft-palate infants can in most instances be controlled (and middle ear aeration maintained), by (a) early myringotomy and aspiration of the middle ear fluid, accompanied by the insertion of a plastic tympanostomy tube, (b) repeat myringotomy and tube replacement as necessary, and (c) prompt treatment of otorrhea. However, whether the long-term gains of this regimen outweigh its inherent inconvenience and complications is not yet established. Careful, comparative studies of outcome regarding otologic and auditory status, speech, intellect, and personality development are urgently needed. One such preliminary study has recently been reported (90).

There appears to be a sharp reduction in middle ear disease after palatal repair, the improvement probably being attributable to the repair rather than to increasing age (88). This constitutes a basis for considering earlier repair than is customary.

Other unanswered questions about otitis in cleft-palate patients involve the age at which myringotomy should first be done; the relative advantages and disadvantages of "permanent" tympanostomy tubes; the usefulness of palatal obturators (82); the role of socio-economic factors in the occurrence of otitis media following palatal repair; reconsideration of the possible value of adenoidectomy in certain patients with intractable otitis media, despite the risk of creating, or of exaggerating preexisting velopharyngeal incompetence (76, 58); and the possible role of the velopharyngeal valving mechanism in Eustachian tube and middle ear pathophysiology.

Other areas that also deserve further investigation include: the embry-

ology and anatomy of the Eustachian tube in relation to skull morphology; histochemical and electron-microscopic study of Eustachian-tube and middle ear mucous membrane; the possible role of surfactant in Eustachian-tube physiology (43); gas composition, pressure, and transport in the Eustachian tube and middle ear; and further biochemical and immunologic characterization of middle ear effusions. Finally, it would appear worthwhile to study spontaneously occurring and experimentally produced middle ear disease in cleft- and non-cleft-palate animals, particularly primates.

V. OROFACIAL GROWTH AND DENTAL ASPECTS

The basic questions confronting dental clinicians who treat children with cleft palate are, first, how does the face and dentition of the child with a cleft differ from normal and, second, how do children with clefts differ from each other?

DEVELOPMENT OF THE DENTITION

Alterations in dentition are most apparent in the region of the cleft, and include a high incidence of missing lateral incisor teeth, ectopic eruption, supernumerary teeth, and smaller central incisors on the side of the cleft (115, 128). In addition, maxillary and mandibular second premolars are frequently absent in persons with clefts of the lip and palate, a still unexplained finding that requires further investigation (132, 149). Enamel hypoplasia in the area of the cleft occurs in both deciduous and permanent teeth, and there is some evidence to suggest that surgical trauma may contribute to this type of defect (126, 139). Patterns of tooth eruption (timing and sequence) in children with clefts remain to be determined, and further studies are also required to determine the patterns of association between various dental anomalies, the type of cleft, and the morphology of the alveolar arch, lip, and nose. There is a suggestion, based on clinical observation, that plaque accumulation is a concomitant of cleft palate. Whether this is due to the oral environment produced by the cleft palate or is attributable to poor oral hygiene is not known.

The form of the maxillary arch in cleft-palate patients is distorted by the cleft in many cases, and surgical closure of the palate affects future growth to some degree. These phenomena have been studied by various methods (167). The limited data and the wide morphogenetic variability observed in these patients do not permit unequivocal conclusions regarding the impact of specific factors to be drawn at this time (152, 159, 111, 163). Quantitative stereophotogrammetric methods (112, 127) show promise as they permit objective mathematical description of the dental study casts and facial photographs in a way that lends itself to data storage and computer analysis. It is apparent from the foregoing that there are indeed some unique aspects to the development of the dentition in cleft-palate patients and that these require more intensive study.

FACIAL GROWTH

Investigation of how facial growth is implicated in the cleft lip and cleft palate syndrome has been approached through cephalometric roentgenography (134, 158). Available studies show that surgically repaired patients tend to have a smaller maxillary complex than non cleft palate persons (122, 130, 132). While adults with unoperated cleft lip and palate apparently possess antero posterior dimensions that approximate those of the non cleft palate population, more studies of persons with unrepaired clefts are needed to resolve this issue (146, 150). In children with unoperated cleft palate, the distances between the pterygoid plates and between the maxillary tuberosities are wider than in non cleft palate children (168). Studies of craniofacial growth in the siblings of cleft palate children are not presently available and would also be advisable, to indicate whether changes in cleft patients are due to the cleft or to the genetic predisposition underlying the cleft.

Structures such as the nasal septum, maxilla, pharynx and mandible may show deviant morphology because they are primarily affected by the clefting, although the possibility remains that at least some of these structures are basically normal and that they develop abnormally because of proximity to adjacent abnormal structures. It is difficult to study problems of this nature clinically, but animal experiments can be designed to test the plasticity of components of the facial skeleton under various conditions (120, 121, 135, 142). Such studies of postnatal development will be even more valuable if viable animal models for craniofacial birth defects can be found.

The question of how accurately facial growth can be predicted takes on added significance when considering the clinical management of children with clefts and other craniofacial anomalies. While some of the studies noted above indicate that surgery may have an effect on growth of the mid-third of the face, other variables must be considered in addition to the surgery. In many cleft-palate children the maxilla is deficient in size at birth, and surgery may in that case serve to make an unfavorable situation worse. Even when the size of the cleft maxilla appears to be adequate prior to surgery, it is possible that these patients may have an inherent tendency towards less growth in the maxillary complex as they mature and perhaps a slower growth rate. These questions are as yet unanswered.

With special reference to the use of the cephalometric roentgenogram for predictive purposes, it is important that landmarks on the cephalogram be located with accuracy and that errors of measurement be reduced to a minimum. These precautions are essential, since rates of facial growth are so slow that errors in technique may well mask the amount of annual growth change (136, 137). It has been demonstrated in studies of normal children that there is a wide range of variability in both the magnitude and direction of growth of the maxilla (113) and only low correlations ($r = +0.5$ or less) between growth increments of the maxilla and mandible (144).

Average growth changes during early development are relatively simple to describe, but adult facial dimensions in a specific individual cannot be predicted precisely from early childhood cephalograms because of wide individual variability and low correlations of facial growth changes. While this limitation is important in research studies, the cephalometric roentgenogram nevertheless can be an extremely valuable clinical tool, both in describing the facial patterns and in documenting the natural history of children with craniofacial birth defects. In some conditions patterns of facial relationships have been shown to grow worse in time; some improve; and others do not change at all (157).

The cephalogram has also been used to describe syndrome-specific patterns of jaw development by defining the relative sites of dysplasia. Certain morphologic characteristics of the mandible appear to be pathognomic in the Pierre Robin, Cornelia de Lange, mandibulofacial dysostosis, clidocranial dysostosis, malignant osteopetrosis, and craniofacial synostosis syndromes (155, 157). Studies of the growth of the premaxillary vomerine complex (156) and of the calvarium following craniectomy for craniosynostosis (141) using the implant method of Bjork (113) should be extended to include investigation of other conditions as well.

Another aspect of facial development that is of specific significance in the clinical management of cleft-lip and palate patients is nasal growth. There are few longitudinal cephalometric studies of nose growth in non-cleft subjects (119, 169) and two (124, 151) in which growth of the nose in normal and cleft children is compared. In addition, the relationship of the shape of the nasal cavity to maxillary arch form has been described in a cleft-palate population (110). More work on this problem would be of value in planning clinical management.

Finally, there is a need to study the natural history of facial growth in children born with clefts and other craniofacial anomalies in relation to a host of other variables: the child's general health and development; birth weight; the presence of associated defects, as for example, congenital heart disease (165); and the pregnancy history. Such investigations will be even more valuable when cleft children whose parents and relatives (i.e., siblings, twins) can be studied simultaneously to determine the presence of microforms of the anomaly in presumably "unaffected" relatives. In this type of investigation, multivariate statistical techniques are required to assess the interdependence of the different variables.

CLINICAL MANAGEMENT

The best age at which to institute orthodontic treatment for cleft-palate children is still an open question. There is evidence suggesting that while early treatment is beneficial for children with bilateral cleft lip and palate, orthodontic treatment prior to the permanent dentition state in children with unilateral cleft lip and palate has no appreciable effect

on the pattern of facial growth (162). In addition, there are peculiar and characteristic problems surrounding long-term retention of the result following the completion of orthodontic treatment (116). Although a number of workers are known to use sophisticated crown and bridge techniques for the retention of orthodontic results, little has been published on this procedure. Long-term interdisciplinary clinical studies are required to shed more light on clinical management problems (140, 153).

In the area of prosthodontics, obturation appears to be the most adequate means of providing satisfactory speech for individuals who possess very short soft palates (170). Also, the extremely wide horseshoe type of cleft-palate defect is not easily repaired surgically, and is probably best managed by the use of prosthesis. The value of speech bulb stimulators remains to be determined, although they are in use in many centers (114, 166). The work of a number of clinicians who are using the palatal lift has been reviewed recently (129), and more information on how these appliances work would be of value. Criteria for the prosthetic approach are needed, and this will require longitudinal studies on the results of long-term obturation.

Dentoalveolar and maxillary surgery are currently important topics in the management of cleft palate. The prognathic appearance that often results when midface growth is deficient has sometimes been corrected by mandibular setback operations, although maxillary advancement seems the more logical approach in such conditions and is being performed with increasing frequency. How early maxillary surgery for repositioning forward can be attempted, what can be expected in the way of improvement, and the long-term results of these operations are still unanswered questions.

Primary bone grafting to establish contiguity in the cleft alveolar arch was introduced in the early 1950's (147, 148, 164) and was enthusiastically adopted in several centers (117). In 1964, Pruzansky (154) called attention to the lack of a sound rationale to support the procedure. Most centers have stopped using primary bone grafting techniques, as the procedure apparently has not achieved the improved results anticipated and does not justify the hazard involved. Furthermore, it has recently been demonstrated (160, 161) that bone grafting in the primary stage of repair of cleft palate may actually be disadvantageous to the child's maxillary growth pattern. Orthopedic procedures, introduced by McNeil (143) are used to realign the maxillary segments prior to surgery in cases of complete clefts of the lip and palate (123, 138). There is some longitudinal evidence indicating that presurgical segmental realignment prior to 2½ years of age remains relatively stable, and that such treatment reduces the probability of a crossbite occurring in the early mixed dentition (131). Further long-term studies of the effects of presurgical orthopedics on later dental development are needed.

VI. SURGICAL ASPECTS

Recent developments and research in this field have allowed many technical improvements in the surgical management of cleft lip and palate. Today's results provide better appearance and function. Clinicians are more critical of their own results, more aware of the interaction of surgical problems with problems in other fields, and much more alert to the need to improve function particularly in the soft palate area (214, 259).

BASIC NEEDS. The earlier section on Anatomical and Physiological Aspects indicated our lack of basic knowledge of variations in the size, shape, and function of the structures of the aural-oral-facial-pharyngeal-laryngeal-respiratory system, their growth patterns, and their vulnerability to surgical scarring.

Although sophisticated methods have been described for tabulating surface size and shape, we lack a convenient, reliable way of recording and assessing the results of cleft lip repair and nasal tip reconstruction (176, 202). Objective comparisons are almost impossible. Consequently, the average practitioner is unable to tabulate the functional results of his palatal repair.

Valid comparisons of one surgical procedure with another have not been made. It has been said that randomized series should not be contemplated in cleft lip and palate surgery since it compromises the surgeon's ethics to subject children to these protocols. Yet, with the lack of definite knowledge that one operation is better than another, and with champions for each, it is quite possible, for example, to say that either operation A or operation B could be used in a particular case. At the time of surgery, if the surgeon honestly does not know whether it would be better to use operation "A" or operation "B" for that particular child, then, and only then, would one of the operations be picked at random and the child entered into a randomized series. If the child does not fit this criterion, he should not be used in the series. This process is obviously slow, because the cases are not numerous, and the results are long in coming, but there seems to be no other way to obtain a valid comparison of operations. Because of the difficulty in developing series of adequate size, collaborative studies may be necessary.

In addition to our problems in evaluating surgical results objectively, reporting methods at scientific meetings and in published periodicals make it impossible to judge whether the material presented is representative of the results obtained. For this reason the reliability of any one operation cannot be judged accurately.

CLEFT LIP REPAIR. Surgeons don't know what size certain structures such as the columella or the philtrum should be when rebuilding these areas, simply because the data are lacking (208). Opinions on the best age for lip repair seem to rest on the individual surgeon's subjective impressions of the type of management that gives the best results. Reliable information is also lacking on the relationship between the age at which the

repair is carried out and the degree of rejection or acceptance of the child by his family. Basic research in wound-healing, the effect of various suture materials on scar formation, and the control of postoperative scarring would be useful (258).

NASAL TIP. The effect of surgery on growth is particularly important with reference to the nasal tip, its alar cartilages, the columella, and also the nasal septum. Distortions of these structures are frequently marked. Though early surgery on these structures is favored by some, the limitations of this surgery have not been defined (175, 197, 222, 252, 254, 259, 291), and it may be prudent to postpone nasal septal surgery until after childhood.

SECONDARY REPAIR. Much repair, originally postponed until the child was a teenager, is presently being done as part of the primary surgery and in the early school years. In general, this has led to fewer problems for secondary repair at a later age, but in some regards it has increased these problems. Excessive scarring around the alar cartilage and nasal vestibular stenosis caused by injudicious surgery can have devastating effects. It would be advisable to study the possible relationships of such secondary deformities to specific deficiencies in the operative technique used for the primary repair.

ALVEOLAR CLEFTS—PRIMARY REPAIR. Opinions still differ as to whether the cleft alveolus should be closed at all, subjected to delayed closure, closed with mucosal pedicle flaps, mucosal periosteal flaps, or closed with bone grafts (180, 187, 210, 218, 221, 230, 239, 276, 282, 289, 304). There is some evidence to show that early bone grafts can restrict the development of the maxilla (273, 277). Though early publications of Nordine (260) and Schuchardt (283) reported tooth migrations into an adjacent bone graft with eruptions through the bone graft, the migration appears to occur only rarely and seems to be more the exception than the rule. One of the greatest needs in this area is the development of methods of realigning alveolar bone and associated tooth buds to allow the teeth to erupt in a position closer to the normal alveolar arch configuration. The preceding section on Orofacial Growth and Dental Aspects gives a more complete discussion of this problem.

BILATERAL CLEFTS. In managing bilateral clefts it is often said that it is twice as hard to obtain results which are half as good. There are still differing results reported from sectioning and non-sectioning the vomer to reposition the premaxilla (173, 213, 256). Presurgical orthopedics appear to be much more important and apparently are used in a higher percentage of patients with bilateral clefts than is the case for those with unilateral clefts (210). The "lip adhesion operation" is particularly effective in bilateral clefts to help mold the protruding premaxilla (217).

There is a difference of opinion as to whether the premaxilla of an infant should be repositioned into the alveolar arch, or whether it should be held

in an anterior position until the rest of the face "catches up with it" (201). Accordingly, there is a need to clarify what happens to the premaxilla after various types of surgical procedures. Valuable information could probably be obtained from studies in developing countries on unoperated clefts (263). Burdi (185) noted that there is no epiphysis in evidence in the prevomerine area. One wonders whether or not sectioning of the vomer can be carried out at almost any level equally well. This should not imply that since there is not an epiphysis, surgery cannot be expected to interfere with growth. Quite the contrary may be the case. Collaborative studies, the assessment of techniques currently in use, longitudinal studies in children being operated on with different techniques, and coordinated studies in developing countries to document the status of alveolar structures in unoperated clefts in older children and adults constitute some of the greatest needs.

HARD PALATE CLEFTS. Closure is being achieved through a variety of techniques with studies claiming to show that the influence on bone growth depends more on age at the time of closure than on the techniques. At this point there are several acceptable operative techniques, but few valid data as to which is better or whether each achieves the same result as measured by the patient's speech, facial growth, and occlusion (243, 251).

Good work has been done on laboratory animals, but spontaneously occurring clefts differ considerably from artificially induced clefts in structure and particularly in blood supply. Consequently, it is questionable whether these studies are comparable to the situation in man (229). For example, the blood supply of the palate in the dog is such that it is almost impossible to do a routine V-Y lengthening procedure without necrosing the flaps.

SOFT PALATE—PRIMARY REPAIR. Much additional information is needed on the anatomy of the soft palate with a cleft. Crucial studies include the structure of the soft palate, its blood supply, the location and direction of its muscles, the role played by the "accessory" velopharyngeal muscles in compensating for palatal inadequacy, the effect of distortions of the tensor palati muscle on Eustachian-tube function, the abnormalities of the Eustachian tube itself, the innervation of these structures, the degree of overlapping of innervation, and the question of whether palates can be reinnervated by inserting pedicle flaps from other areas (190, 194, 195). There is also a question of whether palatal blood supply is enhanced by insertion of a posterior pharyngeal flap. It appears that mesodermal deficiencies could be equally or more important than wound contraction as a prime cause of velopharyngeal incompetence following palatoplasty. However, it is not known whether such a deficiency is one of degree or location, or perhaps a deficiency in precursors for specific mesodermal tissues such as vasoformative or neuroformative tissue. It may be that the palate with a cleft does not develop properly because isometric action and, consequently, work hypertrophy are absent until the palatal repair is carried out.

Research should be conducted to develop standards by which cleft palate operations can be evaluated reliably. In this area particularly there is a great need for a prospective randomized series and collaborative studies so that one operation can be compared objectively with another.

Palatoplasty by various surgical techniques still leaves 20 to 30% of patients with poor speech (214, 309). These problems may be due to velopharyngeal incompetence. Although the cause for this failure rate is more likely to be multifactorial, the number of factors involved and their quantification await detailed scrutiny. At this time what can be done at the time of primary surgery to reduce the speech failure rate is not known. Retropositioning of the palatal structures has been done for years and has not seemed to have altered the figure. Indeed, according to Lindsay those patients with retropositioning operations may not achieve speech as good as those without (237, 238). Is it possible that building the posterior pharyngeal wall forward with a retropharyngeal implant could reduce this figure (179, 309)? One solution appears to be velopharyngeal bridging with a posterior pharyngeal flap at the time of palatal surgery. There is a question, however, as to whether this is warranted in all patients for the sake of 20 to 30% who will have poor speech. Opinions vary as to whether there is a significant difference if this flap is based superiorly or inferiorly (287, 290, 302).

Recent cinefluorographic studies reveal a variety of patterns of motion in the lateral pharyngeal wall during speech in normal subjects and a variety of palatal motion patterns in patients with clefts (285, 286). Objective criteria need to be established wherein subsequent adequacy of the velum can be predicted with accuracy at the time of the primary palatal repair. If the predicted result is an inadequate velum, then a pharyngeal flap or a retropharyngeal implant procedure could be added to the routine soft palate closure.

Areas of further study include evaluation of techniques such as the intravelar veloplasty, the island flap, and the primary posterior pharyngeal flap, with an effort to determine which types of clefts are most benefited by each of these procedures (231, 249, 251, 290, 311). A study of the rate of palatal movement and its fatigability should be fruitful (301). Lack of definitive information still clouds the question of the appropriate age for soft palate closure. While most surgeons in North America and Western Europe believe that this should be done prior to the age of 18 to 24 months, perhaps there is further advantage to closure prior to this time. Evidence that adequate palatal closure has a salutary effect on the ubiquitous problem of middle ear pathology, the possible benefits of avoiding disuse atrophy in the levator muscle and the early establishment of swallowing and crying, all indicate that closure might provide a number of benefits if done much earlier. None of these factors have been clarified by objective studies.

SECONDARY OPERATIONS FOR VELOPHARYNGEAL INCOMPETENCE. There is a great variety of secondary palatal procedures in use at the present time (311). A number of factors must be considered in deciding which of these operations would be most suitable for a particular patient. Research aimed at determining the criteria for choosing one or another of these procedures would be extremely valuable. The posterior pharyngeal flap procedure seems to be the most popular one in this country, but there is considerable conflicting information about the way the flap functions (257, 264). For example, in some patients it seems to allow the superior pharyngeal constrictor to be more effective in assisting closure. In other patients, notably those with very active soft palates which barely lack contact with the posterior pharyngeal wall, it may simply contribute bulk in the area of the levator eminence. The posterior pharyngeal flap may be useful as a tethering force that holds the palate in the posterior position. Subdividing the aperture so that the sum of the areas on either side of the pharyngeal flap approximates 20 square m.m. may be sufficient (220, 298, 299). Perhaps its benefits come from adding mesoderm to a barren area thereby supplying muscle, blood supply, and perhaps even nerve supply (290).

The question of where this flap should be attached has not been answered. Yules and Chase (314) and Owsley et al. (264) are among those who base the flap superiorly and insert it on the nasal surface at the level of the levator papillae to enhance elevation. Others feel that the uvular attachment produces more effective utilization of the superior pharyngeal constrictor function which might be less effective in the higher attachment (184, 257, 264, 288, 312, 303, 316). Stark and Skolnick (285, 286) believe that there is considerable variation in the site of maximum lateral pharyngeal wall excursion from one patient to another which should dictate the type of flap that is used. In a prospective randomized series, Whitaker et al. (302) and Randall (20) were unable to detect a significant difference between superiorly and inferiorly based flaps used as a secondary procedure.

Posterior pharyngeal flaps probably act in different ways in different patients depending on each patient's particular deficiency (311, 314). If this is true, some flaps and pharyngoplasties would be of advantage when used in one type of velopharyngeal insufficiency and another operation would be best for another type of insufficiency. Work should be done to clarify this problem so that the surgeon will be in a better position to choose the appropriate operation for the problems at hand.

To the surgeon, the diagnosis of velopharyngeal incompetence is important from two major standpoints: (1) this is the most important assessment of the results of his primary palatal surgery, and (2) it allows the selection of those patients who will benefit from secondary treatment. Clearly, if the soft palate can be shown to be inadequate for the production of normal speech, a secondary repair, if feasible, should be carried out at the earliest possible time. This decision is not difficult with clearcut incom-

petence, but with borderline incompetence the decision becomes much more difficult. Further research is needed to establish criteria for secondary surgical procedures, and to document the reliability of testing modalities particularly in the very young patient. The section on Speech and Psychosocial Aspects gives a more complete discussion of this subject.

VII. SPEECH AND PSYCHOSOCIAL ASPECTS

This section will explore present information concerning the speech, language, and psychosocial issues involved in cleft palate as they are today and as they provide direction for future research.

SPEECH

Many individuals with treated palatal clefts no longer have serious problems with communication. However, approximately 25% of them fail to develop adequate speech. Disorders of voice quality and consonant articulation are the usual problems found in the latter group following the primary procedures designed to provide intact and functional oral structures. There have been several recent detailed reviews of the literature appropriate to these disorders (349, 396, 415).

Since verbal output is the result of the interaction of many variables, research of a definitive nature is difficult but essential. This discussion will focus on three major areas where additional information is needed. They include anatomical and physiological requirements for speech, its assessment, and the processes and procedures involved in speech therapy.

ANATOMICAL AND PHYSIOLOGICAL REQUIREMENTS FOR SPEECH

Velopharyngeal Closure. Many studies demonstrate that velopharyngeal closure deficits are related to consonant articulation errors (317, 354, 377), hypernasality (409, 410, 412), nasal emission, and, possibly, certain other alterations in voice quality such as hoarseness (370).

The achievement of velopharyngeal closure is now the goal of clinical management. However, investigators continue to wonder whether small velopharyngeal ports, of sizes yet to be determined, are incompatible with good speech (354, 364, 412). An additional question arises about the ages at which such openings might be most influential in determining speech characteristics. Closure requirements may be more important for speech acquisition than for maintenance (354). Additional investigations are required to answer such questions.

Investigators must also begin to study the pressure the palate exerts against the pharyngeal wall (358, 371, 372) and the manner in which these data relate to other measures of velopharyngeal closure and to speech characteristics.

Rate, consistency, and timing of palatal movement are other variables which appear to relate to velopharyngeal competency. These aspects of

function are only now beginning to be studied, and the continuation of this work is essential.

Tonsils and Adenoids. As Cole (340) has pointed out, we know little about the possible relationship of the palatine tonsils to speech behavior. While this matter should be explored, clinical impressions suggest that the tonsil's role is probably limited and that tonsillectomy, when medically indicated, has little or no influence upon speech patterns.

While attitudes regarding the management of adenoidal tissue are less controversial, the need for supportive data is nonetheless clear. Subtelny and Koeppe-Baker (399) raised questions in 1956 about how cleft-palate patients compensate for the gradual, natural decline in the size of adenoidal mass. Clinicians still disagree as to what happens. Some believe that acceptable speech occasionally becomes hypernasal as the person gets older while others question that this occurs. This uncertainty cannot be ignored in setting future research goals.

The surgical removal of adenoids appears to present a problem different from adenoidal reduction as a function of time. Since surgery abruptly alters palato pharyngeal relationships, implications for the patient seem to be worse and hypernasality may be created or intensified subsequent to adenoidectomy. Studies designed to evaluate observations which may have prognostic value are needed. Until such studies have been done, adenoidectomy presents a potential hazard to the effective functioning of the speech mechanism.

Other Variables Related to Velopharyngeal Closure. Other avenues that offer promise for future research include possible sex differences (368), cervical anomalies and pharyngeal depth (332, 380, 399), movement of the lateral pharyngeal walls (355, 356, 394), and consonant-vowel content of the speech sample (330, 334, 375, 401).

Hypothetical Explanations of Velar Function. The development of hypothetical explanations of velar function (352, 376) has stimulated worthwhile research (390) on velar behavior. While no single hypothesis has yet provided definitive answers to questions concerning velar behavior, it is apparent that this approach to problem solving should be encouraged in the future.

Compensations for Velopharyngeal Closing Deficits. Several recent investigations have explored compensatory phenomena related to poor velopharyngeal closure. The role of Passavant's pad (335), expenditure of energy (343, 384, 403) to maintain a given intensity level, alterations in duration of oral port constriction (411) and of consonant sounds (385), variations in utterance rate (359), laryngeal voice quality deviations (366, 370), and aberrant tongue positioning (327, 328, 346) have been identified as possible compensatory adjustments for an inadequate valving mechanism. However, the origins and the natural history of compensatory behavior are presently poorly understood and need further explication.

PHYSIOLOGICAL CORRELATES OF NASALITY

Acoustical Phenomena. Work has been done to increase our appreciation of the complexity of the relationship between the perception of hypernasality and physiological variables involved in its production (333, 386, 387). Information available is not conclusive. Curtis (344) has suggested that nasality is such a complex problem that it may be illogical to get a high correlation between nasality and any single physiological parameter. In short, hypernasality probably involves interaction among a number of components of the vocal tract. However, velopharyngeal coupling deficiencies may constitute the primary basis of the problem. Work in this area will be essential in the future.

Nasal Airway. Little direct attention has yet been given to the influence of the nasal airway upon speech. Warren (410) has reported that nasal pathway resistance is greater in cleft palate than in normal subjects. McWilliams (370) has pointed to variations in both voice quality and articulation in association with airway alterations. This subject requires systematic investigation.

Dentition. Clinical experience and some formal studies suggest possible relationships between maxillofacial deviations and articulation of consonant sounds, particularly sibilants (318, 365, 377, 398, 400). More research should be done in this area. In particular, future studies should be directed toward discovering the influence of maxillofacial structures upon tongue behavior during speech and vice versa.

SPEECH ASSESSMENT

The assessment of speech is the major clinical and research responsibility of the speech pathologist (349, 396, 415). He must understand and be able to differentiate among the bases for the diverse oral communication problems presented by cleft palate patients. He has access to much instrumentation to assist him in these assessments, but his own ear remains his most useful tool in determining the existence of a problem, its nature, and its magnitude. The reliability and validity of these clinical judgments can be increased through research designed to improve understanding of the characteristics of the processes and conditions which influence these judgments.

Velopharyngeal Closure. Observations upon which inferences concerning valving integrity are made must involve only those speech parameters which relate to velopharyngeal closure. In addition, some system for assessing valving competency must be adopted. Data derived both from the listener's evaluation of the speech pattern and from appropriate instrumentation are needed. In the latter regard, no single instrument has yet provided satisfactory answer to clinical or research needs.

Lateral X-ray films or cephalometrics (325, 331, 350, 351, 357, 402) con-

tinue to be widely used. They provide data on the functioning of the oral structures at only one instant in time, thus yielding more limited information than those techniques which permit evaluation of the dynamic functioning of the structures involved. Research should be directed toward broadening our understanding of the possible relationships between lateral X-ray films and other types of observational techniques.

Cinefluorography—dynamic X rays recorded on film or, more recently, video tape, remain valuable although they, too, are limited because of their two-dimensional nature (319, 320, 321, 322, 336, 371, 374, 393, 408). However, Skolnick (394) has described a new video-tape technique that provides a base view of the velopharyngeal valve. This method is new, and certain methodological problems are still to be solved. However, the technique is promising and should be explored in depth.

The storage and retrieval of data from this type of study also continues to present problems. However, computer-assisted measurements may prove useful if appropriate and well-designed studies can be executed in the future.

Aerodynamic techniques—the development of instruments capable of measuring precisely the pressure and airflow associated with speech has resulted in improved, objective methods for assessing velopharyngeal closure as well as for providing a more comprehensive understanding of the physiological basis of cleft plate speech problems (329, 337, 353, 378, 413).

The basic components of aerodynamic measuring systems are flowmeters which record volume rates of airflow and pressure transducers which record airway pressures within the vocal tract. Studies involving airflow and pressure measurements have shown that speech performance depends upon a number of complex variables. More research is indicated to identify the nature and function of these variables and to determine how information derived from pressure-flow studies relate to other types of observations of the speech-producing mechanism and to speech itself.

Electromyography has not been extensively used in cleft-palate clinical and research programs. This undoubtedly reflects the technical difficulties associated with the procedure as well as the complexity of the muscle groups comprising the orofacial region (326, 341, 348, 360, 363). Although the development of the hooked electrode has overcome a number of the disadvantages of needle and surface electrodes, two basic objections to the technique remain. One is inability to verify that the muscle being recorded is, in fact, the muscle being investigated. The other is inability to determine precisely the relationship between electrical activity and muscle contraction. Although muscles are often identified by their electromyographic activity, this procedure is valid only if the somewhat tenuous assumption of what the activity should be is correct. The advantage of electromyography is that it offers an approach to monitoring the motor commands of the central nervous system.

At the present stage of development, electromyography provides some insight into which muscles participate in normal velopharyngeal closure. Data from cleft palate subjects remain quite scarce and for justifiable reasons. The difficulty involved in identifying muscles after surgery poses a formidable task.

Ultrasound as a technique in cleft palate research is quite new and is considered to be in the developmental stage (356, 373). The technique has been applied primarily to studies of the lateral pharyngeal walls (356). In spite of the advantages the technique offers, i.e., it does not require the insertion of tubes or wires in the vocal tract nor does it pose a radiation hazard to the subject, its application seems to be rather limited. Tissue-air interfaces tend to block the passage of the sound beam, and the continuous movement of structures makes interpretation of data difficult.

Tonar (347) is a new and relatively untried instrument designed to measure and modify nasality and phonation. Nasal-to-oral acoustic ratios are generated, and this information is fed to a nasality rating meter. The result is a continuous display of ratios as the persons speaks. Although no data have been presented to substantiate claims made for this instrument, it appears to have value for investigating certain voice disorders and modifying resulting speech behavior. Obviously, more research is needed.

Other Assessment Needs. The evaluation of velopharyngeal competence is basic to all work with cleft-palate patients and to research regarding their speech problems. However, there are other parameters of speech which should be assessed and explored in greater depth. These needs include:

- (a) procedures for describing the development of articulation skills and for accurately identifying variations in articulatory behavior.
- (b) techniques for describing and assessing other speech changes over time.
- (c) methods for describing and assessing language development.
- (d) tools for determining the relative influence of any anatomical or physiological deficits related to the cleft as opposed to variables such as age, hearing, intelligence, socioeconomic status, and other psychosocial factors.
- (e) a common clinical and research language allowing precise communication among clinicians and researchers.
- (f) a system for the organization of resulting information so that it can serve for prognostication.

The needs noted here are relevant to the clinician and researcher alike. However, they also affect all those involved in the physical habilitation of the person with the cleft. These professional people require information about the results of the procedures which they have employed. As they involve themselves in more and more studies designed to compare techniques of primary and secondary management, the necessity for accurate and objective information from the speech pathologist will increase.

SPEECH THERAPY: BEHAVIORAL MANAGEMENT OF SPEECH PROBLEMS

There has been less research and more misunderstanding in the area of speech therapy for people with cleft palates than there has been in any of the other speech areas yet discussed. This is not surprising, because research in therapy is difficult to execute and is complicated by countless known and unknown variables. In spite of these limitations, some studies have been attempted; and further work is indicated.

Several investigators have used training of various sorts to improve velopharyngeal closure (361, 362, 379, 382, 389, 404, 417). No evidence is yet available to suggest that this can be accomplished except, perhaps, under very limited conditions. Velopharyngeal incompetence does not appear to be a problem that can be solved by therapy.

The management of velopharyngeal incompetence has also been approached through obturator reduction (323, 391, 392, 414). However, there is still insufficient evidence that the method is effective. Additional studies are indicated provided they can be tightly designed and well controlled.

Clinical management of articulation problems in children with clefts is another area that has been investigated in only a limited way (338, 388, 405, 406). Future research efforts should be directed toward differentiating those articulation problems which can reasonably be dealt with through speech therapy and those which have a poor prognosis using that approach. It will then be necessary to describe precise treatment protocols and to gather appropriate supporting data on the outcome of their use.

Speech therapy for cleft palate children continues to be used because a problem exists. This undertaking is costly in money, time, and frustration for both clinician and child. Researchers have an obligation to provide information that will help clinicians decide when not to undertake speech therapy as well as when and how it should be implemented.

LANGUAGE

Language skills appear to be somewhat reduced in children with palatal clefts (349, 369, 383, 395). There is a tendency for expressive abilities to be somewhat inferior to receptive capacities and for children with cleft palates to use shorter sentences than do their peers. The origins of these developmental variations and their eventual outcome in adult life remain in question. The problems described are mild, and it is not known how they influence or are influenced by early childhood experience. Attempts should be made to answer these questions.

PSYCHOSOCIAL ASPECTS

Since 1966, several comprehensive reviews have been published on the psychosocial dimensions of the cleft palate problem (349, 367, 369, 396). Since these publications, additional work has been done (324, 339, 342, 407, 416), but the general picture has not changed.

INTELLIGENCE. Cleft palate children tend to achieve slightly lower scores on intelligence tests and on tests of creativity than do their non-cleft-palate peers, but no logical explanations for these findings have been provided.

SCHOOL PROGRESS. No significant differences have been found in the reading abilities of cleft-palate children in comparison to non cleft children, but other areas of school progress have not been studied.

SOCIAL MATURITY. While young children with clefts are suspected of some delay in social maturation, there is little solid evidence to support this contention. Evidence for older children remains ambiguous; but, overall, cleft palate children do not appear to differ greatly from their peers. However, there have been no studies executed to date that can be considered definitive.

ADOLESCENT AND ADULT PROBLEMS. Little research effort has thus far investigated the psychological, social, educational, and vocational status of adolescents and adults with clefts. One recent study (381), however, suggests that they marry later than their siblings and that they drop out of school earlier than siblings who also drop out. These educational differences seem not to hold when the family pattern includes education beyond high school. Much additional work in this area is needed.

PARENTS' ATTITUDES. While much has been written about parents' reactions to and attitudes toward their cleft palate children, the studies have been largely retrospective and have not looked at significant environmental factors from birth onward which may shape or at least influence the behavior of parents and their children. Thus, the area of parental attitudes, child-rearing practices, the family and social milieu, and levels of clinical care have yet to be systematically related to the eventual outcome for the cleft-palate child.

HOSPITALIZATION. There has been almost no work designed to assess the effects of hospitalization upon these children who, in the presence of countless personal and environmental variables, must inevitably encounter this experience, often repeatedly.

ORAL DEPRIVATION. Some writers have felt that deprivation of normal oral activities and the restriction of certain aspects of motor behavior may have lasting psychological effects. These are mere speculations, however, and there is no hard evidence to support or to reject these views.

FACIAL DISFIGUREMENT AND SOCIETY. Too little is known about the effects of facial disfigurement upon eventual life and social roles. Even less certain is the impact of society and its subcultures upon the outcome for the person with a cleft. This area is largely unexplored.

Almost all research in the psychosocial area of cleft palate has suffered from serious problems of design that have either restricted the usefulness of the findings or have made it impossible or dangerous to generalize from them. Future research must deal more effectively with problems of internal and external invalidity. Eventually research in this area must address it-

self to discovering the behavioral characteristics of the subpopulations of children, adolescents, and adults with clefts and to providing a detailed portrait of the environmental and physical correlates of these characteristics.

VIII. CONCLUSIONS AND RECOMMENDATIONS

Unsolved problems of clinical management are numerous, and an evaluation of the state of the art in cleft palate treatment is particularly frustrating because there is inadequate evidence from which to assess the relative value of different therapeutic procedures. There appears to be a well-defined sequence of events that combine to make this so: (a) enthusiastic claims are made for a new type of therapy; (b) the procedure is widely adopted; (c) a flow of favorable clinical reports results; (d) little or no positive evidence develops to support the desirability of the procedure; and (e) there is a sharp drop in the number of clinical reports, again without evidence to support the change. Serious consideration of the following general points, which come largely from the reports of the various subcommittees, should do much to change this state of affairs and thereby improve the effectiveness of our habilitation programs.

A. Heterogeneity

The cleft lip and palate population is not homogeneous. There are crucial variables, some of which are yet to be identified, that provide the bases for the establishment of subgroups. The variables include the type of cleft, extent of other craniofacial impairments, the development of the orofacial complex, type of management, age of management, effectiveness of management, age at the time of evaluation, cultural heritage, psychosocial status, the state of communications skills, and the cosmetic residual following repair of the cleft. It seems likely that commonly observed variations in response to the same surgical or other therapeutic procedures are due in large part to the fact that clefts that appear similar may be quite different. We do not have the tools or the insights to differentiate crucial variations in this population. However, the heterogeneity of the population imposes the responsibility upon investigators to determine in advance which variables to control, and to be aware of the possible interactions among the variables in studying cause and effect relationships. Much research remains to be done in identifying the variables and the nature of their interactions.

B. Evaluation of Present Levels of Care

There is continuing frustration concerning the possibility that there may indeed be centers where the results of treatment are markedly superior to those of other centers. At present, however, we simply do not have the procedures and techniques of documentation and evaluation involving peer participation that enable us to establish the degree of defec-

tiveness of the original and present conditions of the patient. It follows that, if we did and if it could be documented that some centers were achieving superior results, the principles and techniques being followed in those centers could be generalized to other centers to the distinct benefit of persons with clefts.

C. Documentation

In most areas we have far to go in articulating the hypotheses to be tested, in specifying the nature of the observations which have been made or are being made, and in standardizing the procedures of observation and measurement to the end that data from several centers are comparable and that data obtained from observations over time have adequate stability. For example, documentation of the gross anatomy of the cleft structures is lacking. Little has been written about the size, shape, and variations in the deformed areas of the lip; the alar cartilages; the nasal septum; the alveolus; the hard and soft palate; the Eustachian tubes; and the pharynx. Even less is known about how these structures grow or how different management procedures imposed at various times can alter their growth. Until we can improve our documentation skills, the validity of our data will be inadequate. As a consequence we will fail to improve our ability to specify the uniqueness of the individuals with whom we work, our consequent ability to make decisions and predictions affecting them, and our evaluation of the results of different procedures used to correct the aberrant structures.

D. Prediction

Clinicians are faced with making decisions concerning the nature of treatment, choice of procedures, and age for therapy. These decisions are presently made on the basis of loosely accumulated information identified as clinical judgment and experience. Errors have been made in retaining time-honored approaches and in adopting new techniques without adequate documentation and rationale.

We have far to go in becoming dependable predictors. To predict requires that we have the appropriate observational know-how and techniques and that we have identified the relevant variables to be observed. Until we approach this stage we will be limited to individual experiences and the consequent limitation of samples from which to generalize.

E. Longitudinal Studies

The best hope for obtaining the data that will advance knowledge in this field is through long-term longitudinal collaborative studies. Like many health problems which affect children, the status of the cleft disorder frequently changes with maturation and clearly changes with treatment. Research designed to study the impact of this birth defect on the individual in terms of a given parameter must be formulated in such a way

that long-term aspects of the disorder can be evaluated. Because there is such variation in the scope of the disorder over the years from birth to adulthood, all research observations should be accompanied by information which identifies the status of the patients along the maturation and treatment continua.

What is strongly suggested from this review is the need to establish interdisciplinary centers devoted to longitudinal studies of children with clefts and other craniofacial anomalies. Such longitudinal studies can be performed best at a limited number of Centers of Excellence situated in selected geographical areas. Some of the important criteria for the selection of such regional centers are: large and controlled case flow available from birth; availability of adequate treatment personnel and facilities to provide interdisciplinary resources for habilitation; close association of the clinical treatment staff and research members of the unit; maximum assured utilization of staff and facilities; willingness to conduct regular continuing training programs in clinical management; and the facilities and climate conducive to research. Such centers should, in addition, be capable of developing consortia of affiliated satellite institutions to insure maximum utilization of the expertise of both the center and the affiliated hospitals and clinics.

Another benefit of long-term longitudinal studies in which reliable data are obtained by standardized procedures is the ease with which information from different centers may be pooled in a data bank and thus be made accessible for comparison. Furthermore, there is an opportunity to enrich the training of pediatricians, orthodontists, surgeons, and other clinicians by using these data to demonstrate the continuum of morphologic variations that may be expected.

Prospective, longitudinal investigations have a practical application in the clinical management of cleft-palate children since it is only by collecting reliable data that one can deal with the three central problems of management: the best time to treat, the techniques of treatment most appropriate in a particular case, and the effects of treatment. Everyone involved in the care of persons with cleft lip and cleft palate is aware of these questions, all of which have yet to be answered satisfactorily.

The comprehensive research programs suggested here will require long-term institutional commitments.

F. Use of Clefting as a Model

Clefting can be viewed as an experiment of nature. As such, its study can assist us in understanding the normal as well as the pathological processes. Cleft lip and palate is, after all, the most frequent major congenital anomaly amenable to treatment, and its prevalence may be increasing. It provides a good test of the long-term impact of management (care now—results later). It has demonstrated the value of the interdisciplinary approach and has attracted many persons with a variety of backgrounds and

skills. Consequently knowledge derived from research in this area has potential value to many disciplines. Related to this effort is the value of studying the unoperated or otherwise unmanaged cleft. It is most desirable, therefore, that more research be conducted in developing countries where persons with unmanaged clefts exist.

G. Data Banks

Centralized storage of data with convenient retrieval procedures has been used in conducting research in several fields. The data bank has the clear advantage of allowing researchers to pool data over time and population samples so that an appropriate number of subjects or other units of study can be accumulated for a specific project. Such arrangements are particularly appealing in cleft-palate research because of the relative infrequency of occurrence of the defect and the heterogeneity of the population.

There are many problems in establishing such data collections, however. To date few such efforts in the area of cleft lip and palate have been successful. Major problems have to do with specifying the observations to be stored so that the data will be useful for a variety of purposes. Related to that requirement is the additional one that there must be sufficient specificity in the observations that appropriate subgroups of the population can be identified for study. In addition, the observations must be reliable over time and among data "bankers."

Although there are no easy solutions to these problems, several guidelines are suggested for establishing such data collections.

- a. Data banks may be more productive if they are mission-oriented rather than open-ended. They should be created for specified objectives, rather than for the uncritical accumulation of observations on the assumption that the data will eventually be useful for some purpose or other. A preferable approach is to design a data bank for one purpose or set of related purposes which are formulated at the initiation of the project.

- b. For maximal usefulness and reliability of the data, the observations to be stored should be descriptive or documental in nature, not evaluative or judgmental. For example, high fidelity tape recordings of articulation test responses are preferable to information about articulation test scores. Edited tape-recorded samples of connected speech (from which psychological scale values of various aspects of speech can be derived) are preferable to clinical judgments of articulation defectiveness, hypernasality, etc. Copies of cephalograms are preferable to specific measures of velopharyngeal opening or clinical judgments of velopharyngeal status even though such measurements and judgments must eventually be made.

- c. Attention must be given to the methods used for making the observations to be stored in a data bank. For example, if instrumenta-

tion is involved, the same instrument should be used throughout the project; or, if different instruments are used, they should be calibrated carefully. In the same way, procedures not requiring instrumentation must be specified carefully. All "contributors" to the data bank must agree to use the same procedures, and the system must be monitored for the use of the standardized procedures.

d. Procedures for storing the data, methods for retrieving the data, and a system for establishing a protocol for using the data must be established clearly before the data bank is initiated. Experience has shown that, with few exceptions, clinical records are not maintained with the vigor required for the collection of data to be used in research. Maintaining a detailed and somewhat separate record-keeping system for the data bank is expensive even if only one institution is involved. If more than one institution is involved, financial support from outside sources is required.

H. Small Sample Research

There are a number of questions that can be studied meaningfully through the use of small numbers of subjects assembled on some basis that eliminates selection bias. In general, such procedures are applicable to questions about the relationships between variables under very specific conditions. With some exceptions, these are not questions about what is "typical" of the cleft palate population. Instead, very specific, well-delineated, structured questions are asked. An example might be, "What patterns of lingual movement and posture do patients with certain types of velopharyngeal incompetence use during specific speech task?" and "How do those patterns differ from those of normal subjects selected by a highly specific set of criteria?" This kind of research attack has special relevance in the evaluation of various therapeutic procedures administered to carefully selected subjects demonstrating precise and well-defined clinical characteristics.

I. Prevention

Research at the molecular level designed to assist in the prevention of clefting is almost nonexistent. Further efforts in this area should be fruitful.

J. Other Craniofacial Anomalies

Investigation and treatment of major craniofacial anomalies, other than clefts, are in their beginnings. Although this report was not commissioned to consider the problems of persons with these anomalies, concern for them is so intertwined with issues related to clefting and so much a part of the future of the investigators working in the general area that mention of them should be made. Data banking of descriptive information concerning the various anomalies seen, and of the genetic backgrounds and treatments

of persons with them, would be helpful. Prospective research concerning the facial growth of persons with craniofacial anomalies, their language development, their physical health, and their psychosocial adjustments is of considerable importance.

K. The Training of Investigators

There is an urgent need to attract more basic science and clinical investigators into the interdisciplinary settings treating persons with clefts, to design and conduct the research outlined above.

* * * * *

Cleft-palate research carried out during the past 25 years has been largely descriptive. This is understandable when it is remembered that it was done by concerned clinicians seeking to establish the parameters of the problem and to provide better patient care. There can be little doubt about the success of their efforts. Research has increased substantially the cleft palate patient's chances for normal speech, minimized the risks of facial disfigurement, reduced significantly the number of surgical procedures while improving their quality, and offered him help with related health hazards.

If further progress is to be made, however, new directions and methodologies of research must be developed. The future demands projects that are not only well-defined and mission-oriented but that also seek to discover the ways in which many variables act together to influence the clinical result. This kind of research is difficult and demanding. The right questions must first be asked. Then projects must be designed to produce data that can be appropriately interpreted, generalized, and applied. The future will be a demanding time for researchers in cleft palate. However, if the challenges can be met with imagination, creativity, and solid insights derived from research, the coming decades should also be a time of rapid informational expansion and of better care and outcome for the person with cleft palate.

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SPEECH AND PSYCHOSOCIAL ASPECTS

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