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Craniofacial morphology and velopharyngeal physiology in four syndromes of clefting

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CRANIOFACIAL MORPHOLOGY AND VELOPHARYNGEAL PHYSIOLOGY IN FOUR SYNDROMES OF CLEFTING

by

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A dissertation submitted to the Graduate Faculty in Speech and Hearing Sciences in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York.

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Abstract

CRANIOFACIAL MORPHOLOGY AND VELOPHARYNGEAL PHYSIOLOGY IN FOUR SYNDROMES OF CLEFTING

by

Karen J. Golding-Kushner

Advisor: Professor Katherine Harris

Sources of heterogeneity within the population of individuals with cleft palate might predispose certain patients to a particular speech outcome regardless of surgical technique or age at the time of primary palatoplasty. Identification of possible sources of heterogeneity may provide guidance for the nature and timing of treatment and in expectations regarding palate repair. One possible source of variability in the speech production of subjects with cleft palate is skeletal morphology. Subjects with four syndromes associated with cleft palate, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW), were included in this study to examine the possibility that velopharyngeal function in subjects with clefts is related to differences in underlying cranial morphology and resultant vocal tract shape.

The goals of this study were to identify the prevalence of speech abnormalities in a large series of individuals with cleft palate and these four syndromes, and to examine the craniofacial and vocal tract morphology and velopharyngeal function was in a portion of the same sample. Measurements

were made from lateral cephalometric tracings, nasopharyngoscopic and multi-view videofluoroscopic examinations.

Craniofacial morphology was largely syndrome specific and was correlated with vocal tract size and configuration. These characteristics were, in turn, related to differences in velopharyngeal closure patterns, but were not the sole determinants of velopharyngeal insufficiency (VPI). There was a difference in the prevalence and severity of VPI, resonance disorders, and compensatory speech disorders in different syndromes. In general, VPI was more prevalent in the presence of an obtuse cranial base angle and wide pharynx than in a narrow pharynx associated with kyphosis of the cranial base.

Craniofacial morphology and vocal tract configuration were most abnormal in Treacher Collins syndrome. Although subjects with TC had the lowest prevalence and severity of VPI, their patterns of velopharyngeal and lingual movements were most abnormal. Severe hypernasality and compensatory speech disorders were most prevalent in VCF and subjects with VCF who have submucous cleft palate seem to be at a higher risk for speech and resonance abnormalities than subjects with the other three syndromes because of a combination of structural and, possibly, neurologic abnormalities.

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Academia and career would be extremely unrewarding in the absence of a fulfilling personal life. I am fortunate to have a wonderful and extraordinary husband. Without Stuart's patience, support, sense of humor, and encouragement my doctoral education would have been left unfinished 9-1/2 years ago when we moved to Israel. He has helped me through the most challenging experiences in my academic, professional, and personal life, and has also shared the best times. Without his unqualified love my life would be empty.

This thesis is dedicated to my beloved parents, Claire and Louis Golding, of blessed memory. They believed that I could accomplish anything to which I set my mind and from an early age instilled in me the confidence and intellectual curiosity that has brought me to this point. Without their inspiration, this project would never have been undertaken.

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To my family, friends, teachers, and colleagues- I hope that you will not be disappointed.

Karen J. Golding-Kushner
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CHAPTER 1

INTRODUCTION

There have been many studies reporting on the prevalence of velopharyngeal insufficiency and speech disorders following repair of palatal clefts (Jolleys, 1954; Morris, 1973; Lewin et al, 1975; Musgrave et al, 1975; Kaplan et al, 1978; Witzel et al, 1979, 1984; Dorf and Curtain, 1982; Randall et al, 1983; Bardach et al, 1984; Ainoda et al, 1985; Aaronson et al, 1985). These studies have primarily focused on issues such as age at the time of palate repair and the surgical procedure used. Investigators have usually reported that differences in speech quality resulted from these types of treatment effects, but the "success rate" of primary palatoplasty reported in the literature shows marked variability. Recently, consideration has been given to possible sources of heterogeneity within the population of individuals with cleft palate which might predispose certain patients to a particular speech outcome regardless of surgical technique.

A possible source of variability in the speech production of subjects with cleft palate is skeletal morphology. There is evidence that certain morphologic features, such as angulation of the cranial base, have an effect on vocal tract size which may, in turn, influence speech production (Shprintzen, 1982). One way to examine this possibility is to study syndromic subsets of individuals with cleft palate because morphology within a syndrome varies less than in unselected clefts. Subjects with four syndromes associated

with cleft palate, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW), were included in this study to examine the hypothesis that velopharyngeal function in subjects with clefts is influenced by differences in underlying cranial morphology and resultant vocal tract shape.

A reduced pharyngeal width has been observed in Treacher Collins syndrome related to basicranial kyphosis (acute angulation of the cranial base) and in Stickler syndrome in association with a short anterior cranial base (Shprintzen, 1982; Cisneros et al, 1989; Feldman et al, 1989). In contrast, velo-cardio-facial syndrome and van der Woude syndrome are associated with obtuse cranial base angles (platybasia) and a larger than normal pharyngeal width (Shprintzen, 1982; Arvystas and Shprintzen, 1984).

Overt or submucous cleft palate is a frequent finding in all four syndromes (S, TC, VCF, VDW) (Gorlin et al, 1990), but the prevalence of velopharyngeal insufficiency following palate repair in these populations has not been studied in detail. A trend has been observed of a high frequency of VPI in patients with VCF and VDW syndromes (>90%) and a low frequency in S and TC (<20%) (Gereau and Shprintzen, 1988). However, the relationship between craniofacial morphology, pharyngeal width, and speech has not been systematically studied.

Little information is available on speech and resonance patterns following palate repair in subjects with craniofacial syndromes in general, and still less on patients with the four

syndromes. However, if the speech and resonance characteristics were unique, they would provide guidance for the nature and timing of treatment and there would be implications for the way in which families are counselled regarding palate repair. Therefore, the preliminary part of this project is a study to identify the prevalence of resonance and articulation abnormalities in samples of these four syndromic populations followed at a single major craniofacial center. The second part of the project is a study of the morphologic characteristics and velopharyngeal function in a portion of the same sample.

The null hypotheses are:

1. There is no difference in the prevalence of "compensatory" speech disorders (glottal stops, etc.) in different syndromes.
2. There is no difference in the prevalence of resonance disorders in different syndromes.
3. Craniofacial morphology within specific syndromes is not homogeneous (i.e., syndrome specific).
4. Craniofacial morphology is not related to vocal tract (upper airway) size or configuration.
5. There is no difference in the prevalence of velopharyngeal insufficiency (VPI) in association with a "narrow pharynx" versus a "wide pharynx".
6. Cranial base abnormalities are not associated with the frequency of VPI following palate repair or with submucous cleft palate.

7. Craniofacial morphology and airway size or configuration in specific syndromes are not related to differences in velopharyngeal closure patterns.

CHAPTER 2

REVIEW OF THE LITERATURE

Many studies have addressed the relationship between age at the time of primary palatoplasty and speech outcome (Jolleys, 1954; Dorf and Curtain, 1982, 1990; Randall et al, 1983; Ainoda et al, 1985). Dorf and Curtain (1990) found that less than 5% of children undergoing palatoplasty prior to 12 months of age had compensatory articulation in contrast to 90% of children undergoing later repair and attributed surgical success to timing according to stage of phonemic development rather than chronological age regardless of cleft type. Randall et al (1983) reported "better speech results" in children undergoing palatal repair between 3 and 7 months as opposed to 12 to 18 months. Hall and Golding-Kushner (1989) found no significant difference in the prevalence of hypernasality among subjects undergoing palate repair at any two-month interval between 8 months and 18 months, with 84% of all subjects demonstrating normal speech and resonance. Following a review of reports on age of palatal closure and speech outcome, Peterson-Falzone (1988) concluded that 12 months was a critical age.

Other studies have examined the presumed effect of surgical procedure on speech and resonance (Morris, 1973; Lewin et al, 1975; Musgrave et al, 1975; Kaplan et al, 1978; Witzel et al, 1979, 1984; Bardach et al, 1984; Aaronson et al, 1985). Lindsay and Witzel (1990) reported normal speech in 75% of subjects undergoing palate repair with the von

Langenbeck technique. Kaplan et al (1978) reported normal speech in 68% of patients with this procedure. Witzel et al (1979) found no difference in speech outcome for subjects undergoing palate repair with a Von Langenbeck or pushback procedure. Normal speech was reported in approximately 48% of subjects undergoing primary veloplasty (Schweckendiek and Kruse, 1990). In general, these studies have reported that differences in speech resulted primarily from treatment effects, and, as can be seen, "success" statistics from these studies, when provided, varied widely.

Recent consideration has been given to possible sources of heterogeneity within the population of individuals with cleft palate which might predispose certain types of patients to a particular speech outcome regardless of surgical technique. For example, Gereau and Shprintzen (1988) found a strong correlation ($p<.0001$) between adenoid size and presence or absence of VPI. They examined nearly 1000 subjects with nonsyndromic cleft palate using multi-view videofluoroscopy and nasopharyngoscopy and observed that VPI following primary palatoplasty was usually associated with adenoid hypoplasia or obtuse angulation of the cranial base.

It is well known that patients with a syndrome resemble each other despite diversity of racial and ethnic backgrounds (Roberts et al, 1975). By the same token, specific abnormalities of the palate and vocal tract may be characteristic of particular disorders (Shprintzen, 1982). Structural abnormalities together with other anomalies associated with particular syndromes (such as hearing

disorders) may pose potential and predictable hazards to normal speech and resonance. However, little information is available on speech and resonance patterns following palate repair in subjects with craniofacial syndromes, or in individuals with craniofacial syndromes who have submucous cleft palate.

As of 1990, there were 342 known syndromes involving orofacial clefting including 69 genetic syndromes with an autosomal dominant inheritance pattern (Gorlin et al 1990; Cohen and Bankier, 1991). Four of the more familiar genetic disorders are Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW). These four syndromes, each of which is frequently associated with cleft palate, were selected for inclusion in this study to examine the hypothesis that velopharyngeal function in subjects with clefts is influenced by differences in underlying cranial morphology and resultant vocal tract width.

CHARACTERISTICS OF THE FOUR SYNDROMES

Stickler Syndrome (S)

General Description of Stickler Syndrome. Stickler syndrome or hereditary progressive arthroophthalmopathy, is characterized by ocular, orofacial, and skeletal abnormalities (Stickler et al, 1965; Stickler and Pugh, 1967). The ocular findings, first described in 1938 by Wagner (Stickler and Pugh, 1967), have been studied in depth. Myopia has been

reported to occur before 5 years of age in 80% of affected children (Liberfarb and Hirose, 1982; Gorlin et al, 1990). Myopia may worsen with vitreoretinal degeneration and retinal detachment resulting in blindness. Early diagnosis and careful ophthalmologic care can help prevent the severe ocular complications (Schreiner et al, 1973; Wang et al, 1990a). Ocular findings have been diagnosed as early as 2 days after birth (Wang et al 1990a). Skeletal abnormalities include epiphyseal dysplasia, early osteoarthritis with painful and hyperextensible joints, and scoliosis. Mitral valve prolapse has been reported in 50% of cases (Gorlin et al, 1990).

The orofacial characteristics of S include a flat "moon-shaped" face with flat nasal bridge, short nose with anteverted nostrils, micrognathia, and overt or submucous cleft palate (Stickler and Pugh, 1967; Herrmann et al 1975a, 1975b; Jones, 1988; Gorlin et al, 1990). Choanal atresia has been reported (Say et al, 1977). Hearing may be normal or may be characterized by recurrent middle ear disease and fluctuating conductive hearing loss related to cleft palate. Reports of high frequency sensorineural hearing loss have ranged from 7% (Herrmann et al 1975b) to 87% (Liberfarb and Hirose 1982) of Stickler cases, and may be progressive.

Occurrence of S in the General and Cleft Palate Population. The incidence of Stickler syndrome in the general population has not been reported. However, it is the most common genetic connective tissue dysplasia, more common than the better-known Marfan syndrome[1] (Opitz et al 1972). It has been estimated to account for 6.6% of all cleft palate-only patients (Shprintzen, 1988a), and accounts for one-third of all patients with Robin sequence (Herrmann et al 1975a, Sheffield et al, 1987; Shprintzen 1988a, Gorlin et al 1990). It is frequently misdiagnosed as isolated Robin sequence or isolated cleft palate, and is probably underreported or not detected in many cases (Shprintzen et al 1985b, 1985c; Sheffield et al, 1987).

Prevalence of Cleft Palate in S. Reports of the prevalence of cleft palate in Stickler syndrome range from 20% to 36% (Herrmann et al, 1975a; Hall and Herrod, 1975; Liberfarb and Hirose, 1982; Kronwith et al, 1990). The prevalence of clefting may be higher because of underreporting of submucous cleft palate (Cohen et al, 1971; Hall and Herrod, 1975; Shprintzen et al, 1985a), which in one series of subjects was 47% (Herrmann et al, 1975b). Robin sequence occurs in 12% (Herrmann et al, 1975a). Cleft lip has not been reported.

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[1]Marfan syndrome has a frequency of 4 to 6 per 100,000 (Pyeritz and McKusick, 1979)

Treacher Collins Syndrome (TC)

General Description of Treacher Collins Syndrome. Treacher Collins syndrome involves the face, orbits and ears bilaterally (Rogers, 1964; Gorlin et al, 1990). Berry, an ophthalmologist, first described the finding of lower lid depressions in a mother and daughter over 100 years ago (Berry, 1889). Treacher Collins (1900) described malar flattening. The syndrome was labelled mandibulofacial dysostosis (MFD) by Franceschetti and Klein (1949) who further elaborated the morphologic description, although nearly half of their subjects actually had hemifacial microsomia. Characteristic facial features include defects of the lower lids (colobomata, partial or total absence of lower eyelashes), downslanting palpebral fissures, malar hypoplasia (specifically hypoplasia, notching, or clefting of the frontal process of the zygomatic bone which forms the inferotemporal orbital rim), maxillary hypoplasia, curvature of the inferior mandibular border with malocclusion including open bite which worsens with time, bilateral auricular and middle ear malformations, and preauricular extension of the hairline toward the cheek (Franceschetti and Klein, 1949; Roberts et al, 1975; Mafee and Valvassori, 1981; Fitz and Noyek 1981; Jones, 1988; Gorlin et al, 1990; Wang et al 1990b). The mastoids are frequently sclerotic and not air filled (Gorlin and Sedano, 1971). Maximum conductive hearing loss secondary to middle ear malformations is common (Beighton, 1971; Selder, 1973).

Occurrence of TC in the General and Cleft Palate Population. The incidence of Treacher Collins syndrome has been estimated as 1:10,000 live births (Roa and Moss, 1984). However, it may be undetected in mild cases (Rogers, 1974; Gorlin et al, 1990) and has been misdiagnosed as isolated Robin sequence (Shprintzen et al 1985c). Treacher Collins syndrome accounted for 3.8% of the cleft palate-only and .2% of the cleft lip +/- cleft palate[2] population at a major craniofacial center (Shprintzen et al 1985c) and accounted for 7% of infants with Robin sequence (Shprintzen 1988a).

Prevalence of Cleft Palate in TC. As in all syndromes, reports of the prevalence of cleft palate in TC vary depending on the ascertainment bias of the reporting institution (ophthalmologic center versus cleft palate center, etc), diagnostic techniques (such as the use of nasopharyngoscopy in the identification of submucous clefts), the inclusion or exclusion of submucous clefts in the total number of cleft cases reported, and sample size. The prevalence of cleft palate-only in TC has been reported to range from 25% to 40% (Gorlin and Sedano, 1971; Roberts et al, 1975; Peterson-Falzone and Pruzansky, 1976; Jones, 1988; Kolar et al, 1985; Gorlin et al, 1990, Vallino et al, 1991). Submucous cleft palate may occur in TC (Fara et al 1971; Weatherly-White et al 1972; Walker, 1974), and may have a prevalence of 10 to 30% (Peterson-Falzone and Pruzansky, 1976; Shprintzen et al, 1979,

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[2]cleft lip with or without cleft palate

Vallino et al, 1991). The exact prevalence of clefts in TC is difficult to determine from published reports because only some authors include submucous cleft palate (SMCP) with all clefts. Peterson-Falzone and Pruzansky (1976) described the palate in multiple TC subjects as foreshortened and applied the term "congenital palatal insufficiency (CPI)," the category in which they also included submucous clefts[3]. Underdiagnosis of submucous clefts is common, as clearly demonstrated when selected studies are reviewed. For example, Shprintzen et al (1979) reported from an institution with a reputation in the treatment of cleft palate and craniofacial disorders (ascertainment bias) where nasopharyngoscopic examination of proposita and morphologic examination of relatives are routine. They diagnosed overt clefts or submucous clefts in 12 of 20 TC subjects (60%). As with Stickler syndrome, submucous cleft palate, although not suspected because speech was normal, was diagnosed in several subjects and their relatives by careful peroral examination or by endoscopy.

Robin sequence is a common finding in TC, possibly because of the inherent mandibular hypoplasia (Shprintzen, 1988a). Cleft lip has been described as rare in TC (Rogers, 1964; Gorlin et al, 1990), but was, interestingly, listed as

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[3]Kaplan (1975) noted that 100% of 240 cases of "short palate" he examined were found to have submucous cleft palate. This suggests that subjects described as having a "foreshortened" palate may actually have SMCP or occult SMCP (OSMCP), indicating a higher frequency of clefts than actually reported. Subjects with "CPI" also probably have SMCP or OSMCP.

a finding in one of Berry's two original subjects and her son (1889). Peterson-Falzone and Pruzansky (1976) had 1 subject of 25 with cleft lip (4%).

Velo-cardio-facial Syndrome (VCF)

General Description of Velo-cardio-facial Syndrome. VCF was first delineated by Shprintzen and colleagues in 1978, although subjects with similar characteristics were described in earlier reports by Sedlackova and colleagues in 1955 (Sedlackova, 1967) and by Strong (1967). Frequent features of the syndrome include overt or submucous cleft palate, cardiovascular anomalies (ventriculoseptal defect, tetralogy of Fallot, or right-sided aortic arch and others), characteristic facial appearance (vertically long face, prominent nose with squared nasal root and narrow alar base, flattened malar region, narrow palpebral fissures, narrow nasal passages, bluish suborbital congestion or "allergic shiners," retrognathia), and learning disabilities. Other findings include small stature, slender hands and digits, abundant scalp hair, pharyngeal hypotonia, and mildly dysmorphic auricles with flattened helical folds. Less frequent findings include Robin malformation sequence, inguinal and umbilical hernias, hypospadias, scoliosis, and sensorineural hearing loss (Shprintzen et al 1978; Young et al, 1980; Shprintzen et al, 1981; Arvystas and Shprintzen 1984; Golding-Kushner et al, 1985; Williams et al, 1985; Beemer, 1986; Meinecke et al, 1986; Williams et al, 1987; Jones, 1988; Johnson and Ceino-Sena, 1990; Stevens et al,

1990; Gorlin, 1990). Ophthalmologic findings include tortuosity of the retinal vessels and posterior embryotoxin (Fitch, 1983; Mansour et al, 1987). Medial displacement of the internal carotid artery is another vascular feature (MacKenzie-Stepner et al, 1987b; D'Antonio and Marsh, 1987). Holoprosencephaly has been reported in a single case (Wraith et al, 1985). VCF has also been reported to occur with the CHARGE association and DiGeorge sequence (Shprintzen, 1987, 1990).

Occurrence of VCF in the General and Cleft Palate Population. Velo-cardio-facial syndrome has been reported to be the most common syndrome of clefting, accounting for 8.1% of the cleft palate-only population at a major craniofacial center (Shprintzen et al, 1985b) and 13% of the Robin population (Shprintzen, 1988a). No data are available on the prevalence of VCF in the general population, but could be as high as 1 in 15,000 (R. J. Shprintzen, personal communication, July 17, 1991).

Prevalence of Cleft Palate in VCF. Reporting a possible ascertainment bias, Shprintzen et al (1981) indicated that all cases of VCF examined at that time had cleft palate, including 28% with overt clefts and 71% with SMCP, 38% of which were

occult submucous clefts of the palate[4] (Croft et al, 1978; Lewin et al, 1980; Croft et al, 1981). A cleft palate/SMCP prevalence rate of 98% was subsequently reported (Williams et al, 1985). Hypernasality has been reported in some subjects in whom no cleft was diagnosed (Meinecke et al, 1986). However, OSMCP could not be ruled out in those subjects because nasopharyngoscopy was not performed. In another series of 26 subjects with VPI who were probably affected with VCF only 2 had repaired overt clefts of the soft palate (Stern et al, 1977). About 15% of all VCF subjects present with Robin sequence (Shprintzen, 1988a). Cleft lip has not been reported except in the single case of holoprosencephaly who had premaxillary agenesis, a form of that sequence (Wraith et al, 1985).

Van der Woude Syndrome (VDW)

General Description of Van der Woude Syndrome. The earliest reports of Van der Woude syndrome were published in the mid-1800's by Demarquay and Murray (Gorlin et al, 1990). It was subsequently described in detail by Van der Woude (1954) and Cervenka et al (1967). Almost all of the reports have focussed on the genetic transmission of the disorder. It

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[4]Occult submucous cleft palate (OSMCP) can, by definition, only be diagnosed by nasopharyngoscopy or during surgery. The palatal defect, a deficient or absent musculus uvulae (m.u.) with or without muscular diastasis, exists on the dorsal side of the palate, and is not visible on peroral examination. In normal subjects, the m.u. bulge adds bulk to the dorsal surface of the elevated palate (Azzam and Kuehn, 1977), and provides a target for medial motion of the lateral pharyngeal walls (Skolnick, 1975; Croft et al, 1978; Lewin et al, 1980).

is characterized by cleft lip and/or cleft palate associated with lower lip pits or conical elevations, and congenitally absent premolars. Expression of clefts is variable, ranging from bilateral complete cleft lip and palate, to submucous cleft palate (Dronamraju, 1971; Ranta and Rintala, 1983; Shprintzen et al, 1980; Burdick et al, 1987; Jones, 1988; Murray et al, 1990). Ankyloglossia has been reported (Burdick et al, 1987). Manifestations of VDW other than orofacial features occur infrequently, but cardiac defects have been reported (Gorlin et al, 1990).

Occurrence of VDW in the General and Cleft Palate Population. The incidence of all expressions of VDW has been estimated to be 3.58 per 100,000 live births (Burdick, 1986; Gorlin et al 1990), but is probably underreported because of failure to identify mild expressions (e.g., SMCP or lip pits only), especially when the family history is negative (Cervenka et al, 1967; Burdick et al, 1985). Van der Woude syndrome accounts for 1% to 3% of all cleft lip and palate cases (Gorlin et al, 1990; Murray et al, 1990). VDW represented 4.5% of the cleft palate-only and 4.5% of the cleft lip +/- cleft palate population at a major craniofacial center (Shprintzen, 1988a) and 6% of all new patients registered at a major craniofacial center over a 4 year period (Shprintzen et al, 1980).

Prevalence of Cleft Palate in VDW. Cleft palate-only, including overt and submucous cleft palate, was present in 33% of 67 VDW subjects of Shprintzen et al (1980), with an overt cleft rate of 21%, a figure also cited by Gorlin et al, 1990. Earlier prevalence figures of 16% (Janku et al, 1980; Burdick et al, 1985) and 17% (Cervenka et al, 1967) for cleft palate-only in VDW may represent underreporting of submucous clefts, diagnosed in Shprintzen's series using nasopharyngoscopy.

CEPHALOMETRIC STUDIES AND THE CRANIAL BASE

In a review of palatal and pharyngeal anomalies in common syndromes of clefting, Shprintzen (1982) indicated that acute angulation of the cranial base (kyphosis) was frequent in Stickler syndrome and Treacher Collins syndrome, while velo-cardio-facial syndrome and van der Woude syndrome were associated with platybasia or obtuse cranial base angles.

A "steep" skull base was observed in one of Herrmann's early Stickler cases (Herrmann et al, 1975a), but no measurements were provided. Saksena et al (1983) assessed 21 affected and 18 normal members of 8 families in the only published cephalometric study on Stickler syndrome. Subjects ranged in age from 3 years to adult. Affected subjects had marked shortening of the overall length of the cranial base and the length of the posterior cranial base, with short midfacial height and long total and lower face height. In contrast, Glander (1990), who examined 20 cephalographs of

Stickler subjects, found only slight shortening of the posterior cranial base, and facial height measures were normal. The mean cranial base angle was 129 degrees[5]. Stickler subjects with Robin sequence demonstrated relative maxillary and mandibular retrognathia, but non-Robin Stickler subjects did not.

Craniofacial morphology in Treacher Collins syndrome has been studied extensively, with abnormalities identified in the size and contour of the cranial base and mandible. Cleft and noncleft TC subjects have not been described separately to date. An abnormally acute cranial base angle in TC, as low as 105 degrees, has consistently been observed by cephalometric analysis (Garner 1967a, 1967b; Roberts et al, 1975; Shprintzen et al, 1979; Mafee and Valvassori, 1981; Grayson et al 1985, 1986; Peterson-Falzone and Figueroa 1989; Arvystas and Shprintzen, 1991). This was also identified in dry skull analyses (Dahl et al, 1975; Herring et al, 1979) and using anthropometric methods (Kolar et al, 1985, 1987).

Furthermore, growth of the cranial base in normals is essentially complete by 14 years (Riolo et al, 1974; Grayson et al, 1985) with minimal change in the flexure of the cranial base over time[6] (Riolo et al, 1974). However, basicranial kyphosis in TC may have late onset or worsen over time by as

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[5]Mean cranial base angle (N-S-B) for normals is 130 degrees (Riolo et al, 1974).

[6]N-S-B in normal males becomes slightly more acute, with a mean reduction of .5 degrees; the angle becomes slightly more obtuse in normal females with a mean increase of 1.5 degrees from 6 to 16 years. The sex difference is about 2 degrees. (Riolo et al, 1964).

much as 20 degrees (Garner 1967a, 1967b; Roberts et al, 1975; Peterson-Falzone and Figueroa, 1989). It has also been observed that the anterior and posterior cranial base lengths are both short in TC (Roberts et al, 1975).

The skull base in Stickler syndrome and TC is also narrowed in the transverse dimension. Shprintzen (1982) measured the interpterygoid distance on submentovertical radiographs (taken with a cephalostat for stabilization) in three Stickler subjects and 7 TC subjects. The mean interpterygoid distance for normals was 57 mm in contrast to a mean for S of 44 mm and for TC of 34 mm. Hypoplasia of the pterygoid process of the sphenoid bone, especially the lateral plate, was observed in a dry adult skull by Dahl et al (1975). Transverse narrowing was also reported based on anthropometric measures (inferred by measuring the intertragus distance) of 32 TC subjects, including 18 with cleft palate (Kolar et al, 1985, 1987).

The mandible in TC is hypoplastic and dysmorphic (Rogers, 1964; Gorlin and Sedano, 1971; Dahl et al, 1975; Mafee and Valvassori, 1981; Grayson et al, 1986; Gorlin et al, 1990). Roberts et al (1975), using serial cephalographs, indicated that the mandible was short and had a "peculiar" curve of the inferior border which did not change over time. Measurements of a 15 week dried fetal skull suggested that both the basicranial and mandibular findings are primary abnormalities in Treacher Collins syndrome. Behrents et al (1977) found that in comparison to a normal age-matched fetal head the TC fetus showed slight kyphosis of the cranial base. The body of

the mandible was highly distinctive, with little ossification in the central region which was bowed resulting in sharp curvature of the lower border. Formation and growth of the condyle was defective and the mandible was posteriorly positioned. These basicranial and mandibular abnormalities of early onset could result in a congenitally narrow vocal tract.

Velo-cardio-facial syndrome is associated with an abnormally obtuse cranial base angle (Shprintzen, 1982; Meinecke et al, 1986; Glander, 1990), although normal (Johnson and Ceino-Sena 1990) and acute (Meinecke et al, 1986) angulation have been reported in a few subjects. Arvystas and Shprintzen (1984) studied the craniofacial morphology of 13 subjects with VCF using lateral cephalographs. VCF subjects had obtuse basicranial angles with a mean of 137 (range 128-144 degrees) which was significantly different from normal at the .01 to .001 level. The maxilla and mandible were morphologically normal, but the mandible was abnormally retrognathic in relationship to the maxilla. Arvystas and Shprintzen stated that the platybasia caused an abnormal relationship between the facial bones and cranium, contributing to the appearance of malar deficiency and prominence of the nasal bridge as well as to an unusually wide pharynx. Glander (1990) reported a mean cranial base angle of 133 degrees in 26 subjects with VCF.

Shprintzen (1982) reported that an obtuse cranial base angle was frequent in van der Woude syndrome. However, no cephalometric studies on VDW have been published.

VOCAL TRACT

Pharyngeal Width

In their analysis of a dried TC skull, Dahl et al (1975) observed that maxillary retrusion together with an acute cranial base angle resulted in anteroposterior shortening of the bony nasopharynx. The maxilla was hypoplastic, and its width was reduced. This, together with a backward inclination of the maxilla, resulted in decreased vertical height of the nasopharynx.

It has been observed that certain syndromes were associated with a markedly abnormal pharyngeal width (Shprintzen et al, 1979; Shprintzen, 1982). TC and S have been categorized as "narrow pharynx syndromes of clefting" and VCF and VDW as "wide pharynx syndromes of clefting" (Shprintzen, 1982). The pharyngeal airway was studied in 11 TC subjects (including 9 with cleft palate) using lateral cephalograms, nasopharyngoscopy and multi-view videofluoroscopy (Shprintzen et al, 1979). The TC pharynx was severely hypoplastic with lumen size reduced in the transverse dimension and, to a lesser degree, in the anteroposterior dimension. Narrowing was noted throughout the entire vertical height of the pharynx from the cranial base to the larynx with marked reduction in the lateral dimensions (measured from right to left lateral pharyngeal wall) and some reduction in

the anteroposterior dimensions[7]. The mean inter-LPW width of normal subjects was 32 mm (range 22 to 44 mm), and of nonsyndromic cleft subjects was 36 mm (range 19 to 48 mm)[8]. The pharyngeal width in TC (including the TC subjects with clefts) was extremely narrow, with a mean inter-LPW distance of 14 mm (range 5 to 22 mm). In contrast, 28 of 30 VCF subjects had inter-LPW widths over 40 mm (mean and range were not specified), markedly wider than both normals and nonsyndromic cleft subjects. All of the VCF and 9 of the 11 TC subjects had cleft palate. Van der Woude syndrome was also categorized as a wide pharynx syndrome of clefting by Shprintzen (1982), but no measurements were reported.

Stickler syndrome was also observed to be a narrow pharynx syndrome of clefting (Shprintzen, 1982). The inter-LPW diameter was not reported but the interpterygoid distance seen on submentovertical radiographs was measured. Schafer (1982) and Shprintzen (1982) indicated that this distance determined the transverse pharyngeal width because the lateral aspects of the pharynx are suspended from the pterygoid plates (Bosma, 1976). The mean interpterygoid distance for three S subjects was 44 mm, compared to the mean for normals of 57 mm and for TC subjects of 34 mm.

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[7]Measurement was made at the narrowest distance between the right and left lateral pharyngeal walls as seen on frontal view videofluoroscopy. The narrowest distance was usually near the base of the tongue, corresponding roughly to the Lum 6 level in the current study.

[8]A wider than normal pharynx in isolated cleft subjects was consistent with Maue-Dickson's earlier report of increased pharyngeal width of fetal heads with clefts without increase in width of the fetal heads (Maue-Dickson et al 1976).

Glander (1990) used lateral cephalometric tracings to compare lumen depth and height in subjects with S and VCF. He found that the Stickler airway was longer and narrower than the VCF airway. Robin sequence did not affect the measurements in either group. Glander did not report measurements on any normal subjects.

The airway studies of Schafer (1982) and Shprintzen (1982) supported the observation of Dahl et al (1975) that the size of the supralaryngeal vocal tract was directly related to a constellation of inherent skeletal anomalies. Specifically, basicranial kyphosis (as in S and TC) results in downward flexion of the clivus and depression of the sphenoid complex reducing both the anteroposterior dimension and the height of the nasopharynx. Maxillary hypoplasia (as in S and TC) results in abnormal approximation of the perpendicular pterygoid plates resulting in marked narrowing of the transverse dimension of this space and causing obstruction at the oropharyngeal and hypopharyngeal level. Retrognathia and mandibular hypoplasia could further constrict the hypopharyngeal space (Roberts et al, 1975).

Conversely, Shprintzen (1982) observed that posterior displacement of the cranial base occurs with an obtuse angle, increasing pharyngeal depth. Just as basicranial kyphosis contributes to airway narrowing in S and TC, platybasia contributes to excessive pharyngeal width in VCF and VDW.

Length of the supralaryngeal airway has not been studied extensively. Roberts et al (1975) stated that the hyoid in TC subjects was usually at the level of C-3, the same vertical

level as normals. In contrast, Shprintzen et al (1979) observed antero-inferior displacement of the hyoid, suggesting elongation of the TC vocal tract. Herring et al (1979) observed the TC larynx itself to be vertically elongated, widened laterally, and shortened anteroposteriorly, with a shortened vocal ligament and large arytenoid cartilages.

Airway Function

Dimensions of the lumen reviewed in the previous section might be expected to have implications for both airway function and speech production. Although little has been written on speech and resonance in the cleft syndromes in this study, there is a significant literature on the airway, especially in TC and S. These studies were reviewed because behavior of the vocal tract in terms of airway obstruction may relate to the lumen as a vocal tract.

TC and S subjects have a high prevalence of airway problems (Herring et al, 1979; Shprintzen et al, 1979; Johnston et al, 1981; Brouillette et al, 1982; Sher et al, 1986; Shprintzen, 1988a). Higher infant mortality than in the normal population has been reported (Stickler et al, 1965; Hall, 1974; Herrmann et al, 1975a; Herring et al, 1979). Difficult or impossible endotracheal intubation and significant anesthetic and postanesthetic problems associated with airway problems management of TC patients is common (Ross, 1963; Beighton, 1971; Handler et al, 1979; Roa and Moss, 1984; Miyabe et al, 1985). These difficulties have

been attributed to a variety of structural abnormalities, including pharyngeal hypoplasia (Peterson-Falzone and Pruzansky, 1976; Shprintzen et al, 1979; Herring et al, 1979), difficulty in visualizing the epiglottis and vocal folds (Ross, 1963; Lopez and James, 1968), choanal atresia (Roberts et al, 1975), mandibular hypoplasia (Ross, 1963; Peterson-Falzone and Pruzansky, 1976; Schafer, 1982; Sher et al, 1986; Shprintzen, 1988a), and restricted oral opening (Peterson-Falzone and Pruzansky, 1976). These findings are not mutually exclusive, and all may play a role in airway compromise, surgical difficulty, anesthetic risk, and speech disorders.

Airway narrowing predisposes a subject to obstructive sleep apnea (OSA)[9]. OSA and obstructive "awake" apnea was found in 25% of the TC and 14% of the S infants studied at one Center, often in association with Robin sequence (Sher et al 1986; Shprintzen 1988a). OSA also occurred in 13% of the infants with VCF and Robin sequence at the same Center, although VCF is associated with a wide pharynx (Sher et al 1986; Shprintzen 1988a). Gorlin et al (1990) reported that OSA had been found in about half of the neonates with VCF. There have not been reported cases of OSA or OAA associated with van der Woude syndrome.

Airway obstruction in various syndromes has been attributed to glossoptosis (Johnston et al, 1981; Sher et al, 1986; Shprintzen, 1988a). However, just as there are multiple

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[9]OSA is operationally defined as 30 apneic episodes in a 7 hour sleep period; an apnea is defined as cessation of airflow from the nose and mouth for 10 seconds (Sher et al, 1986).

patterns of velopharyngeal closure during speech, endoscopic examination has revealed multiple mechanisms of airway obstruction in addition to glossoptosis. These include blockage of the airway by compression of the tongue and palatal tags against the posterior pharyngeal wall ("palatoglossopharyngeal junction") observed in S and TC, and sphincteric pharyngeal collapse which was observed in subjects with S, TC, and VCF (Sher et al 1986; Shprintzen 1988a). Acute cranial base angulation combined with micrognathia in narrowing the size of the lumen was implicated as contributory to predisposing infants with S and TC to obstruction. In VCF, obstruction was attributed to pharyngeal hypotonia and/or mandibular retrognathia.

OSA has been reported as a complication of palatoplasty and pharyngoplasty in TC (Crysdale, 1981; Roa and Moss, 1984) necessitating tracheotomy or pharyngeal flap revision, complicating treatment of VPI. OSA has been reported as a complication of pharyngeal flap surgery in TC and S because of a small airway and in VCF because of pharyngeal hypotonia (Shprintzen et al, 1981; Shprintzen, 1988b).

Choanal atresia has been reported in TC (Roberts et al, 1975) and S (Say et al, 1977). Roberts et al (1975) speculated that the short cranial base length and obtuse angulation of the palatal plane, together with an acute cranial base and normal anterior face height, reduces the size of the posterior choanae. Say et al (1977) believed this represented an extreme expression of midface deficiency. Small or absent paranasal and maxillary sinuses have also been

reported in TC (Gorlin and Sedano, 1971; Mafee and Valvassori, 1981). These findings together with the middle ear anomalies, suggest generalized hypoplasia of the head and neck air spaces in TC (Shprintzen et al, 1979). A small nasal capsule was reported in VCF, related to the obtuse cranial base (Arvystas and Shprintzen, 1984). These observations might be expected to contribute to abnormalities in nasal and oral resonance.

SPEECH

Although there have been many reports describing large numbers of subjects with Stickler, Treacher Collins, and velo-cardio-facial syndromes, and several on van der Woude syndrome, the majority have focused on the ophthalmologic, morphologic, airway, and genetic aspects of these conditions. The prevalence of hypernasality and other speech disorders in these populations has not been adequately studied. Most of the available information on speech is anecdotal.

Stickler Syndrome

Herrmann reported "nasality" in 29% of his subjects, and "speech impairment" in one subject without further description or correlation with palatal morphology (Herrmann et al, 1975a). Hall (1974) noted only one case of hypernasality in five subjects with repaired clefts.

In at least two reports (Cohen et al, 1971; Shprintzen et al, 1985c) family members of affected subjects were found to

have submucous clefts that had not been suspected because of normal speech.

There were only two reports on S by speech pathologists with nonspecific and contradictory information. In the first report, a general catalogue of communication disorders in 105 syndromes, articulation and resonance disorders related to cleft palate and voice disorders were listed as "frequent" findings in Stickler syndrome (Siegel-Sadewitz and Shprintzen 1982). The articulation, resonance, and voice disorders were not described. However, in a later report, hyponasality was reported as a frequent finding in Stickler subjects (Gereau and Shprintzen, 1988).

Treacher Collins Syndrome

Speech may be normal in TC, even in a severely affected patient (Peterson-Falzone, 1981). However, severe vocal tract constriction and hypoplasia of other resonating cavities might be expected to have a negative effect on both oral and nasal resonance, and cleft palate might be associated with VPI. Other potential sources of abnormal speech in TC subjects are hearing loss, abnormal tongue posture, and open bite. Unfortunately, most studies in TC have focused on morphologic, otologic, and surgical considerations. Speech production has been addressed by only a few investigators. Massengill et al (1971) intended to provide articulation and resonance data on two subjects with TC. However, the photographs included in

the paper indicated that the subjects were affected with hemifacial microsomia, not with TC.

Articulation in TC. Using cephalometry, Garner (1967a, 1967b) observed a skeletal open bite and noted that the available tongue space was diminished because of mandibular hypoplasia and retrognathia. He speculated that these two factors act to force the tongue down and forward, and described the dental effect (flaring of the teeth) but not speech. Murray et al (1975) stated that tongue movement and articulation in TC may be improved by craniofacial surgery but did not describe the presurgical or postsurgical speech patterns of his subjects, nor was palate morphology described.

Peterson-Falzone and Pruzansky (1976), described an abnormal articulatory posture noted on a lateral cephalogram in one TC subject with "CPI" in whom /s/ was produced with a raised tongue dorsum obstructing oral emission of air. This description is identical to the posture for a nasal snort (Trost, 1981), an abnormal compensatory error which is a known component of the "cleft palate speech" disorder and not unique to TC (Hoch et al, 1986).

Vallino et al (1991) described speech characteristics of 20 TC subjects including 8 with cleft palate and 2 with SMCP. Results were not differentiated by palate morphology. Articulation was normal in 2 subjects, and 9 subjects produced

combined auditory and visual distortions[10]. Compensatory errors were reported, including glottal stops, laryngeal compensations, pharyngeal fricatives, velar stops, and posterior nasal fricatives. However, the number of subjects with these errors was not stated. Difficulty with bilabial closure and interdentalization of tongue-tip sounds was attributed to open bite, but did not occur in every subject.

Voice and Resonance in TC. VPI and hypernasality have been described as frequent findings in TC, even in the absence of cleft palate (Beighton, 1971; Peterson-Falzone and Pruzansky, 1976; Peterson-Falzone, 1981; Sparks and Millard, 1981). In these studies, identification of cleft palate was based solely on oral examination. As noted previously, insufficient diagnostic scrutiny may have resulted in failure to diagnose submucous clefts. Hypernasality has also been reported in TC as a sequela of maxillary advancement (Crysdale 1981).

Peterson-Falzone (1981) observed that limited oral opening in TC related to mandibular hypoplasia, and abnormal height of the tongue dorsum at rest caused by the curved mandibular body (also noted by Schafer, 1982) may contribute to clinical descriptions of a "muffled" voice quality. She

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[10]"Auditory distortion" refers to a distortion that is heard by a listener. "Visual distortion" refers to the way the speaker's articulatory gestures look during the speech act. This does not necessarily affect the sound as it is heard by the listener. An example is interdental protrusion of the tongue-tip during production of apical /n/, which looks distorted but is heard as normal.

suggested that the muffled quality was linked to abnormal resonating characteristics of the supralaryngeal vocal tract or may result, at least in part, from aberrant laryngeal vibratory patterns.

Siegel-Sadewitz and Shprintzen (1982) indicated that articulation, voice, and resonance were frequently abnormal in TC, but provided no further information. However, Gereau and Shprintzen (1988) stated that, as in Stickler syndrome, resonance in TC is frequently hyponasal.

In summarizing the results of the only acoustic study on TC to date, Peterson-Falzone (1988) found that crowding of the oral cavity and pharyngeal space caused damping and abnormal frequency location of the vowel formants. However, she indicated that even when obvious VPI is present, the effect of this crowding on the vowel formants in producing a peculiar muffled quality overrides what would otherwise be clearly hypernasal speech. Unfortunately, these data were presented at an ASHA meeting in 1984 and never published, and no further analysis was done (S. Peterson-Falzone, personal communication, April 16, 1991). No information was available about the methods, subjects, cleft status, or results of clinical (perceptual) evaluation. Still, hypernasality was described as a frequent finding in TC (Peterson-Falzone, 1988).

Vallino et al (1991) reported normal voice quality in 55% of 20 TC subjects, and mild hoarseness in 1 subject. Forty percent had normal resonance, and 25% were hypernasal. An additional 25% had "mixed hypo- hypernasality/muffled"

resonance. The hyponasality was attributed to constricted nares or "some type of obstruction" preventing adequate airflow during production of nasal consonants. No subject had hyponasality alone. As noted above, half of these subjects had cleft palate, but resonance and voice characteristics were not reported as a function of cleft history.

Velo-cardio-facial Syndrome

Hypernasality and articulation disorders are common in VCF (Shprintzen et al, 1978; Siegel-Sadewitz and Shprintzen, 1982; Meinecke et al 1986; Stevens et al, 1990). The severity was generally not reported, but one case was said to be "mildly" hypernasal by Williams et al (1985). Golding-Kushner et al (1985) reported that hypernasality in most cases was severe, and that most subjects had severe articulation disorders.

Van der Woude Syndrome

The term "cleft palate speech," presumably referring to glottal stops, pharyngeal fricatives, and nasal snorting, was said to characterize the speech in several subjects with van der Woude syndrome, who were also described as hypernasal (Burdick et al, 1987). Siegel-Sadewitz and Shprintzen (1982) stated that articulation and resonance problems related to cleft palate are common in VDW. Glass et al (1979) also stated that hypernasality was common in VDW, but the degree of nasality was only given for one subject, who was moderately hypernasal. Gereau and Shprintzen (1988) reported that

hypernasality was "routine" in VDW following palatoplasty. On the other hand, normal speech and resonance has also been reported, as in the case of a subject's father who was found to have VDW and a submucous cleft palate on examination (Shprintzen et al, 1980).

VELOPHARYNGEAL CLOSURE

Gereau and Shprintzen (1988) examined the frequency of velopharyngeal insufficiency in 32 S, 14 TC, 64 VCF, and 28 VDW subjects with cleft palate using multi-view videofluoroscopy and nasopharyngoscopy. They reported that VPI was "rare" in syndromes with an acute cranial base (TC and S). Only 1 (7%) TC and 5 (16%) S had VPI. On the other hand, VPI was present in the majority of subjects with "wide pharynx" syndromes, occurring in 26 (93%) VDW and 62 (97%) VCF subjects. The degree of VPI was not stated. Also, all VCF and VDW subjects with good V-P closure had large adenoids. The prevalence of VPI in 500 nonsyndromic cleft palate subjects at the same institution was 14% (Hall and Golding-Kushner, 1989).

Fluoroscopic examination revealed poor velar motion in 26 subjects ascertained through a cardiology clinic who probably were affected with VCF (Stern et al, 1977). In the only description of velopharyngeal movement patterns using multi-view videofluoroscopy, Shprintzen et al (1978) reported that VPI in velo-cardio-facial syndrome was characterized by absent

or poor LPW motion. VPI in velo-cardio-facial syndrome was initially attributed to pharyngeal hypotonia (Shprintzen et al, 1978). Subsequently, additional contributory factors in VPI were said to be the excess pharyngeal space (related to the obtuse cranial base angle) together with palatal deficiency (Arvystas and Shprintzen, 1984). Adenoid hypoplasia in VCF further diminishes the likelihood of adequate velopharyngeal closure, because the adenoid is the primary point of velar contact during speech in children with normal and cleft palate (Subtelny and Koepp-Baker, 1956; Skolnick et al, 1975; Croft et al, 1981; Siegel-Sadewitz and Shprintzen, 1986; Gereau and Shprintzen, 1988).

CHAPTER 3

METHODS

PART I: PREVALENCE OF SPEECH DISORDERS IN FOUR SYNDROMES

SUBJECTS

Registration and database records of the Center for Craniofacial Disorders of Montefiore Medical Center and the Albert Einstein College of Medicine (CCFD) from January 1976 through December 1988 were reviewed. 2936 patients were registered during that 13 year period. All patients with cleft palate without cleft lip or alveolus who had a primary syndromic diagnosis of Stickler syndrome (S), Treacher Collins syndrome (TC), Van der Woude syndrome (VDW), or Velo-cardio-facial syndrome (VCF) were identified, yielding a total of 129 patients or 4% of the total registration. The type of cleft palate included overt cleft palate (CP), submucous cleft palate (SMCP), or occult submucous cleft palate (OSMCP).

DATA COLLECTION

Medical records of all identified patients were reviewed to verify the diagnosis and cleft type, and to obtain demographic, speech and resonance data. The following information was obtained on each subject:

1. Date of birth and chronological age at time of referral to CCFD, gender
2. Referring diagnosis and reason for referral

3. Established diagnosis (S, TC, VCF, VDW)
4. Cleft type (CP, SMCP, OSMCP)
5. Age at time of palate repair, if done
6. History of glossopexy or tracheotomy in infancy to relieve upper airway obstruction
7. Audiometric status in each ear, based on testing at the time of speech and other examinations (testing included pure tone air and bone conduction thresholds, speech reception and speech discrimination, tympanometry, acoustic reflexes)
8. History pertaining to articulation development
9. Articulation, nasal resonance, oral resonance, voice, and receptive and expressive language status based on formal evaluation at the time of referral to CCFD by an ASHA certified speech-language pathologist.

A copy of the data collection form for the prevalence study appears in Appendix A-1.

Verification of Diagnosis

Syndromic diagnoses were confirmed by a dysmorphologist, medical geneticist, and/or genetic counselor experienced in the identification of craniofacial syndromes who reviewed records or examined the patient. Diagnoses were based on findings other than craniofacial morphology as assessed by cephalometry, VPI, or airway size. Any patient with a

questionable expression of the syndrome or unconfirmed cleft was excluded.

DIAGNOSTIC PROCEDURES AT CCFD

Perceptual Evaluation of Speech

Standard evaluation procedure at CCFD for all patients includes independent perceptual assessment of oral and nasal resonance, articulation, vocal quality, and vocal pitch by at least two ASHA certified speech pathologists experienced in the evaluation and treatment of speech disorders related to cleft palate and velopharyngeal insufficiency[11].

Speech Sample

Clinical, endoscopic, and videofluoroscopic examinations at CCFD were performed with a standard speech sample which included production of sounds in isolation, C-V combinations, and phrases, to allow for perceptual evaluation and observation of a full range of velopharyngeal gestures under various conditions of intraoral pressure and phonemic complexity (Shprintzen and Golding-Kushner, 1989; Golding-Kushner et al, 1990).

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[11]Between 1976 and 1988 there were 6 speech-language pathologists on the CCFD Team including three at any given time.

The speech sample used at CCFD on which nasality and articulation ratings for Part I of this study were based included the following:

ma-ma-ma	Jerry's slippers	kitty cat
pa-pa-pa	fifty-five	baby boy
ti-ti-ti	sustained /s/, /f/	table top
Stop the bus	Popeye plays baseball	
Suzy sees Sally	counting 1-10	

This speech sample was designed to include the following phonetic contexts:

1. Repetitions of different C-V combinations, where the consonant was a sample of both voiced and unvoiced plosives, and a nasal consonant /m/ paired with both high and low vowels (e.g., /i/ and /a/).
2. Production of sustained voiceless fricatives (/s/ or /f/), critical for revealing phoneme specific VPI or phoneme specific closure (Shprintzen and Golding-Kushner, 1989).
3. Utterances including nasal to non-nasal transitions and non-nasal to nasal transitions, as produced during counting one-two, seven-eight, etc.

As part of the perceptual evaluation at CCFD, hypernasality and hyponasality were rated on separate 4 point scales as absent, mild, moderate or severe. Vocal pitch was rated as

normal, high, or low for age and sex. Vocal quality was rated as normal or hoarse.

Speech and resonance data for this study were obtained by review of the independent evaluations which were done at the time of referral to CCFD or at the time of instrumental assessment[12].

PART II: CRANIAL AND VOCAL TRACT MORPHOLOGY IN FOUR SYNDROMES

SUBJECTS

Experimental Subjects

A subset of subjects from Part I of the study was identified for whom a lateral cephalogram and recordings of nasopharyngoscopic and multi-view videofluoroscopic examinations were available. To be included, all three records had to have been obtained over no longer than a six month period, except for adults who had completed facial and cranial growth, as part of a standard clinical examination. Any subject with a pharyngeal flap or other pharyngoplasty, or who had undergone orthognathic surgery was excluded. These subjects were excluded because the surgical procedure could have affected perceptual evaluation, cephalometric measurements, and/or velopharyngeal movements. The study was

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[12]Interrater reliability for speech, resonance, and voice judgements made by KJG-K and R. Shprintzen, both of whom examined most of the 129 subjects in this part of the study, was previously established to be high, with independent ratings at above a 95% level of agreement (Golding, 1981).

primarily retrospective although some subjects were added as data became available. Forty-five CCFD patients, including 43 from the initial prevalence study, served as subjects for morphologic and physiologic analysis[13].

Control Subjects

Fifteen subjects were obtained from the Montefiore Medical Center Orthodontic Program to serve as controls for the morphologic (cephalometric) measures. The control subjects were orthognathically normal and had no history of craniofacial disorders or speech abnormalities, had never had surgery to the head or neck, and presented to the Orthodontic program with Class I (dental) malocclusions only. These normal controls were drawn from a similar geographic region as the experimental subjects, and the control group was similar in racial composition to the experimental group. Certain cephalometric measurements made on the controls were compared with published norms to confirm that they were skeletally normal.

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[13]Examinations of velopharyngeal function were available on only 8 subjects with Treacher Collins syndrome and cleft palate only. In order to maintain a minimum of 10 subjects per syndrome group, two TCS subjects with cleft lip and palate (one unilateral, one bilateral) were added to the experimental group. Their cephalographic, nasopharyngoscopic, and videofluoroscopic data were included with the other repaired-cleft subjects.

MORPHOLOGY: CEPHALOMETRY

Examination Procedure

All lateral cephalograms were taken with the patient's head stabilized in a Sieman's cephalostat with a cathode-to-object distance of five feet and an object-to-film distance of 13 cm. In order to assure standard head position both within and between subjects, cephalographs were taken in the natural head position with the teeth in centric occlusion and with the subject instructed not to swallow or speak and to breathe quietly.

Preparation of Materials

Each radiograph was traced on clear acetate paper. By convention, the skeleton and facial profile were traced with solid lines, the soft tissue with broken lines. The soft tissue of the vocal tract that was traced included the posterior pharyngeal wall, adenoid, soft palate, and tongue, along with the epiglottis and any visible laryngeal structures. Tonsils that were visible in the airway were traced to differentiate them from the soft palate but were ignored in assessing the size of the pharyngeal lumen. The tracings were photocopied and identified only by subject number. All measurements were made on the photocopied sheets.

Cephalographs of the 45 experimental subjects and 15 control subjects were traced and measured by the investigator following a training procedure. Linear measurements were made

to the nearest 0.5 mm, and angles were measured to nearest 0.5 degrees.

Training. To establish the investigator's reliability as a tracer and in the identification of landmarks, an initial series of 35 films was traced. The investigator and an Instructor in the Orthodontic program of Montefiore Medical Center independently traced and measured cephalographs of 15 normal and 20 cleft subjects. The orthodontist was experienced in the procedure and his measurements served as the standard. After the first 11 tracings, any discrepancies of more than 5 mm or 5 degrees were jointly reviewed to determine if redefinition or increased specificity of criteria for landmark selection was necessary, and, if so, measurements were repeated. Agreement between measurements of 90% or better indicates very high reliability (Guilford, cited in Williams, 1968). Therefore, the investigator retraced and/or remeasured discrepant planes and angles until 93% agreement between the two tracers was obtained.

Interrater Reliability

A second measurement was made for each plane and angle on the cephalometric tracings of 23 experimental subjects by a post-doctoral dental fellow at Montefiore to establish interrater reliability. He did not participate in the initial training procedure, did not know the purpose of the study, and was not familiar with the syndromes included in the study.

Cephalometric Analysis: Landmarks, Planes, and Angles

The following landmarks were identified according to standard procedure described by Jacobson and Caulfield (1985) (Figure 3.1):

Or = Orbitale; lowest point on the inferior rim of the orbit

Po = Porion; most superiorly positioned point of the external auditory meatus; machine porion is that point on the ear rods of the cephalostat and may be more easily visualized. Machine Po was used.

Cranial base landmarks.

S = Sella; geometric center of the pituitary fossa of the sphenoid bone, located by visual inspection

N = Nasion; most anterior point on the frontonasal suture in the midsagittal plane

B = Basion; most inferior posterior point on the anterior rim of the foramen magnum, located using straight edge parallel to FH (defined below)

Maxillary and Mandibular landmarks.

ANS = Anterior nasal spine; anterior tip of the nasal spine (the sharp bony process of the maxilla at the lower margin of the anterior nasal opening)

PNS = Posterior nasal spine; posterior spine of the palatine bone constituting the hard palate, located using a line perpendicular to FH

Ar = Articulare; point at the junction of the posterior border of the ramus and the inferior border of the cranial base (occipital bone)

Go = Gonion; point on the curvature of the mandible located by bisecting the angle formed by lines tangent to the posterior ramus and the inferior border or the mandible

Me = Menton; lowest point on the shadow of the symphysis of the mandible seen on the lateral cephalograph located by using a line parallel to FH and moving the straight edge upward until it touches the inferior border of the symphysis

Ptm = Pterygomaxillare; lowest point of pterygomaxillary fissure

Pg = Pogonion; most anterior point on chin located by moving line perpendicular to FH until it first reaches chin

Gn = Gnathion; point on chin midway between Me and Pg

Reference Planes. The following reference planes were drawn:

FH = Frankfort Horizontal; plane formed by straight line intersecting Orbitale and Porion, used as referent for other measures to control for changes affected by head position

H = Horizonal; geometric horizontal generally corresponding to horizontal edge of film

Vertical= line perpendicular to H

PPl = Palatal plane; intersects ANS and PNS

MPl = Mandibular plane; intersects Go and Gn

HPl = Hyoid plane; horizontal to FH, through the point at which the hyoid bone enters the pharynx; a novel plane

Linear Measurements. The following standard linear measurements were made:

ANS - PNS = length of hard palate

N - S = anterior cranial base length

S - B = posterior cranial base length

Angular Measurements. The following standard angular measurements were made:

H-FH = angle formed by H and FH planes to correct for lack of true horizontal orientation of FH.

H-N-S = angle formed by H and anterior cranial base (nasion-sella) to obtain a measure of vertical height of sella

N-S-B = cranial base angle (nasion-sella-basion)

N-S-Ar = cranial base angle using ramus (similar to N-S-B)

FH-MPl = angle formed by FH and mandibular plane; a measure of vertical facial height

Vocal Tract. Some of the vocal tract measurements were validated in previous studies, including that of Laniado (1987). Measurements which were developed or modified for this study are indicated by an asterisk.

V = inferior tip of velum

PNS - V = velar length

ANS-PNS-V = palatal angle at rest; the relative "drape" of the velum

*PPl-PPW = airway angle formed by the palatal plane and line tangent to the posterior pharyngeal wall (PPW); If the PPW was irregular, the tangent was drawn as the "best fit" to parallel the course of the vocal tract

*A-PPW = vocal tract angle formed by lines tangent to PPW and superior boundary of vocal tract (as the airway curves toward nasal passages or adenoid)

MPl-H = distance from mandibular plane to superior most point on hyoid on line constructed perpendicular to mandibular plane

Anteroposterior depth of the lumen and soft tissue thickness of the PPW was obtained at six levels by construction of the following lines parallel to the palatal plane (Figure 3.2):

VELOPHARYNGEAL LEVEL:

*Lum 1: PNS to PPW, excluding any soft tissue

*Lum 2: midpoint of velum between PNS and V to PPW

OROPHARYNGEAL LEVEL:

*Lum 3: V to PPW

*Lum 4: PPW to tongue with origin at intersection point of mandibular plane with PPW

HYPOPHARYNGEAL LEVEL[14]:

*Lum 5: PPW to tongue or epiglottis closest to antero-inferior tip of odontoid process

*Lum 6: PPW to anterior airway boundary (tongue, epiglottis) closest to midpoint of C-3

THICKNESS OF PPW:

*PPW 1: PPW to skull base or cervical spine tangent at plane of Lum 1

*PPW 2: PPW to cervical spine at plane of Lum 2

*PPW 3: PPW to cervical spine at plane of Lum 3

*PPW 4: PPW to cervical spine at plane of Lum 4

*PPW 5: PPW to cervical spine at plane of Lum 5

*PPW 6: PPW to cervical spine at plane of Lum 6

AIRWAY HEIGHT

Vertical height of the larynx and vocal tract was measured using the following lines constructed perpendicular to the palatal plane (Figure 3.2):

*PPl-V: palatal plane to inferior tip of velum; oropharyngeal airway height

*PPl-HPl: palatal plane to inferior reference line (hyoid plane); total oro- and hypopharyngeal airway height

*Lower airway height (LAH): difference between PPl-V and PPl-HPl; hypopharyngeal airway height

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[14]The term hypopharyngeal usually refers to the subglottic or lower airway. It is used here to refer to the lowest one-third of the supraglottal vocal tract. The larynx itself and the subglottal vocal tract were not examined.

Computer Analysis

All cephalometric tracings were digitized and stored using the Pentax CMS-6000 Information/Image Management System (IMS). The IMS is a software package run on an IBM-AT compatible which has the ability to digitize and store any video image, recorded or live. The stored images may then be subjected to various procedures, such as annotation, tracing, enlargement, and/or measurement of surface areas. Measurement is by computation of the number of pixels within a user-defined boundary. All computer measurements in this study were developed specifically for this project.

A Panasonic color video camera (PK-959) was used for recording the images to be digitized with tracings mounted on a free-standing light-box 18 inches from the camera lens. A line-drawing portion of the software program utilizing a mouse peripheral was used to trace the lumen and skeletal airway frame which was outlined during the initial tracing procedure. It was necessary to identify a referent for use in converting the pixel measurements into meaningful units to correct for any magnification differences which may have occurred when the original radiographs were obtained or as a result of the input procedure to the IMS system. Machine porion, or the shadow of the ear rods of the cephalostat, which has a known area of 1 cm, appeared in every cephalograph and was selected as the standard referent. The area of the tracing of Po on each cephalograph was measured in pixels and was also was computed in mm^2 using the formula:

$$\text{area} = (\text{diameter}/2) \times 3.14$$

These two measurements of Po were then used as referents for conversion of the other computer measurements into millimeters using the formula:

$$\frac{X \times \text{Po area}}{\text{Po pixels}}$$

where X = the computer measurement in pixels to be converted.

The following areas were computed in machine units (pixels) (Figure 3.3):

BLOCK: area enclosed in the skeletal frame defined by the following referent lines:

FH = superior reference line

HPl = hyoid plane; inferior reference line constructed parallel to FH through the point at which the hyoid bone intersects the pharynx

PtmPl = pterygomaxillary plane; anterior reference line constructed perpendicular to FH through PTM

BPl = basion plane; posterior reference line constructed perpendicular to FH through basion

AW (AIRWAY): lumen area within the skeletal frame, bounded anteriorly by the velum and tongue, and posteriorly by the posterior pharyngeal wall, with any tonsilar tissue present ignored; actual lumen

AD (ADENOID): area of the adenoid

VT (VOCAL TRACT): area within the skeletal frame including **AW** and **AD**; maximum lumen with adenoid removed

The following measurements of relative adenoid and airway size were also made:

PCTVTAD: Percent of the vocal tract filled with adenoid tissue: [AD/(AW + AD)] x 100

PCTSKAW: Percent of the skeletal airway frame (BLOCK) occupied by airway: (AW/BLOCK) x 100

Linear measurement of the block reference planes were made to allow comparison of block width and length, as follows:

BL WDTH: PTM plane to basion plane, corresponding to anteroposterior depth of the skeletal frame of the airway

BL HGT: FH plane to hyoid plane, corresponding to the height of the skeletal frame of the airway

PART III: VELOPHARYNGEAL PHYSIOLOGY IN FOUR SYNDROMES

Physiological data pertaining to velopharyngeal closure using direct imaging techniques of nasopharyngoscopy and multi-view videofluoroscopy were obtained on the 45 subjects who had undergone cephalometric analysis. Subjects with normal speech did not undergo multi-view videofluoroscopy so that unnecessary radiation could be avoided. Also, some subjects were uncooperative for nasopharyngoscopy or were examined before nasopharyngoscopy was routine for every patient at CCFD. In those cases, analysis was limited to

cephalometry and a single velopharyngeal imaging procedure. A total of 76 videotapes of the 45 subjects were analyzed to obtain data of velopharyngeal function. There were 39 nasopharyngoscopic studies and 37 multi-view videofluoroscopic examinations. Thirty-one of the subjects had data from both nasopharyngoscopy and videofluoroscopy (Table 3.1).

Speech Sample

Analysis of velopharyngeal component gestures from both endoscopic and fluoroscopic studies was usually made at maximum closure during production of isolated, sustained, voiceless fricative /s/ to ensure that differences in phonetic context would not confound the analysis. The phoneme /s/ was selected because it was included in all studies and, based on preliminary review of examinations to be analyzed, was generally representative of the speaker's "best" closure pattern.

Abnormal lip, tongue, and glottal activity associated with "cleft palate speech" is known to have a bidirectional effect on velopharyngeal insufficiency (Golding, 1981; Hoch et al, 1986; Henningsson and Isberg, 1986). Specifically, when glottal stops, pharyngeal fricatives, or nasal snorting (posterior nasal fricative) are produced, there is a decrease or even elimination of lateral pharyngeal wall motion. The nasal snort may even be accompanied by outward movement of the lateral pharyngeal walls (Golding-Kushner, 1991; Henningsson and Isberg, 1991; Hoch et al, 1986; Henningsson and Isberg, 1986). Therefore, in order to make accurate statements about

the effect of underlying craniofacial morphology on velopharyngeal movements, VP measurements were made during correct articulation only, and not during production of abnormally produced phonemes. Movement was examined for intersyllabic and intrasyllabic consistency, the presence of sound specific VPI or sound specific closure, and consistency on repeated attempts of the same speech task to determine the "habitual" degree and pattern of VP closure. When inconsistencies in VP valving were present, measurements were made at maximum movement and a notation was made indicating whether or not this was consistent with the habitual movement. Thus, if the subject did not produce /s/ with correct tongue placement and oral air stream direction, or if VP gestures on /s/ were different from other normally produced phonemes because of an aerodynamic artifact, sustained /f/ was used. When this sound was also abnormally articulated, a voiceless plosive (/p/ or /t/) was used, where "best" velopharyngeal performance was observed. For each subject, a notation was made indicating if the sound used for analysis was representative of the speaker's maximum velopharyngeal closure and habitual velopharyngeal closure[15]. The position of the tonsils was examined by endoscopy and fluoroscopy to ensure that analysis was not influenced by their presence which may affect velopharyngeal closure (Shprintzen et al, 1987; MacKenzie-Stepner et al, 1987a).

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[15]Habitual movement refers to the general pattern of velopharyngeal motion observed during connected speech.

NASOPHARYNGOSCOPY

Examination Procedure

All nasopharyngoscopic examinations were performed by the investigator or one other expert endoscopist using a flexible end-viewing fiberoptic nasopharyngoscope (Machida 3-L 3 mm diameter endoscope prior to 1990, Machida 2-L 2 mm diameter nasopharyngoscope after 1990) with a 400W high intensity cold light source (Machida RG-400). Examinations with the Machida 3-L were preceded by two-stage administration of topical anesthesia (Shprintzen and Golding-Kushner, 1989). The larger nasal passage was determined by visual inspection and sprayed with a solution of 2% Pontocaine (aqueous tetracaine hydrochloride) mixed in equal parts with 0.5% phenylephrine. A strip of cotton orthopedic bandage (Webril) 3 mm wide and 8 cm long was saturated with 2% Pontocaine and inserted into the sprayed nostril using a small bayonet forceps. The packing was left in place for 5-10 minutes and removed immediately prior to examination. Examinations performed with the 2 mm endoscope were preceded only by the initial spray because the smaller endoscope causes virtually no discomfort even without anesthesia eliminating the need for total numbing of the nasal passage (Golding-Kushner and Shprintzen, 1990). There was no difference between the endoscopes in the size or quality of the endoscopic image (Golding-Kushner and Shprintzen, 1990).

Recording

Examinations were performed with the endoscope connected to a tripod-mounted camera (currently Panasonic PV-S445D) and

recorded on videotape. Examinations prior to 1980 were recorded on super-8 mm movie film with a motion-picture camera (GAF 250XL) with simultaneous sound. A Sony portable VCR in beta format (SL-2000 with AC-220 power adapter) was used from 1980-1984, and a VHS format VCR after 1984.

Preparation of Materials for Analysis of Velopharyngeal Gestures

The original tape segments were located on film, or VHS or Beta videotape, and copied in chronological order to a master videotape (VHS) with the examinations preceded by subject ID number. Studies which had been initially recorded on motion picture film were converted to videotape. Isolation of frames to be analyzed was accomplished using the Panasonic AG-1950 stereo Hi-Fi videocassette recorder, a professional quality video editing unit. The frames to be traced and measured were then photographed using the Polaroid Freeze-frame Video Recorder, and any identifying information appearing in the photograph, such as the Subject's initials, diagnosis, or date of examination, was covered with opaque tape. The ID number and context (i.e., rest position, /s/, /p/, /t/) were written on the photograph. The photographs were then traced on clear acetate paper, and the tracings were digitized, stored, and annotated using the IMS, following the same procedure as used for cephalometric tracings.

Analysis of Velopharyngeal Gestures

Analysis of velopharyngeal closure was done according to the protocol developed by a multidisciplinary International Working Group (IWG) of experts in nasopharyngoscopy and multi-view videofluoroscopy (Golding-Kushner et al, 1990). All measurements were based on endoscopic views where all, or most of the VP orifice was visible in a single field of view during production of the sound to be analyzed.

Measurement Ratios[16]. Displacement ratios were computed for each component of the velopharyngeal valve to describe the distance travelled by the structure relative to the maximum distance possible (i.e., to close the velopharyngeal port). The displacement of each structure was measured relative to the resting position of the opposing structure. Movements of the velum, right lateral pharyngeal wall, left lateral pharyngeal wall, and posterior pharyngeal wall were rated separately with a ratio computed for each structure. The procedure for computing each ratio is specified in the sections that follow. If a measurement could not be made because of inability to visualize a structure, a notation of

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[16]Measurements of absolute size are essentially impossible to obtain from videofluoroscopic and nasopharyngoscopic images for many reasons which are discussed by Golding-Kushner et al (1990). For example, using a standard sized referent placed in the field of vision may interfere with velopharyngeal valving. Endoscopic images are subject to multiple sources of distortion (Pigott and Makepeace, 1982) such as variable proximity to the image being measured and the angle of view of the sphincter. In any case, the relative distance traversed by a structure is a more valid measure of velopharyngeal closure than the absolute distance which has different meaning in a small pharynx than in a large one. Therefore, movement ratios defining the percentage of the velopharyngeal port affected by a particular gesture were computed.

"could not visualize" (CNV) was made. This occurred when the pharynx was large or angulated, making it impossible on endoscopic studies to see both lateral pharyngeal walls simultaneously.

Velar Displacement: (Figure 3.4.) A line was constructed between the midpoint of the velum and the posterior pharyngeal wall along the trajectory of the movement of the velar midpoint (identified as the midpoint of the musculus uvulae, central depression on the velar surface, or anatomic midline of a flat velum). The rest position of the velar midpoint (during nasal inspiration) was defined as 0.0 on a ratio scale. The point where the reference line intersected the posterior pharyngeal wall or adenoid at rest was defined as 1.0 on the ratio scale. The point of maximum movement of the velum along the reference line established the degree of velar movement relative to points 0.0 and 1.0.

Lateral Pharyngeal Wall Displacement: (Figure 3.5.) A horizontal line was constructed to intersect the most medial position of the lateral pharyngeal wall on each side at rest. The rest position of each lateral wall (during nasal inspiration) was defined as 0.0 on a ratio scale. The intersection point of the reference line on the opposite lateral wall was defined as 1.0 on the ratio scale. The point of maximum movement of each lateral wall along the reference line established the degree of lateral movement between points 0.0 and 1.0. Each lateral wall was assessed separately(R-LPW,

L-LPW). If there was movement away from the opposite lateral wall, this was recorded as -0.1.

Posterior Pharyngeal Wall and Passavant's Ridge Displacement: (Figure 3.6.) A line was constructed between the posterior pharyngeal wall (PPW) or location of Passavant's Ridge (PR), if present, and the midpoint of the velum (as defined above). The rest position of the velar midpoint (during nasal inspiration) was defined as 1.0 on a ratio scale. A reference line was constructed along the movement trajectory of the PPW or PR midpoint. The point at which the reference line intersected the posterior pharyngeal wall at rest was defined as 0.0 on the ratio scale and the point of maximum movement of the posterior pharyngeal wall along the reference line established the degree of PPW movement relative to points 0.0 and 1.0.

Adenoid Size: The area of the adenoid (Figure 3.4) and the area of the entire closure plane were traced and measured using the IMS. Relative adenoid size (NAD- naso adenoid) was then computed using the formula:

$$\frac{\text{adenoid size}}{\text{total closure plane area}} = \text{\% vp closure plane occupied by adenoid}$$

Velopharyngeal Gap Description.

Size of the Gap: The IMS was used to trace and measure the entire closure plane at rest, and the velopharyngeal gap during the target phoneme. Calculation was made of the

percentage (ratio) of the VP orifice closed during the segment(s) analyzed, with 1.0 representing complete closure (i.e., 100 percent movement or closure), and 0.0 representing the rest position during nasal inspiration (absence of movement, i.e., gross VPI). If only bubbling was seen, but no gap could be defined (i.e., a "pin hole" gap), this was recorded as 0.9.

Shape of the Gap: The coronal, sagittal, circular system described by Skolnick et al (1973) for classification of closure patterns was used to describe the shape of the gap (Figure 3.7). The shape of the gap was described, not the shape of the movement pattern. Both circular and circular with Passavant's ridge closure patterns were described as circular gaps. Small central triangular gaps were listed as circular. Lateral gaps were described as right, left, or bilateral. Irregularly shaped gaps were listed as "other."

Intrarater and Interrater Reliability

Intrarater reliability was based on repeated measurements by the investigator who retraced and remeasured 30 randomly selected nasopharyngoscopic studies two months following completion of the initial tracings. Interrater reliability was based on independent measurement by the investigator and a second observer who was an expert in nasopharyngoscopy.

MULTI-VIEW VIDEOFLUOROSCOPY

Examination Procedure

All videofluoroscopic examinations were performed by a single radiologist and speech pathologist. Barium contrast was instilled nasally prior to each examination to enhance delineation of soft tissue. All subjects were examined in at least lateral and frontal projections because both of these views are essential to providing direct visualization of all the components of closure (Shprintzen and Golding-Kushner, 1989). Most subjects were also examined in an en face view, either base (in the majority of cases) or Towne projection. The field of radiation in each view was kept as narrow as possible and each examination was completed in less than two minutes to minimize radiation exposure (Isberg et al, 1989).

Lateral view. The lateral view allows visualization of velar (V) and posterior pharyngeal wall (PPW) motion, and provides an unobstructed view of lingual gestures necessary for correct interpretation of velopharyngeal movement. The tongue is beneath the velum and therefore out of the endoscopic field of view which may lead to an erroneous interpretation of palatal motion. For example, the tongue may lift the velum into the plane of closure even when the velum has no intrinsic movement. A false positive impression of palatal motion may also occur when large tonsils are retrodisplaced into the airway. When that occurs, the tongue may push a tonsil which in turn may displace the velum. Lingual gestures are not distinguishable on other fluoroscopic

views or endoscopy, and misinterpretation of apparent velar motion could result. When this occurred during production of /s/, an alternate phoneme on which abnormal tongue movement did not assist velar motion was selected for analysis (in all views) instead of /s/, as discussed previously (see ***Speech Sample***).

Frontal view. In the frontal (postero-anterior) view, the degree, level, and contour of movement of the left and right lateral aspects of the pharyngeal walls (L-LPW, R-LPW) over the vertical extent of the pharynx during phonation is visible.

En face view. In the base view, the subject is in the "sphinx" position with the plane of velopharyngeal closure perpendicular to the x-ray beam. This en face view allows observation of the velum, posterior pharyngeal wall and both lateral walls simultaneously. This view is comparable to the nasopharyngoscopic view except that movement at multiple vertical levels is visible. In the Towne projection, another en face view, the head is flexed and the x-ray beam is perpendicular to the closure plane at its most superior level in the nasopharynx. The x-rays are emitted from above the plane rather than from below.

Recording

Videofluoroscopic examinations were performed using a standard Phillips fluoroscopic table with video capacity built into the image intensifier. The video signal was routed to a video tape machine, initially a Sony EV-210 1" reel-to-reel, then a Sony Beta format VCR (SL-2000 with AC-220 power adapter), and most recently a Panasonic AG-1950 professional quality VHS format VCR.

Preparation of Materials for Analysis of Velopharyngeal Gestures

Complete examinations of the experimental subjects were edited in chronological order onto a master videotape (VHS-format) using the Panasonic AG-1950. Examinations were separated by the subject's identification number, with no other identification. For each study, the frame showing the rest position immediately preceding sustained /s/ and the frame showing maximum closure were identified using the same Panasonic VCR and a flat screen monitor (Panasonic CT-1112V). The rest position image was traced on clear acetate in solid lines. The tracing was left in place and frames were advanced individually until the frame containing maximum closure was located and traced in broken lines. This was repeated for each view. If movement patterns were inconsistent and /s/ did not represent best closure, additional frame pairs identified as "habitual" closure and/or "maximum" closure were traced.

Analysis of Velopharyngeal Gestures

As described in the previous section, analysis of velopharyngeal closure was done according to the protocol developed by the International Working Group (Golding-Kushner, et al 1990). Displacement ratio measures were made from the tracings. The en face view (base or Towne) tracing was input to IMS system as described for the cephalometric and endoscopic tracings, and area ratios were computed from that view.

Measurement Ratios. See **NASOPHARYNGOSCOPY**: *Measurement Ratios*, above.

En Face Views (Base and Towne). Analysis was made of the degree of displacement of the velum, lateral pharyngeal walls, and posterior pharyngeal walls, and of the size, shape, and position of the gap. The same criteria and procedures were applied as were used for nasopharyngoscopy. The base view procedures are illustrated in Figures 3.8 to 3.10. The Towne view is identical to nasopharyngoscopy (Figures 3.4 to 3.6).

Frontal View. Lateral pharyngeal wall (LPW) motion in the area of the velopharyngeal orifice, usually in the region of the second cervical vertebra (C-2), was analyzed. Movement at lower levels may be tonsillar and was not used for the quantitative LPW analysis. LPW movements were analyzed in terms of displacement, contour, direction, and symmetry of movement. There was no analysis of the velopharyngeal gap

from this view because it can not be adequately defined. However, the presence of barium blowing through the sphincter suggesting VPI was noted.

LPW Displacement: (Figure 3.11.) A vertical reference line was constructed to correspond to the anatomic midline between the lateral pharyngeal walls at rest (i.e., during quiet respiration). The remainder of this procedure was done for each lateral pharyngeal wall separately (R-LPW, L-LPW). The medial most point on the LPW at maximum constriction during phonation was identified. A horizontal reference line perpendicular to the vertical reference line was constructed through that point across the midline. The rest position of the LPW intersected by the horizontal line was defined as 0.0 on a ratio scale. The point on the opposing lateral wall at rest intersected by the horizontal reference line was defined as 1.0 on the ratio scale. The point of maximum movement along the reference line established the degree of LPW movement relative to points 0.0 and 1.0. For example, movement to midline (the vertical reference line) was rated 0.5. Movement away from the opposite lateral wall was recorded as -0.1.

LPW Contour: (Figure 3.12.) Contour refers to the vertical extent of movement of each LPW, or how much of the lateral wall along its height moved. Contour was described as "shelf" if movement is localized or discrete thus resembling a horizontal or shelf-like projection, "balloon" if movement

was broad based, "vertical" if the entire wall moved as a unit, or "irregular."

Direction: The direction or vector of movement was described as medial, superomedial, or outward.

Symmetry: Symmetry of displacement, contour, and movement vector of the right and left lateral pharyngeal walls was noted and described.

Lateral View. Analyses made from this view were of the degree, contour, and direction of velar and posterior wall displacement, as well as of abnormal "compensatory" lingual, velar, and pharyngeal gestures. Analysis was based on examination with the head in a neutral position.

Velar Displacement: (Figure 3.13.) The vector of velar movement along its trajectory was used for analysis because it corresponds to the perceived plane of closure on endoscopic examination. The point on the velum closest to the posterior pharyngeal wall at maximum constriction was identified. A line drawn from that point to the same point on the velum at rest defined the vector of movement. This line was extended to intersect the posterior pharyngeal wall or adenoid at rest, and served as a reference line. The point at which the reference line intersected the velum at rest was defined as 0.0 on a ratio scale. The point where the reference line intersected the posterior pharyngeal wall at rest was defined

as 1.0. The point of maximum movement of the velum along the reference line established the degree of velar displacement relative to points 0.0 and 1.0.

Velar Direction and Contour: The direction of velar movement was described relative to the plane of the hard palate as superior, posterior, posterosuperior, or tip-hinge (the velar tip elevates toward the posterior pharyngeal wall with no velar eminence, as if swinging on a hinge).

Posterior Pharyngeal Wall and Passavant Ridge Displacement: (Figure 3.14) The midpoint of the moving PPW or Passavant ridge at maximum constriction was identified and the location of the same point on the posterior pharyngeal wall at rest was defined as 0.0 on a ratio scale. These two points identified the trajectory of movement of the ridge and were connected to form a reference line. The point on the velum at rest which was intersected by the reference line was defined as 1.0. The point of maximum displacement of the posterior pharyngeal wall along the reference line established the degree of movement relative to points 0.0 and 1.0. Passive posterior pharyngeal wall motion and discrete ridges were measured in the same way, and not differentiated in the analysis.

PPW Direction: The direction of PPW motion was described as anterior or anterosuperior.

Velopharyngeal gap: A valid measurement of "gap size" can not be made from the lateral projection[17]. However, barium seen blowing up between the velum and posterior pharyngeal wall suggests the presence of VPI and was noted.

Intrarater and Interrater Reliability

Independent measurements were made by two observers, the investigator and a radiologist with over 20 years of experience with videofluoroscopic phonation studies. The measurements on twenty subjects were repeated jointly by both observers one month after the initial measurements were made. The second measurement was referred to as the "group" rating, and was the measurement used in subsequent analyses.

PART IV: STATISTICAL METHODS

STATISTICAL METHODS FOR PART I: PREVALENCE STUDY

Descriptive statistics for the 129 subjects were generated for each variable by established diagnosis and for the four syndrome groups combined into two pharyngeal width groups. Increasing subgroup size by collapsing data into two

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[17]Sinclair et al (1982) found that lateral fluoroscopy frequently underestimated the degree of VPI when compared with base view fluoroscopy and endoscopy. The presence of an apparent gap may be equally misleading, especially in patients with very active LPW movement and sagittal closure patterns, in which case the midline approximation of the lateral pharyngeal walls mechanically prevents contact between the velum and posterior pharyngeal wall. In this situation the lateral view would suggest VPI even if complete velopharyngeal closure was effected.

groups was necessary to increase the power of statistical analysis and reduce the chance of Type II errors[18]. Stickler syndrome and Treacher Collins syndrome were paired to form a narrow pharynx group, and velo-cardio-facial syndrome and van der Woude syndrome were paired to form a wide pharynx group (Shprintzen, 1982).

Means and standard deviations were used for analysis of variables that were somewhat normally distributed, and medians and ranges were used for analysis of continuous variables measured along ordinal scales. Relative frequencies and percents were generated for categorical variables. Box plots were drawn for each group and used to visualize differences between groups.

Differences among syndrome groups with regard to categorical characteristics were tested for significance using a Pearson Chi-square analysis provided assumptions were met (Siegel, 1956). When possible in the event expected cell frequencies were less than 5, the investigator collapsed categories in a meaningful way. Two by two tables with expected cell frequencies were then analyzed using Fisher's Exact Tests (Siegel, 1956). Distributions of continuous variables were examined to determine whether they met assumptions of normality. Because many of the variables were

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[18]The four syndrome groups which ranged in size from 10 to 13 subjects were clinically large groups considering that these syndromes are rare in the general population and not all individuals with these syndromes have cleft palate. However, because of the large number of dependent variables the individual syndrome groups were too small for valid application of inferential statistical analysis.

measured along ordinal scales, and others had skewed or irregularly shaped distributions, the Kruskal-Wallis nonparametric analogy to the analysis of variance was used to test differences among syndromic groups for these continuous variables (Siegel, 1956). For particular variables measured along ordinal scales, for which the scale contained few categories and assumptions were met, the Mantel-Haenszel Chi-square test was used to assess the significance of monotonically increasing trends among syndrome groups (Siegel, 1956).

A post-hoc analysis of severity of hypernasality was performed to assess differences between pairs of syndrome groups and for selected contrasts (VCF x narrow, VDW x narrow). This was done using the Wilcoxon Rank-Sum Test (Siegel, 1956). Because these represented multiple comparisons, a Bonferroni multiple comparison procedure was incorporated into the analysis whereby the overall Type I error was divided by the number of post-hoc analyses, and the adjusted level of error was used to assess the significance of post-hoc differences.

STATISTICAL METHODS FOR PART II: MORPHOLOGY AND PHYSIOLOGY

Cephalometry

Skeletal, soft tissue, and airway measurements were taken on normal and syndromic subjects. Descriptive statistics as referenced above were generated for normal and affected subjects, for both the syndrome and pharyngeal width groups. Differences between the narrow and normal groups, between the

wide and normal groups, and between the narrow and wide groups with regard to continuous variables were tested using the Wilcoxon Rank Sum Test. Differences with regard to gender were assessed using the Fisher's Exact Test. A second analysis of differences in vocal tract size was done excluding two subjects with TC and one each with S and VDW who had undergone adenoidectomy.

Nasopharyngoscopy and multi-view videofluoroscopy

Descriptive statistics with reference to physiologic characteristics were generated for the syndrome and pharyngeal width groups. Differences between the narrow pharynx and wide pharynx groups were tested using Wilcoxon Rank Sum Tests for continuous variables, and Chi-square tests for categorical variables, provided assumptions were met. For dichotomous variables, differences were assessed using Fisher's Exact Test.

Differences among the four syndromes

Descriptive statistics for the four syndrome groups (S, TC, VCF, VDW) were compared for each variable, although inferential statistics could not used for analysis of within (pharyngeal width) group comparisons. The distribution of measurements of subjects within a diagnostic (syndrome) group often suggested that at least some of these differences were syndrome specific rather than specific to a pharyngeal width group. Characteristics which appeared to be syndrome specific in their presence or severity are described.

Intrarater and interrater reliability

For selected characteristics, measurements were obtained from two independent raters or from two independent raters and the two raters working as a group. For each pair of ratings, scatterplots were drawn to determine whether the degree of agreement was linear. The degree of association was measured using Pearson and Spearman correlation coefficients. The square of the Pearson correlation reflects the ratio of the variances for the two raters, indicating further agreement in responses (Cronbach, 1979).

All tests of significance were performed at a Type I error of .05, and were two-tailed. All analyses were performed using SAS (1985).

INTERRATER AND INTRARATER RELIABILITY: PEARSON COEFFICIENTS

Interrater Reliability of cephalometric measurements

Pearson correlation coefficients and levels of significance for the degree of association of interjudge measurements of cephalometric tracings are listed in Appendix B-1. Based on Guilford's guide for interpreting the magnitude of correlation (cited in Williams, 1968), almost all of the measurements were highly (r =.70 to .90) or very highly (r>.90) correlated, indicating good interrater reliability. Two measurements were only moderately reliable in one condition. They were the measurement of nasopharyngeal angle

(A-PPW) in narrow-pharynx subjects, and the palatopharyngeal angle (PP1-PPW) in wide-pharynx subjects. All correlations were highly significant ($p<.001$) except for the A-PPW measure for the narrow-pharynx group.

Intrarater and interrater reliability of nasopharyngoscopic measurements

Pearson correlation coefficients for intrarater and interrater comparisons of displacement ratios and velopharyngeal gap size measurements are listed in Appendix C-1. All of the coefficients were very high ($r>.90$, $p<.0001$), indicating very good reliability.

Interrater Reliability of multi-view videofluoroscopic measurements

Pearson correlation coefficients computed to determine interrater reliability are listed in Appendix D-1. Based on Guilford's classification of correlations (cited in Williams, 1968), reliability of the independent measurements of the two judges was moderate to high. Interrater agreement on the presence or absence of VPI based on frontal and lateral views was very high at 97%. The Pearson correlation coefficients indicated that agreement was better for each rater with the group rating than for the independent ratings with each other, with high or very high agreement on each variable. The result of the group measurement was the value used for analysis of velopharyngeal gestures.

Table 3.1. Nasopharyngoscopic (NASO) and multi-view videofluoroscopic (MVF) examinations analyzed to obtain data on velopharyngeal closure in subjects with Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

DIAGNOSIS	NASO ONLY	MVF ONLY	NASO/MVF	TOTAL
S	1	1	8	10
TC	2	2	6	10
VCF	1	3	9	13
VDW	4	0	8	12
TOTAL:				
SUBJECTS	8	6	31	45
EXAMINATIONS				76

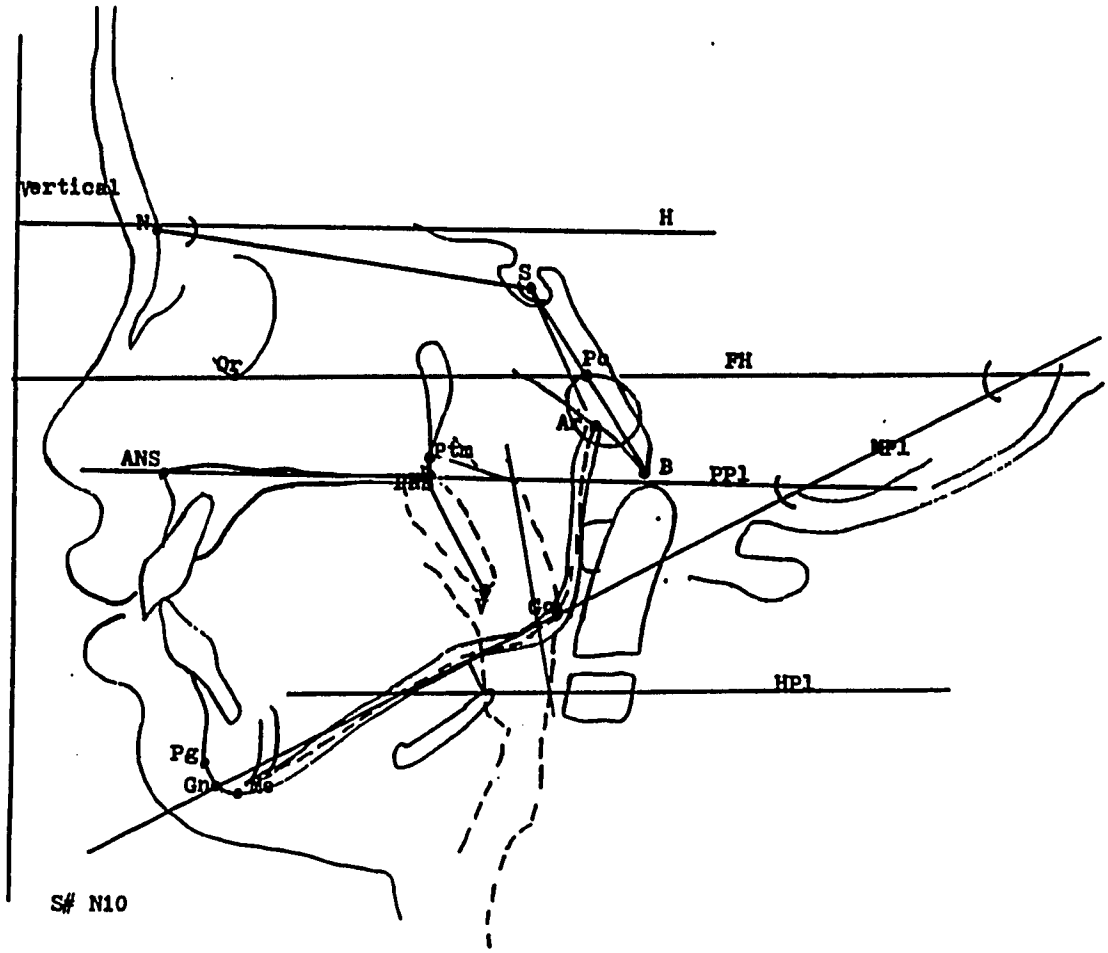

Figure 3.1. Cephalometric tracing of normal subject: skeletal and palatal landmarks, reference planes, and angles.

LEGEND: Points: Ar= articulare; ANS= anterior nasal spine; B= basion; Gn= gnathion; Go= gonion; Me= menton; N= nasion; Or= orbitale; Pg= pogonion; PNS= posterior nasal spine; Po= (machine) porion; Ptm: pterygomaxillary fissure; S= sella; V= velar tip
Planes: FH= Frankfort horizontal; H= geometric horizontal; HPl= hyoid plane; MPl= mandibular plane; N-S= anterior cranial base; PPl= palatal plane; S-B= posterior cranial base
Angles: H-N-S= sella height; MPl-PPl, MPl-FH= mandibular plane angle; N-S-B, N-S-Ar= cranial base angle
Connecting lines: N-S= anterior cranial base; S-B= posterior cranial base; ANS-PNS= hard palate; PNS-V= velar length

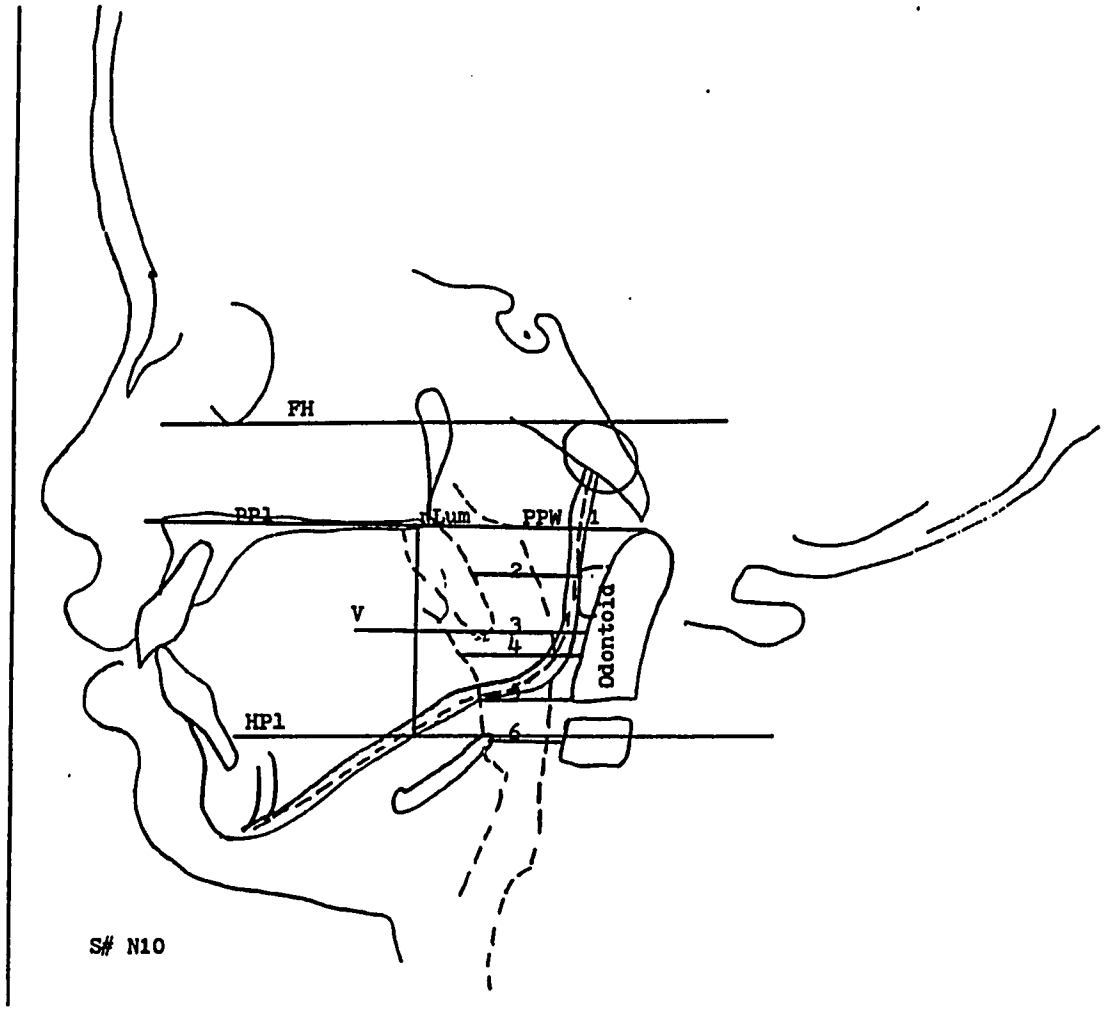

Figure 3.2. Cephalometric tracing of normal subject: lumen depth and posterior pharyngeal wall measurements.

LEGEND: Lum= lumen, PPW= posterior pharyngeal wall; level 1 is at palatal plane; level 3 is at velar tip; level 2 is midpoint between 1 and 3; level 4 is a level of intersection of mandibular plane with PPW; level 5 is at lower odontoid border; level 6 is at midpoint of C-3.

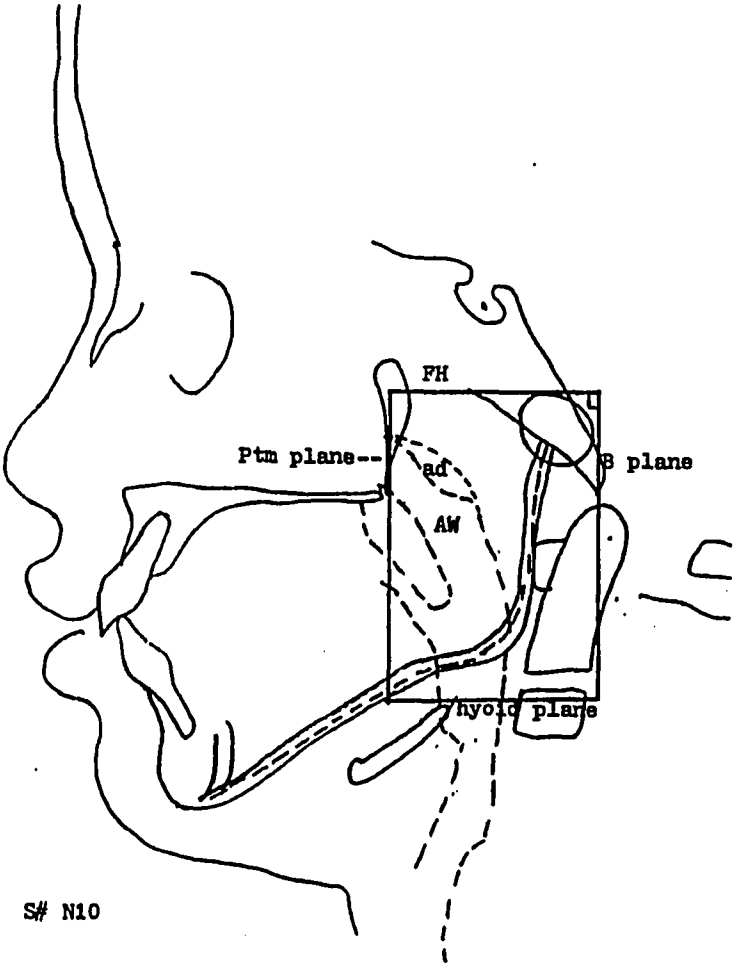

Figure 3.3. Cephalometric tracing of normal subject: skeletal frame (BLOCK) and vocal tract area measurements.

LEGEND: FH= Frankfort horizontal; PTM plane= plane through pterygomaxillary fissure; B plane= plane through basion; ad= adenoid; AW= airway

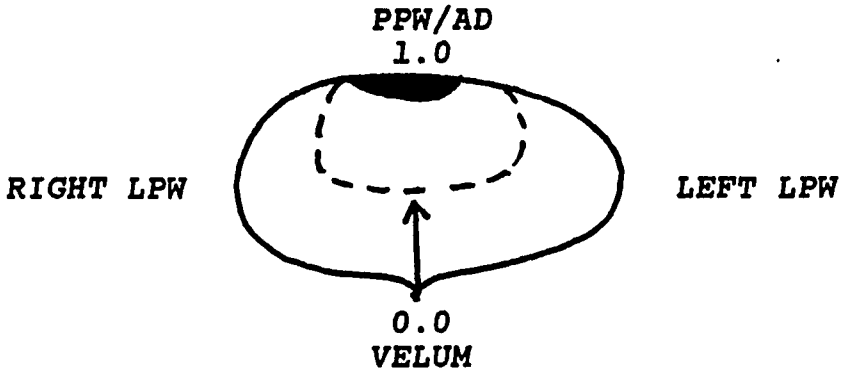

Figure 3.4. Nasopharyngoscopy and Towne view fluoroscopy: Velar displacement.

KEY: PPW= posterior pharyngeal wall; Ad= adenoid; LPW= lateral pharyngeal wall.

Rest position is traced with a solid line. Position of structures during speech is traced in broken lines. Maximum velar movement to the adenoid (the target of the movement trajectory in this case) represents a ratio of 1.0; absent velar motion is 0.0. Velar displacement in this subject is 0.5.

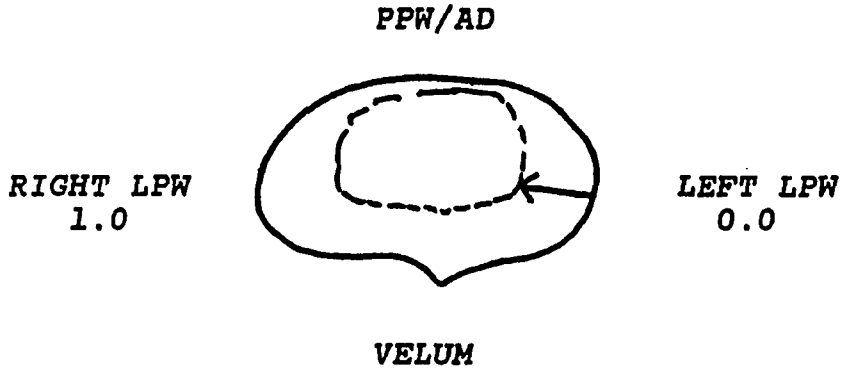

Figure 3.5. Nasopharyngoscopy and Towne view fluoroscopy: Lateral pharyngeal wall displacement.

KEY: PPW= posterior pharyngeal wall; Ad= adenoid; LPW= lateral pharyngeal wall.

Rest position is traced with a solid line. Position of structures during speech is traced in broken lines. Maximum movement of left LPW (L-LPW) toward right LPW (R-LPW) represents a ratio of 1.0; absent L-LPW motion is 0.0. L-LPW displacement in this subject is .3. Right LPW ratio is not shown.

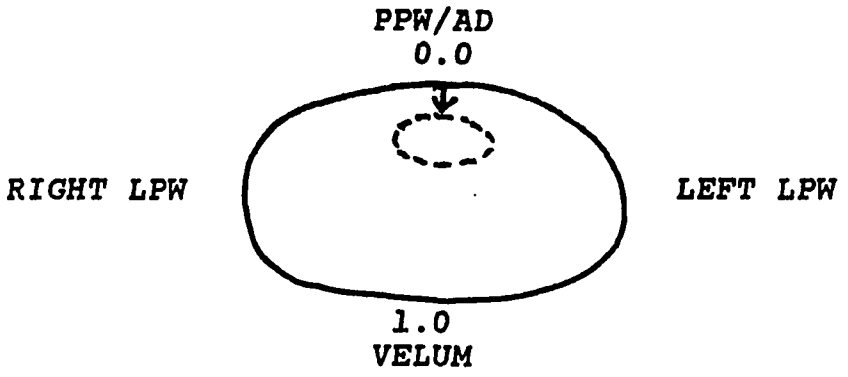

Figure 3.6. Nasopharyngoscopy and Towne view fluoroscopy: Posterior pharyngeal wall displacement.

KEY: PPW= posterior pharyngeal wall; Ad= adenoid; LPW= lateral pharyngeal wall.

Rest position is traced with a solid line. Position of structures during speech is traced in broken lines. Maximum movement of the PPW to the velar rest position represents a ratio of 1.0; absent PPW motion is 0.0. PPW displacement in this subject is .1.

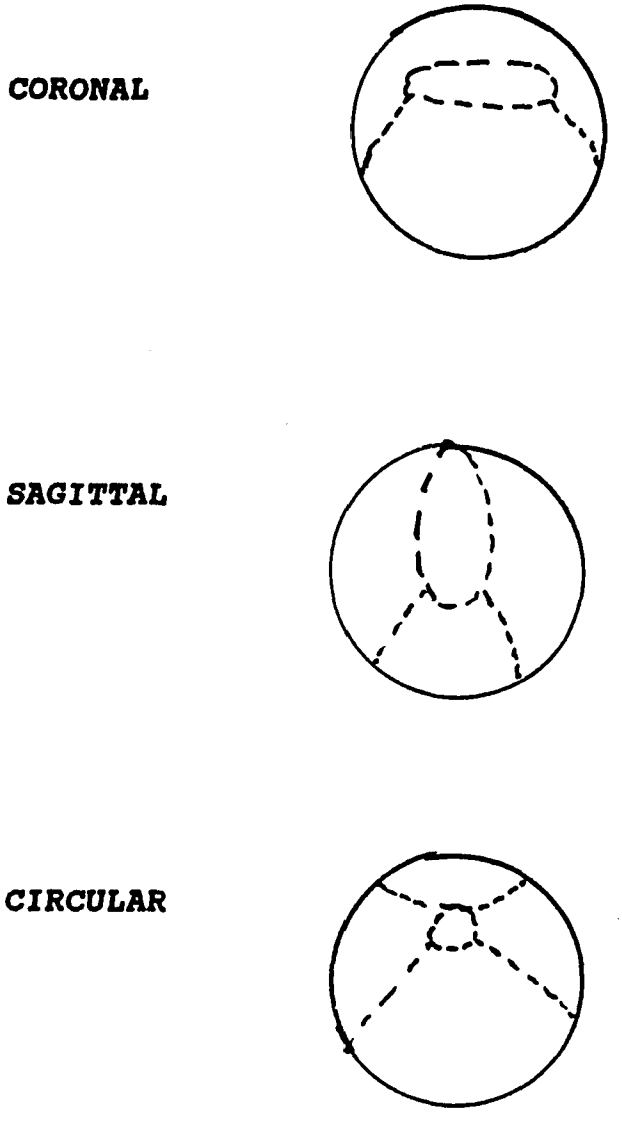

Figure 3.7. Nasopharyngoscopy and en face videofluoroscopy: shape of velopharyngeal gap.

Rest position is traced with a solid line. Position of structures during speech is traced in broken lines.

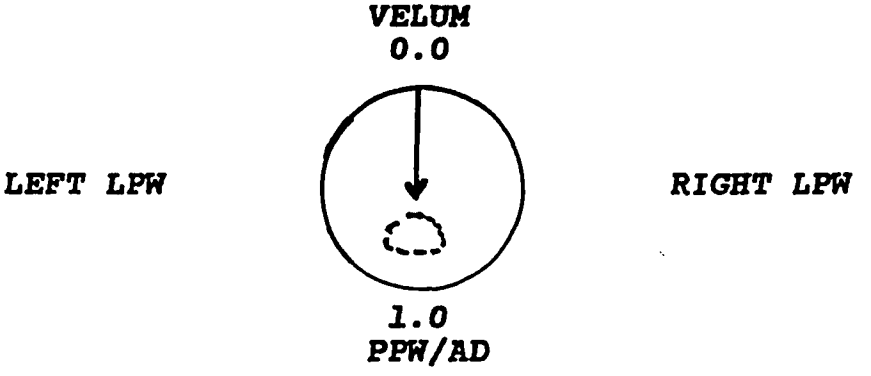

Figure 3.8. Base view videofluoroscopy: Velar displacement. KEY: PPW= posterior pharyngeal wall; AD= adenoid; LPW= lateral pharyngeal wall.

Rest position is traced with a solid line. Position of structures during speech is traced in broken lines. Maximum velar movement to PPW represents a ratio of 1.0; absent velar motion is 0.0. Velar displacement in this subject is 0.8.

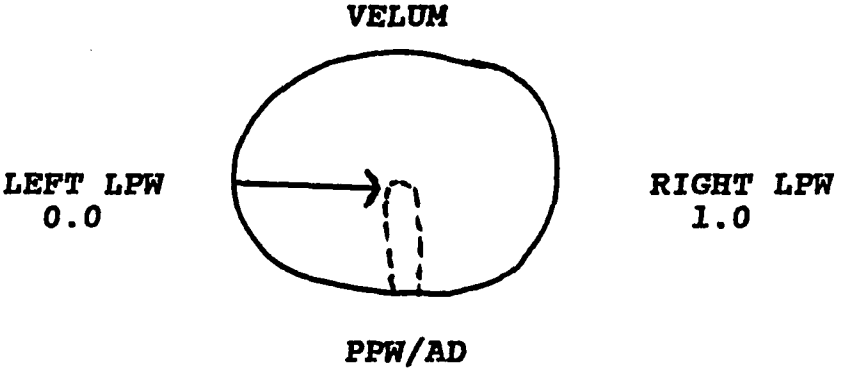

Figure 3.9. Base view videofluoroscopy: Lateral pharyngeal wall displacement.

KEY: PPW= posterior pharyngeal wall; Ad= adenoid; LPW= lateral pharyngeal wall.

Rest position is traced with a solid line. Position of structures during speech is traced in broken lines. Maximum movement of left LPW (L-LPW) toward right LPW (R-LPW) represents a ratio of 1.0; absent L-LPW motion is 0.0. L-LPW displacement in this subject is .5. Right LPW ratio is not shown.

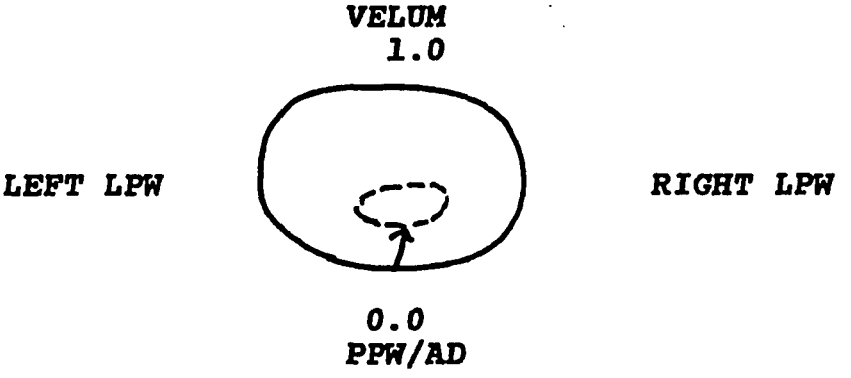

Figure 3.10. Base view videofluoroscopy: Posterior pharyngeal wall displacement.

KEY: PPW= posterior pharyngeal wall; Ad= adenoid; LPW= lateral pharyngeal wall.

Rest position is traced with a solid line. Position of structures during speech is traced in broken lines. Maximum movement of the PPW to the velar rest position represents a ratio of 1.0; absent PPW motion is 0.0. PPW displacement in this subject is .3.

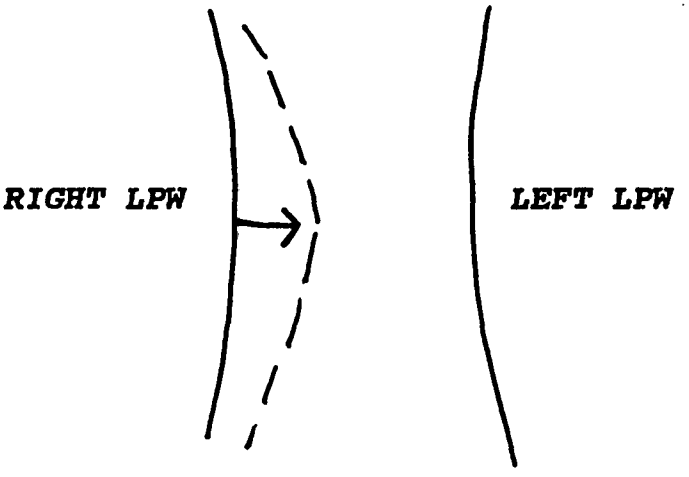

Figure 3.11. Frontal view videofluoroscopy: Lateral pharyngeal wall (LPW) displacement.

Rest position is traced with a solid line. Position of structures during speech is traced in broken lines. Maximum movement of the Right LPW (R-LPW) to the left LPW represents a ratio of 1.0; absent LPW motion is 0.0. R-LPW displacement in this subject is .3.

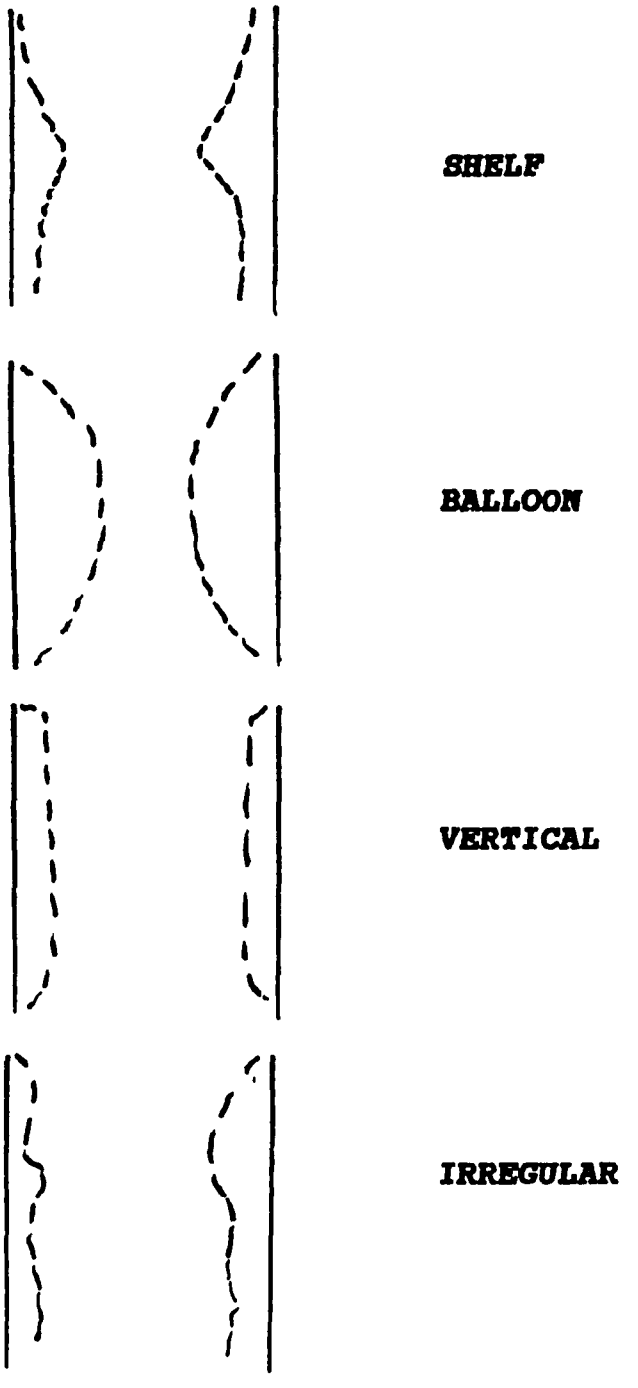

Figure 3.12. Frontal view videofluoroscopy: Contour of lateral pharyngeal wall motion.

Rest position is traced with a solid line. Position of structures during speech is traced in broken lines.

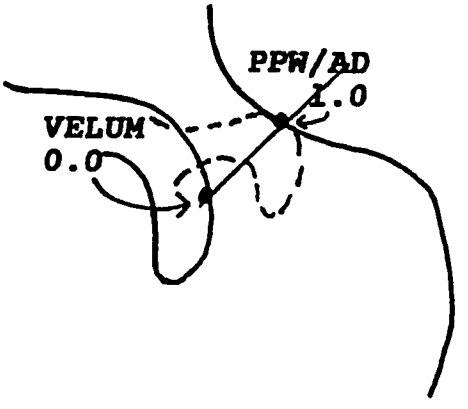

Figure 3.13. Lateral view videofluoroscopy: Velar displacement.

Rest position is traced with a solid line. Position of structures during speech is traced in broken lines. Maximum velar motion to the posterior pharyngeal wall (PPW) or adenoid (ad) along the trajectory of velar movement represents a ratio of 1.0; absent velar motion is 0.0. Velar displacement in this subject is 1.0.

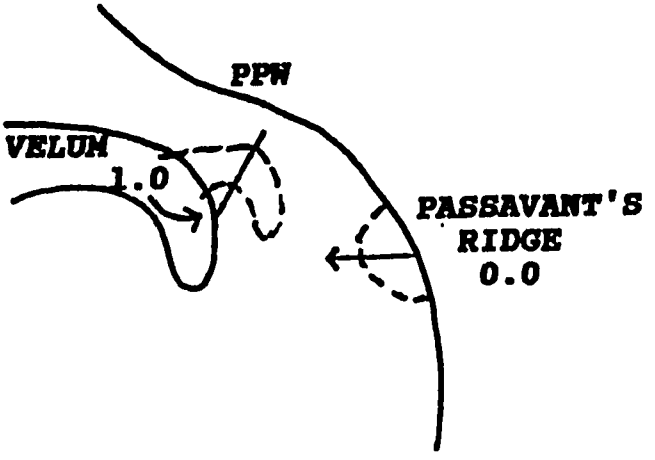

Figure 3.14. Lateral view videofluoroscopy: Displacement of the posterior pharyngeal wall (PPW) or Passavant's ridge.

Rest position is traced with a solid line. Position of structures during speech is traced in broken lines. Maximum movement of the PPW or Passavant's ridge toward the velar rest position represents a ratio of 1.0; absent PPW motion is 0.0. PPW displacement in this subject is 0.3.

CHAPTER 4

RESULTS

PART I: PREVALENCE OF SPEECH DISORDERS IN FOUR SYNDROMES

Population and speech characteristics of 129 subjects with cleft palate associated with Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), or van der Woude syndrome (VDW) were analyzed. Descriptive statistics and results of inferential statistical analyses for each variable are included in Appendix A-2 to A-21. Raw data for individual subjects are included in Appendix A-22.

Demographic and Clinical Data

Established Diagnosis. There were 29 subjects with Stickler syndrome (22.5% of the subjects in the prevalence study), 11 with Treacher Collins syndrome (8.5%), 74 with velo-cardio-facial syndrome (57.4%), and 15 with van der Woude syndrome (11.6%) (Appendix A-2).

Gender. There were 50 males and 79 females, representing 38.8% and 61.2% of the total respectively. Chi-square analysis showed no difference in the distribution of males and females among the four syndromes or two pharyngeal widths (Appendix A-2).

Age at time of referral to CCFD. The median[19] age at time of referral for the group as a whole was 5 years 1 month, and the range was from birth to 57 years. The referral age was different for the four syndrome groups (Kruskal-Wallis Test[20], $p<.01$), with median referral ages from youngest to oldest as follows: 1-9 for S, 5-4 for VCF, 8-0 for VDW, and 12-0 for TC. A two-way comparison showed a difference in age at referral for the narrow pharynx and wide pharynx groups ($p<.05$) with the wide-pharynx syndrome subjects older at time of referral (6-0 for wide pharynx versus 3-9 for narrow). However, 75% of all patients were 12 years old or younger at the time of referral (Appendix A-2).

Cleft type. There was no difference in the prevalence of overt clefts in the wide and narrow pharynx groups. Submucous cleft palate was more prevalent in wide-pharynx syndromes than in narrow-pharynx syndromes (Chi-square, $p<.0001$). Most subjects with S and VDW had overt cleft palate. Most subjects with TC and VCF had submucous clefts. Occult SMCP occurred only in VCF and accounted for 34% of the VCF clefts. The data on type of cleft palate according to pharyngeal width and syndromic diagnosis appears in Appendix A-3.

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[19]For many variables where the distribution of values was not normal the median was a more valid measure of central tendency than the mean and is, in those cases, the statistic on which discussions are based.

[20]The Kruskal Wallis test (Chi-square approximation) is a test of significance for continuous variables where the assumption of homogeneity is not met. It is a nonparametric analogy of ANOVA.

Age at time of palate repair. There were 52 subjects with repaired cleft palate. No subject with submucous cleft palate had surgical repair. The median age at time of repair was 1 year 3 months. There was no difference in age at palate repair for the two pharyngeal widths or four diagnostic groups (Kruskal-Wallis Test) (Appendix A-4).

Referring Diagnosis. The frequency distribution of referring diagnoses (the diagnoses with which patients were referred) among the 129 subjects according to established diagnosis and pharyngeal width is listed in Appendix A-5. The most common diagnoses which were made prior to referral to CCFD were cleft palate (29.5% of all subjects), speech disorder or VPI (23.3%), and Robin sequence (14.7%). Small cell size prevented valid statistical analysis of this variable. However, 90% of the patients referred with Robin sequence had a narrow-pharynx syndrome and every patient referred with a speech-related diagnosis or a diagnosis of VPI had a wide-pharynx syndrome.

Reason for referral. The reasons for referral to CCFD are listed in Appendix A-6. More than half of the 129 subjects (56%) were referred to CCFD because of speech impairment or hypernasality. The second most common reason given for referral was cleft palate, accounting for 13% of the referrals. Seven percent of the patients were identified when they accompanied family members who had been referred but had not themselves been referred.

Small cell size precluded valid statistical analysis of this variable, but several interesting referral patterns were apparent when the narrow and wide pharynx groups and the four syndrome groups were compared. Consistent with the trends observed in referring diagnoses, the wide-pharynx syndromes accounted for 85% of the speech referrals. Poor speech or hypernasality was given as the reason for referral for 72% of the VCF and 53% of the VDW subjects, but only for 34% of the Stickler and 9% of the TC subjects. All five subjects referred because of failed pharyngeal flap surgery and 74% of those referred because of poor speech were found to have VCF. In contrast, the narrow-pharynx syndromes (S and TC) accounted for 80% of the airway referrals. Apnea or airway problems were cited as the reason for referral in 27% of the TC and 17% of the Stickler subjects, but in only 3% of the VCF and none of the VDW subjects. There did not appear to be any other differences among the groups for reason of referral, except that no TC subject with cleft palate was referred because of the cleft.

History of glossopexy or tracheotomy in infancy to relieve upper airway obstruction. Twelve percent of the subjects had required surgery in infancy for treatment of upper airway obstruction, and the need for surgery was significantly greater in the narrow pharynx syndromes ($p<.00001$). About one-third of the S and TC subjects had undergone temporary glossopexy or tracheotomy which was

required in only 2 of the subjects with VCF and in none of the subjects with VDW (Appendix A-7).

Audiometric status. Audiometric data (based on the 3-frequency average of 500 Hz, 1000 Hz, and 2000 Hz) are reported in Appendix A-8. Eighty-five percent of the subjects with VCF and 93% of the subjects with VDW had normal hearing bilaterally at the time of speech evaluation. A severe bilateral mixed hearing loss was present in only one subject who had TC. That subject had been fitted with amplification in infancy and aided hearing was within normal limits on threshold and speech discrimination testing. The remaining subjects had mild or moderate conductive hearing loss in the worse ear[21]. Small cell size precluded valid statistical analysis of this variable. However, the results were consistent with the known association of Stickler syndrome and Treacher Collins syndrome with hearing loss, and these two diagnoses accounted for 30% of the study population but 66% of the subjects with hearing loss.

Receptive and expressive language. Data were available on 126 subjects. Chi-square analysis indicated a difference in language skills between the narrow and wide pharynx groups and among the four syndrome groups ($p<.01$), with a very high prevalence of delays in subjects with VCF. Normal language development was documented in most of the subjects with VDW

[21]Two Stickler subjects with moderate hearing loss had a mild sensorineural component.

and at least half of the S and TC subjects. However, 85% of the subjects with VCF demonstrated delayed language skills. Language data according to diagnosis are listed in Appendix A-9. Language did not appear to be related to hearing acuity (Appendix A-10).

Prevalence of Articulation Disorders

Articulation Development. The frequency distribution of predominant articulation development characteristics for each syndrome and pharyngeal width group are listed in Appendix A-11. Small cell size precluded valid statistical analysis of this variable. Therefore, categories of errors were combined to ascertain a profile of the prevalence of compensatory errors which might be related to cleft palate, velopharyngeal insufficiency, or vocal tract abnormalities. A distinction was made between "compensatory" errors and "obligatory" errors. The former (glottal stops, etc.) are errors in learning affecting place and/or manner of sound production which can only be corrected by speech therapy. In contrast, obligatory errors result directly from an anatomic defect, are not easily amenable to therapy, and often self-correct when the underlying structural cause of the error is corrected; compensatory errors do not (Golding-Kushner, 1990, 1991). Obligatory errors include nasal emission and reduced intraoral pressure related to VPI or fistulae, and certain articulation distortions related to hearing loss, palatal fistulae, or malocclusion.

In this study, the category of "normal" articulation included all noncompensatory speech production. That is, a subject was considered as having normal speech production if the only errors were developmental (i.e., phonologic, not phonetic), or obligatory.

Articulation and diagnosis: The articulation development of 50% to 60% of the subjects with each diagnosis except for VCF was normal or characterized by errors which were not compensatory, including developmental and obligatory errors. As noted above, cell size was not large enough for valid statistical analysis of articulation. However, as seen in Figure 4.1, there was an extremely high prevalence of glottal stop speech disorders in VCF, occurring in 88% of the cases. About 40% each of the VDW and S subjects had glottal speech development, but only 1 TC subject had this problem.

In contrast, a pattern consisting predominantly of tongue backing errors occurred only in the narrow pharynx syndromes. Tongue backing and isolated nasal snorting occurred in 40% of the subjects with TC. One subject with S (4%) presented with isolated nasal snorting.

Articulation and age at Referral: Data on articulation development prior to any therapeutic intervention were analyzed separately for 26 subjects in this study who were referred to CCFD prior to age 2 years and the 120 subjects referred at a later age. The most common reason for referral in subjects over 2 years of age was a speech disorder

which may have introduced an ascertainment bias (Appendix A-12). As seen in Figure 4.2, there was a slightly higher prevalence of glottal speech disorders in S subjects referred late than in S subjects referred early. Data were available for only one subject with TC who was referred early, and only one late referred subject with TC had glottal speech. There was no apparent difference in the prevalence of compensatory speech errors for early and late referrals in the wide pharynx group.

Articulation and cleft type: Glottal stop errors were produced by 56% of the subjects with repaired cleft palate and 71% of the subjects with SMCP or OSMCP. As seen in Figure 4.3, speech patterns were fairly consistent within each diagnostic group regardless of cleft type, with the highest prevalence of both glottal speech and SMCP in velo-cardio-facial syndrome. Most subjects with VCF had glottal speech regardless of cleft type. Tongue backing errors were not related to type of cleft.

Articulation and hypernasality: Kruskal-Wallis Test analysis indicated a significant relationship between severity of hypernasality and type of articulation development patterns ($p<.0001$). Subjects with the most severe hypernasality ratings during correct articulation production had early articulation histories of glottal and compensatory errors. Median hypernasality ratings were as follows: normal articulation: .5 (mild or intermittent hypernasality); tongue

backing: 1.0 (mild hypernasality); glottal speech: 2.0 (severe hypernasality).

Articulation and audiometric status: Only one subject with S had speech errors (sibilant distortions) which were believed to be related to a moderate high frequency mixed hearing loss. A statistical relationship was found between articulation and hearing (Kruskal-Wallis Test, $p<.01$). However, examination of the data suggested that covariation was related to diagnosis. 82% of the subjects with glottal speech had normal hearing, but 60% of the subjects with tongue backing errors had moderate hearing losses (and Treacher Collins syndrome). 60% of the subjects with normal articulation had normal hearing.

Articulation and language: As seen in Figures 4.4A and 4.4B, approximately 70% of the subjects with delayed language had glottal speech, and about 70% of the subjects with glottal speech had delayed language. Approximately one-third of the subjects with normal language also had glottal speech. Tongue backing did not appear to have any relationship to language. Data are listed in Appendix A-14.

Prevalence of Resonance Disorders

Oral Resonance. Over 90% of the subjects had normal oral resonance. Most of the subjects with abnormal oral resonance had narrow-pharynx syndromes (Fisher's Exact Test, $p<.001$). The oral resonance of half of the TC subjects was described as

"muffled," a term which is widely used in the clinical literature but for which the acoustic correlate has not been studied. There were 3 S and 1 VCF subject with "potato-in-the-mouth" resonance related to tonsilar hypertrophy. All of the subjects with VDW had normal oral resonance. (Appendix A-15).

Nasal Resonance. Analysis was limited to resonance data obtained during correct articulation because the presence of compensatory articulation errors may affect both the perception of hypernasality and the velopharyngeal movements that control coupling of the oral and nasal cavities (Golding-Kushner, 1989). Subjects who had undergone pharyngoplasty were also excluded because the surgery may have decreased the severity of hypernasality or caused hyponasality. Data were analyzed on 93 subjects.

Hypernasality: Data on the prevalence and severity of hypernasality according to pharyngeal width and diagnosis are listed in Appendix A-16. Hypernasality was significantly more prevalent in the wide pharynx group than in the narrow pharynx group (Fisher's Exact Test, $p<.0001$), although more than half of the subjects in both groups were hypernasal (Figure 4.5.).

Severity of hypernasality, analyzed for those cases in which hypernasality was present, was also significantly different for the four syndrome subgroups and two pharyngeal width subgroups (Kruskal-Wallis Test, $p<.0001$), and is

displayed in Figure 4.6. The mean degree of hypernasality for each syndrome group from mildest to most severe was: TC: 1.0, S: 1.4, VDW: 1.7, VCF: 2.3. There was a significant difference in the severity of hypernasality between velo-cardio-facial syndrome and the narrow pharynx syndromes (Wilcoxon Rank Sum Test, $p<.0001$), but not between van der Woude syndrome and the narrow pharynx syndromes. Every subject with VCF was hypernasal.

There was a significant relationship between hypernasality and cleft type (Fisher's Exact Test, $p<.05$). Data on hypernasality and cleft type are in Appendix A-17. Most subjects with normal resonance had repaired clefts, but most subjects with hypernasality had SMCP or OSMCP. However, 70% of the subjects with repaired clefts and 87% of the subjects with SMCP were hypernasal. Hypernasality was not related to hearing loss (Wilcoxon Rank Sum Test, p=ns) or to vocal quality (Fisher's Exact Test, p=ns) (Appendix A-18).

The prevalence of hypernasality among subjects with repaired (overt) cleft palate who were ascertained in infancy (and, therefore, not referred because of speech problems) was examined separately. Results are listed in Table 4.1. Speech data following palate repair were available on only one subject with TC, who had mild to moderate hypernasality. The similarity between Stickler syndrome and van der Woude syndrome was striking, with a 46% hypernasality rate for S and 40% for VDW. Interestingly, the mean hypernasality severity rating in S was 1.4 (mild to moderate) but for VDW was 0.5 (very mild or intermittent). Every VCF subject was severely

hypernasal following primary palate repair. The prevalence of hypernasality in S, VCF, and VDW was higher than the 14% prevalence of VPI following palate repair among subjects with non-syndromic cleft palate at the same institution (Hall and Golding-Kushner, 1989).

Hyponasality: Six subjects were hyponasal, two each with S, TC, and VCF; hyponasality was intermittent or mild in all cases. Although neither prevalence nor degree of hyponasality were statistically different for pharyngeal width or diagnostic group comparisons, examination of the frequency distribution suggested differences. The narrow pharynx syndromes accounted for 37% of the study population but 67% of the hyponasal subjects, and 20% of the subjects with TC were hyponasal (Figure 4.7). Data are shown in Appendix A-19.

Prevalence of Voice Disorders

Results of perceptual voice analysis were available on 125 subjects. One subject with Stickler syndrome was excluded because he had a tracheotomy at the time of his speech evaluation.

Vocal quality. Chi-square analysis revealed no significant difference in the prevalence of hoarseness in narrow-pharynx and wide-pharynx syndromes. However, of the twenty subjects who were hoarse, fourteen (70%) had VCF and five (25%) had S (Appendix A-20). Vocal quality was not related to history of glossopexy/ tracheostomy in infancy (Fisher's Exact Test) (Appendix A-20). As noted above, vocal

quality was not related to hypernasality. Almost 80% of the subjects with normal vocal quality and 93% of the hoarse subjects were hypernasal (Appendix A-18).

Vocal pitch. Small cell size precluded valid statistical analysis of this variable, but most subjects (78%) had normal vocal pitch. A higher than normal pitch was perceived in 28% of the VCF (21/53) and 20% of the TC (2/10) subjects. Of the 24 subjects with high pitch, 21 (88%) had VCF. All three subjects with low pitch had narrow pharynx syndromes. Perceived vocal pitch was not related to history of glossopexy or tracheotomy in infancy (Appendix A-21).

PARTS II AND III: MORPHOLOGY AND VELOPHARYNGEAL PHYSIOLOGY IN FOUR SYNDROMES

Subjects

Age, gender, and cleft-type of the 45 experimental and 15 control subjects are included in Table 4.2. There were 10 subjects with S, 10 with TC, 13 with VCF, and 12 with VDW. Wilcoxon Rank Sum analysis showed no difference in age distribution for subjects in the narrow pharynx group and wide pharynx group. The median age was between 7 and 8 years for both groups. However, the median age of subjects with TC was 16 years which was 7 years older than the next "oldest" group, VDW. Fisher's Exact Test revealed no difference in gender between the narrow and wide pharynx groups. There 18 males

and 27 females. There were a total of 21 subjects with repaired overt cleft palate (CP) and 24 with SMCP, including 5 with OSMCP. There were more cases of SMCP in the wide pharynx group (Wilcoxon Rank Sum Test, $p<.0001$).

PART II: CRANIAL AND VOCAL TRACT MORPHOLOGY IN FOUR SYNDROMES

MORPHOLOGY: CEPHALOMETRY

Normal Subjects

Median age of the control group was 9 years, and there was no difference in the age (Wilcoxon Rank Sum Test) or gender distribution (Fisher's Exact Test) between the control and experimental groups.

Cephalometric measurements of control subjects

The mean cephalometric measurements for the control group were within 1 S.D. of Riolo's (1974) published norms for skeletal morphology, confirming that they were skeletally normal subjects (Appendix B-2). Cephalometric tracings of one of the normal subjects were reproduced in Figures 3.1 through 3.3.

Cephalometric measurements of experimental subjects

Descriptive statistics for each variable for the control, pharyngeal width groups and syndromic groups are listed in alphabetical order in Appendix B-3, along with the level of significance of differences between groups for the three

comparisons made on each variable (narrow pharynx x wide pharynx, narrow pharynx x control, wide pharynx x control). A summary of the statistically significant differences between the wide pharynx and narrow pharynx groups is in Table 4.3. Complete raw data on the experimental and normal subjects are in Appendix B-5 and B-6 respectively.

The pharyngeal width group comparisons described in this results section are arranged according to the type of characteristic measured (skeletal, soft tissue, airway), and differences refer to statistically significant differences between the pharyngeal width groups and normals on the Wilcoxon Rank Sum Test. Characteristics attributed to specific syndromes reflect differences suggested by examination of the distribution of measurements within each group but do not reflect statistically significant differences, and statements were made about specific syndromes only when there appeared to be a lack of homogeneity within the pharyngeal width group. These trends are illustrated using bar graphs or pie charts, and are summarized in Table 4.3 which also contains the results of statistical analysis according to pharyngeal width. Cephalometric tracings of a subject with each of the four syndromes appear in Figures 4.8 to 4.11.

Skeletal measurements.

Cranial base. The cranial base angle (N-S-B) was acute (124^0) in the narrow pharynx group ($p<.001$) and obtuse

(138°) in the wide pharynx group[22] ($p<.01$). There were no statistical differences in the height of sella turcica (H-N-S) on any comparison (Figure 4.12). The anterior cranial base (N-S) was abnormally short in the narrow pharynx group ($p<.01$) but normal in the wide pharynx group. As seen in Figure 4.13, the anterior cranial base was shortest among subjects with Stickler syndrome. The posterior cranial base (S-Ba) was abnormally short in the wide pharynx group ($p<.01$), especially in VCF (Figure 4.14), but normal in the narrow pharynx group, although shortening also occurred in some subjects with S. There was no attempt to correlate morphological measurements with history of Robin sequence. Glander (1990) compared Robin and non-Robin Stickler and VCF subjects and found that Robin and non-Robin Stickler subjects differed only in anterior facial contour measurements. He also reported that Robin sequence had no effect on VCF or on other skeletal, lumen, or soft tissue measurements in Stickler.

Mandible. The mandibular body (Go-Me) was short in the narrow pharynx group ($p<.01$) and normal in the wide pharynx syndromes, but was not different between the narrow and wide pharynx groups. The distribution of measurements in VCF seemed short, like the narrow pharynx syndromes, but normal in VDW (Figure 4.15). Length of the ramus (Ar-Go) was normal on all comparisons, but as seen in Figure 4.16, was

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[22]The cranial base angle measurement N-S-Ar was abnormally acute in the narrow pharynx syndromes but normal in the wide pharynx syndromes. This measurement may be influenced by mandibular characteristics extraneous to the cranial base.

shorter than even the shortest control group value in 25% of the subjects with TC and longer than the longest normal value in 50% of the subjects with VDW.

The Frankfort horizontal (H-FH) was steeply inclined in the narrow pharynx group ($p<.05$), but appeared to be relatively normal in S and steep only in TC (Figure 4.17). The mandibular plane angle with FH as a reference (FH-MPl) was also steep in the narrow pharynx group ($p<.001$). As seen in Figure 4.18, it was steepest in TC and flatter than the flattest control group value in 25% of the subjects with VDW. The mandibular plane angle formed with the palatal plane (MPl-PPl) was not statistically different from normal in the narrow or wide pharynx groups but was most obtuse in TC (Figure 4.19). The distance from sella to the intersection of the ramus with the posterior cranial base (S-Ar) was not different for the pharyngeal width comparisons, but was above the upper range of the control group in 50% of the subjects with VDW (Figure 4.20), consistent with their tendency towards an obtuse mandibular plane.

Palatal Measurements. Length of the hard palate (ANS-PNS) did not differentiate the narrow and wide pharynx groups from each other, but was abnormally short for both pharyngeal widths ($p<.01$). However, hard palate length was related to cleft type, and was abnormally short in repaired cleft palate ($p<.05$) but normal in both SMCP and OSMCP. Physical dimensions of the hard and soft palate according to cleft type are listed in Appendix B-4.

The velum was abnormally thin (V WDTH) in the wide pharynx group ($p<.01$), but the distribution of values suggested that this was because of an especially thin velum in VCF (Figure 4.21). Further analysis indicated that velar thickness was normal in repaired clefts but abnormally thin in SMCP ($p<.01$) and even thinner in OSMCP (Figure 4.22), suggesting that the statistical difference between pharyngeal widths may have reflected an interaction effect. There was a higher prevalence of SMCP in the wide pharynx syndromes and all cases of OSMCP had velo-cardio-facial syndrome.

The velum (PNS-V, PP1-V) was abnormally short in the wide pharynx group ($p<.001$) and was not statistically different for different cleft types. However, as seen in Figure 4.23, the range of measurements in OSMCP suggested shorter velar length in this type of cleft than in SMCP, a difference which may have been obscured from statistical significance by the small sample size. Also, velar length in Stickler syndrome was similar to velar length in the wide pharynx syndromes but the range of measurements was larger (Figure 4.24).

Velar drape (ANS-PNS-V) was significantly different for the narrow and wide pharyngeal width groups ($p<.05$), but neither group was different from normal. The angle at which the soft palate hung down into the pharynx was much more acute in TC than in the controls or in any other syndrome (Figure 4.25).

Soft tissue measurements.

Adenoid. Area of the adenoid (AD) as measured on lateral cephalographs was abnormally small in the narrow pharynx group ($p<.05$) and normal in the wide pharynx group, but was not statistically different between the pharyngeal width groups. The distribution of adenoid area measurements within each syndrome suggested that it was especially small in TC (Fig. 4.26). Relative adenoid size (PCTVTAD), or the proportion of the vocal tract space which was filled with adenoid tissue, was not different for the narrow or wide pharynx groups. Measurements according to syndrome are illustrated in Figure 4.27 and show that the relative adenoid size was smallest in TC with a median of 0%. The adenoid filled 4% or less of the vocal tract in subjects with VCF. Scatterplots showing the relative adenoid size (PCTVTAD) according to age in TC and VCF are in Figure 4.28. They clearly illustrate that adenoid size was a function of age in TC, but not in VCF. In subjects with TC who were younger than 15 years of age, the adenoid filled 40% to 80% of the vocal tract, but older subjects had no adenoid tissue. However, 6 of 9 subjects with VCF who were younger than 8 years old had adenoid tissue filling 0 to 20% of the vocal tract.

Thickness of the posterior pharyngeal wall. PPW thickness was not different from normal at any level in the narrow pharynx group but was abnormally thin in the wide pharynx group at the highest three levels measured, corresponding to the velopharynx (PPW 1-2, $p<.001$) and upper

oropharynx (PPW 3, $p<.05$). The narrow and wide pharynx groups were different from each other at three measurement levels in the velopharynx (PPW 1-2, $p<.01$) and lower oropharynx (PPW 4, $p<.05$), with thicker PPW 4 measurements in TC than in any other syndrome (Figure 4.29).

Airway (Lumen) measurements.

Airway depth. Anteroposterior depth of the vocal tract in the narrow and wide pharynx groups was significantly different from each other and from the controls at the velopharyngeal (Lum 1-2) and oropharyngeal (Lum 3-4) levels ($p<.001$). The lumen measurements were short in the narrow pharynx group and long in the wide pharynx group, validating the pharyngeal width classifications. Although not different from the controls, the narrow and wide pharynx groups also differed from each other at the level of the hypopharynx (Lum 5-6) ($p<.001$), with measurements in both groups clustered at extremes within the normal range. Comparison of the lumen length measurements according to diagnosis suggested some syndrome specific patterns. The range of Lum 1 measurements in S was the same as the range for the controls, although the distribution was definitely skewed to the shorter end of the normal range, suggesting slight reduction in lumen depth at the velopharyngeal level; the TC lumen depth at this level was severely reduced (Figure 4.30). The overall distribution of S measurements in the oropharynx (Lum 3-4) were similar to normal; only the TC group was very narrow (Figure 4.31). Lumen depth at the hypopharyngeal level (Lum 5-6) was reduced

in both of the narrow pharynx syndromes, TC more than S, but was not different from the controls for the wide pharynx group. However, half of the subjects with VCF had Lum 5 measurements above the upper limit of values of the controls (Figure 4.32).

The anteroposterior depth of the skeletal frame of the airway (BL WDTH) measured from the pterygomaxillary fissure to basion was abnormally small in the narrow pharynx group ($p<.01$) but was not different from normal for the wide pharynx group. The narrowed skeletal frame seemed primarily to affect TC subjects, 60% of whom had widths below the smallest normal value. There were two S subjects with small widths, but also two S subjects in whom the value was above the normal range (Figure 4.33).

Airway height: Measurements of vertical height of the vocal tract (LAH or velum-hyoid, MPl-Hy, PPl-Hy) were abnormally long in the narrow pharynx group ($p<.01$). Vocal tract height in the wide pharynx group was not different from normal. Comparison of the measurements between syndromes suggested that VDW was similar in airway height to S, and that the airway height in VCF was shortened, even when comparison was made using the airway height measure not affected by velar length (PPl-Hy, Figure 4.34).

The height of the skeletal frame of the airway (BL HGHT) which measured the vertical distance from the Frankfort horizontal to the hyoid plane was not different from normal in either the wide or narrow pharynx groups, and the groups were

not different from each other. However, the TC measurements were skewed to the long range of normal as a group, and the VCF measurements were clustered near the shortest values within the normal range (Figure 4.35).

Airway size and shape: The area of the skeletal frame of the airway (BL area) in the experimental groups was not different from the controls. However, the airway area (AW) was smaller than normal in the narrow pharynx group ($p<.05$) and normal in the wide group. This was true of TC but not S (Figure 4.36).

Relative vocal tract size, or the percentage of the skeletal frame which contained lumen (PCTSKAW), was abnormally low in the narrow pharynx group ($p<.01$) and abnormally high in the wide pharynx group ($p<.01$). The difference between the narrow and wide pharynx groups was highly significant, at a .0001 level of confidence. As seen in Figure 4.37, VCF and VDW were fairly homogeneous on this measurement, and both were abnormal. However, the decreased proportion of lumen seen in TC was not as prevalent or severe in S, in which the measurement seemed to be minimally reduced in comparison with the control group.

The nasopharyngeal angle (A-PPW) was abnormally obtuse in the narrow pharynx group ($p<.001$) but not different from normal in the wide pharynx syndromes. Again, an examination of the measurements within each syndrome suggested that S and VDW subjects were more similar to each other than to TC or VCF. The TC nasopharyngeal angle was more obtuse than normal

in almost every subject. The angle in over 25% of the subjects with VCF was more acute than all of the controls (Figure 4.38). The obliquity of the angle in TC was consistent with the tendency of the vocal tract to course downward and backward from nasopharynx to hypopharynx, rather than downward. The inferoposterior course of the TC vocal tract was suggested by several other variables. For example, the angle formed by the intersection of the palatal plane with the posterior pharyngeal wall (PPl-PPW) was not statistically different for any group comparison. However, the angle was much more obtuse in TC than in the other three syndromes (Figure 4.39).

PART III: VELOPHARYNGEAL PHYSIOLOGY IN FOUR SYNDROMES

NASOPHARYNGOSCOPY

Speech sample used for nasopharyngoscopic analysis

Analysis was made during production of sustained /s/ for all subjects except for 4 in the wide pharynx group (1 VCF, 3 VDW). For those subjects, analysis was performed during maximum closure while producing /p/ (3 subjects) or /t/ (1 subject). Fisher's Exact Test revealed no difference between groups in the analysis of whether the phoneme used was representative of either the habitual degree of closure or the maximum degree of closure. In all subjects except for one with VDW, the phoneme used for analysis reflected both habitual and maximum closure.

Analysis of velopharyngeal gestures of the experimental subjects

Results of analysis of the endoscopic examinations appear in Table 4.4. Raw data for each subject is contained in Appendix C-2. The Wilcoxon Rank Sum Test revealed significant differences between the narrow and wide pharynx groups in the degree of velar displacement ($p<.01$), occurrence of VPI ($p<.0001$), and severity of VPI ($p<.01$) (Table 4.5). In comparison to the narrow pharynx group, the wide pharynx group had less velar motion, a higher prevalence of VPI, and larger velopharyngeal gaps when gaps occurred. Prevalence of VPI for each syndrome group was similar to the prevalence of hypernasality in the larger sample of 129 subjects included in Part I of this study except for a higher prevalence of VPI in the van der Woude syndrome subgroup than of hypernasality in the larger group.

Velopharyngeal Gap Description.

Velopharyngeal gap size: Severity of VPI according to syndrome group based on endoscopic observation is displayed in Figure 4.40. Review of the distribution of measurements suggested that the size of the velopharyngeal gaps tended to be larger in VCF than in VDW. In fact, when VPI occurred, gap size in VDW was similar to gap size in S. Gross VPI, or complete absence of closure, occurred only in VCF and 25% of the VCF subjects closed less than 10% of the velopharyngeal port during speech. Conversely, 50% of the subjects with VCF closed between 86% and 97% of the port as viewed

endoscopically. VCF was the only group with this type of bimodal distribution of ratios. Occurrence and severity of VPI were lowest in TC.

Velopharyngeal gap shape: Fifty percent of all subjects with VPI had gaps oriented in the coronal plane indicating a lack of LPW motion (Table 4.4). Twenty-eight percent had gaps which were circular or oriented in the sagittal plane indicating the presence of a central defect. Gap shape according to pharyngeal width and syndrome is represented in Figures 4.41 and 4.42. There did not appear to be any pharyngeal width or syndrome specific differences in gap shape except that 70% of the gaps in VCF were coronal or gross. There was only one TC subject with a gap detected, and the shape of the gap was coronal.

Lateral pharyngeal wall displacement: LPW displacement was not statistically different for the narrow and wide pharynx groups. However, as seen in Figure 4.43, there were differences related to syndrome. VCF was the only syndrome in which 25% of the subjects had no LPW motion and 50% had motion which was negligible (less than 10% toward the opposite LPW). In fact, 75% of the subjects with VCF had LPW displacement ratios below .20. In contrast, S, TC, and VDW had subjects in whom LPW motion approached the pharyngeal midline (.4 to .5), and no subject with TC had a right-LPW ratio which was less than 35%. Distribution of LPW displacement ratios in VDW and S were similar to each other.

Adenoid Size: Relative adenoid size at the plane of velopharyngeal closure measured from the endoscopic view was not significantly different for the wide and narrow pharynx groups. However, as seen in Figure 4.44, the adenoid filled less than 15% of the pharynx at the area of velopharyngeal closure in half of the subjects with VCF. The median adenoid size for the subjects with VDW was only slightly below the median size in subjects with S and TC.

MULTI-VIEW VIDEOFLUOROSCOPY

Subjects

As indicated in Table 3.1, lateral and frontal view videofluoroscopic data were available on 37 subjects who had cephalometric analysis. In addition, a base view examination had been performed on 22 of the subjects. Every potential rating could not be made on every subject because of occasional technical problems with the original examinations, such as a poor barium coat on lateral pharyngeal wall or a "false" view related to head position or superimposition of other anatomic structures on the structure to be analyzed.

Speech sample used for videofluoroscopic analysis

Analysis was made during production of sustained /s/ for all subjects except for 2 narrow pharynx and 2 wide pharynx subjects (2 TC, 1 VCF, 1 VDW). For those subjects, analysis was performed during maximum closure while producing /p/ (2 subjects) or /t/ (2 subjects). The same phoneme was used for videofluoroscopy and nasopharyngoscopy in all cases in which

both examinations were done. Fisher's Exact Test identified no difference between the number of subjects in the wide and narrow pharynx groups in which the habitual and maximum degree of closure were different, or in the phoneme used for analysis. The phoneme used for analysis represented maximum closure in all cases, and represented the habitual closure pattern in 92%. In three subjects (1 TC, 2 VCF), the maximum closure was not habitual, but was elicited during examination when verbal prompting for correct production was provided.

Analysis of velopharyngeal gestures of the experimental subjects

Results of videofluoroscopic analysis are in Table 4.5. Raw data are listed in Appendix D-5. The narrow and wide pharynx groups were statistically different from each other in the presence or absence of VPI as identified on both frontal and en face projections ($p<.01$), but not from lateral projection (Table 4.6) and in velopharyngeal gap size measured from the en face view (Wilcoxon Rank Sum Test, $p<.05$). VPI occurred more often and with greater severity in the wide pharynx group.

Velopharyngeal gap description.

Velopharyngeal Gap size. The mean size of the velopharyngeal gaps measured from en face view videofluoroscopy for each of the syndromes is illustrated in Figure 4.45. The largest gaps occurred in subjects with VCF,

and the smallest occurred in TC. The mean gap size and distribution for S and VDW appeared similar.

Shape of gap. Gap shapes corresponding to normal closure patterns were represented in similar frequency in both the narrow and wide pharynx groups. All wide pharynx subjects examined fluoroscopically had VPI, and gross VPI occurred only in VCF. The distribution of gap shape according to pharyngeal width and syndrome is illustrated in Figures 4.46 and 4.47.

Velar displacement. Velar displacement was measured from en face and lateral projections. As seen in Figure 4.48, base view analysis suggested that relative velar motion was best in TC and worst, at times absent, in VCF. The relative amount of velar motion in S and VDW were similar. The displacement ratio derived from en face view was comparable to the velar ratio from nasopharyngoscopy, and the rank ordering of syndromes according to the amount of velar motion was the same.

The velar displacement ratios derived from lateral view had better interrater reliability and reflected a larger range of motion. VCF was the only group in which absence of velar motion occurred, and the only group in which the velum never contacted the posterior pharyngeal wall. In contrast to the observation in the en face view, the median velar displacement ratio in VDW was much lower than in VCF or any other syndrome. In fact, because of a bimodal distribution, subjects with VCF

had the highest median ratio for this variable but also the lowest velar displacement ratios (Figure 4.49).

Direction of velar motion: The direction of velar motion as seen on lateral view videofluoroscopy was posterior in 46% of the subjects and posterosuperior in 38% (Appendix D-2). Two subjects with VCF had no velar motion and one had "tip-hinge" motion. Posterior motion occurred in 2 subjects with TC and 1 with VDW. Inadequate sample size precluded valid statistical analysis of this variable.

Posterior pharyngeal wall displacement. The Wilcoxon Rank Sum Test revealed no difference between the pharyngeal width groups with regard to PPW displacement in any fluoroscopic view. Subjects with S had much more posterior pharyngeal wall motion than subjects in any other group when measured from base view fluoroscopy (Figure 4.50). However, subjects with TC and VDW had the most movement, and VCF the least when observed from lateral view, which is the view that affords an unobstructed observation of PPW displacement (Figure 4.51).

Direction of posterior pharyngeal wall motion. Fifty-one percent of the subjects had anterior movement of the posterior pharyngeal wall. Forty-one percent had no PPW motion. One subject each had anteroinferior (TC), anterosuperior (VDW), or outward (VCF) motion (Appendix D-3).

Lateral pharyngeal wall displacement. Although the narrow and wide pharynx groups were not statistically different with regard to LPW displacement, it was worse in VCF than in any other syndrome (Figure 4.52). Mean LPW displacement ratios in the other syndromes were similar to each other. Ratings were similar from en face and frontal view, but were more reliable from frontal view (Appendix D-1).

LPW Contour: There was no significant difference between the narrow and wide pharynx groups, and the shape distribution based on frontal view fluoroscopy among the four syndrome groups appeared to be the same. 50% of all of the subjects had "balloon" shaped LPW displacement, and 70% had either balloon or shelf-like movement (Appendix D-4). Half of the subjects with VCF had absent or vertical LPW motion, more than in any other syndrome.

LPW Direction and Symmetry: There was no apparent difference between the narrow and wide pharynx groups in the direction of LPW motion observed on frontal view videofluoroscopy. Over 90% of all subjects had medial motion of the LPW's. One subject with S had superomedial motion, one subject with VCF had no LPW motion, and one subject with VCF had outward LPW motion.

Table 4.1. Prevalence and severity of hypernasality following palate repair for subjects undergoing primary palatoplasty at Montefiore Medical Center.

Diagnosis	CP	N	Percent subjects with hypernasality	Mean severity rating
S	15	13	46	1.4
TC	2	1	(100)	(1.5)
VCF	4	4	100	3.0
VDW	5	5	40	0.5
NON-SYNDROMIC		500	14**	not reported

CP= number of subjects with overt cleft palate only
N= number of subjects on whom resonance data were available
S= Stickler syndrome
TC= Treacher Collins syndrome
VCF= velo-cardio-facial syndrome
VDW= van der Woude syndrome

**Hall and Golding-Kushner (1989)

Table 4.2. Age, gender, cleft-type, and resonance of control and experimental subjects on whom cephalometric, nasopharyngoscopic, and videofluoroscopic measurements were made. Significance levels are listed for differences between narrow pharynx (NAR), wide pharynx, and control (CTL) groups.

VARIABLE	CONTROL Yr-Mos N= 15	NARROW PHARYNX (S, TC) N= 20	WIDE PHARYNX (VCF, VDW) N= 25	S N= 10	TC N= 10	VCF N= 13	VDW N= 12	P[23] NAR x CTL	P WIDE x CTL	P NAR x WIDE
AGE										
MEDIAN	9-0	7-7	7-2	5-5	16-3	6-1	9-1	ns	ns	ns
RANGE	7-0, 11-0	3-6, 42-0	4-1, 38-0	3-1, 21-1	5-1, 42	4-1, 30	5-1, 39			
GENDER										
MALE	6	10	8	5	5	6	2	ns	ns	ns
FEMALE	9	10	17	5	5	7	10			
CLEFT										
OVERT	0	13	8	8	5	0	8			<.0001
SMCP	0	7	12	2	5	8	4			
OSMCP	0	0	5	0	0	5	0			
POST ADENO-TONSILLECTOMY										
NO	15	17	24	9	8	13	11	ns	ns	ns
YES	0	3	1	1	2	0	1			
HYPERNASALITY mean severity	0	.88	1.9	1.15	0.6	2.3	1.5			
HYPONASALITY mean severity	0	.08	0	0	.15	0	0			

S= Stickler syndrome; TC= Treacher Collins syndrome; VCF= velo-cardio-facial syndrome; VDW= van der Woude syndrome
ns = not significant

[23]Probability values were derived from the Wilcoxon Rank Sum Test, except for gender differences which were derived using Fisher's Exact Test.

Table 4.3. Abnormal morphologic characteristics of Stickler (S), Treacher Collins (TC), velo-cardio-facial (VCF), and van der Woude (VDW) syndromes.

VARIABLE	CHARACTERISTIC	S	TC	VCF	VDW	NAR x CTL	NAR x WD	WIDE x CTL
SKELETAL:								
N-S-B	cranial base angle	A	A	O	O	***	***	**
N-S-Ar	cranial base angle	A	A			***	***	
N-S	anterior cranial base	S				**	**	
Go-Me	mandibular body	S	S	S		**		
N-MPl	mandibular plane		O		A	***	***	
N-FH	Frankfort horizontal		O			*		
S-Ba	posterior cranial base			S			*	**
MPl-PPl	mandibular plane				A			
Ar-Go	ramus length				L			
S-Ar	sella to ramus				L			
ANS-PNS	hard palate	S				**		**
SOFT TISSUE:								
PNS-V	velar length	S		S	S			***
ANS-PNS-V	velar drape		A				*	
PPW 1-2	PPW at velopharynx			TN	TN		***	***
PPW 3	PPW at high oropharynx			TN				*
PPW 4	PPW at lower oropharynx		TK				*	
Ad mm	adenoid area		S		L	*		
PCTVTAD	relative adenoid size		S	S				
AIRWAY DEPTH:								
Lum 1	A-P depth pharynx (pal. plane)		S	L	L	***	***	***
Lum 2	A-P depth pharynx (vel midpt)	S	S	L	L	***	***	***
Lum 3-4	A-P depth oropharynx		S	L	L	*	***	**
Lum 5	A-P depth upper hypopharynx		S			***	***	
Lum 6	A-P depth lower hypopharynx	S	S			*	**	
BL WDTH	A-P depth skeletal frame		S			*	**	
AIRWAY HEIGHT:								
LAH	airway height velum-hyoid	L	L		L	***	*	
MPl-Hy	hyoid position		L			*	*	
PPl-Hy	airway height pal plane-hy		L	S		**	**	
BL HGHT	height skeletal block		L	S				
AIRWAY SIZE AND SHAPE:								
AW mm	airway area	S	S			*	**	
PCTSKAW	percent lumen in skel. frame		S	L		**	***	*
A-PPW	nasopharyngeal angle		O			***	**	

A=ACUTE; O=OBTUSE; S=SHORT, SMALL; L=LONG, LARGE, LOW; TK=THICK; TN=THIN

* $p < .05$
** $p < .01$
*** $p < .001$

Table 4.4. Displacement ratios, adenoid size and characteristics of velopharyngeal (V-P) gestures based on nasopharyngoscopy. Significance levels for differences between narrow pharynx (NAR) and wide pharynx groups listed.

VARIABLE Mean S.D. Range	NARROW PHARYNX N= 17	WIDE PHARYNX N= 22	p: NAR x WIDE[24]	S N= 9	TC N= 8	VCF N= 10	VDW N= 12
VELAR DISPLACEMENT	.87 .19 .45, 1.0	.61 .38 0, 1.0	.009	.81 .2 .45, 1.0	.94 .16 .55, 1.0	.57 .42 0, .95	.64 .37 .05, 1.0
POSTERIOR PHARYNGEAL WALL DISPLACEMENT	.04 .09 0, .3	.05 .11 0, .33	ns	.06 .12 0, .3	.01 .03 0, .08	.03 .09 0, .3	.07 .13 0, .33
LEFT LATERAL PHARYNGEAL WALL DISPLACEMENT	.3 (N=11) .15 0, .5	.18 (N=21) .15 0, .38	ns	.24 (N=6) .15 0, .4	.37 (N=5) .13 .18, .5	.11 .14 0, .38	.24 (N=11) .13 0, .38
RIGHT LATERAL PHARYNGEAL WALL DISPLACEMENT	.3 (N=12) .15 0, .5	.19 (N=18) .15 0, .46	ns	.23 (N=7) .16 0, .46	.38 (N=5) .07 .3, .5	.12 (N=9) .15 0, .46	.26 (N=9) .12 0, .44
MEDIAN % V-P CLOSURE PLANE FILLED W/ADENOID	43 0, 80	30 0, 75	ns	43 0, 75	44 0, 8	15 0, 75	38 .07, 61
N & PERCENT OF SUBJECTS WITH VPI (+/- VPI)	8 47%	21 95%	.0008[25]	7 78%	1 12%	10 100%	11 92%
PERCENT OF V-P CLOSURE ACHIEVED (Severity of VPI)	91% 17 43, 100	71% 34 0, 100	.004	83% 21 43, 100	99% 04 89, 100	58% 43 0, 97	81% 19 40, 100
SHAPE V-P GAP*							
SA, CI	2	6		2	0	2	4
CO	4	11		3	1	7	4
L, B	2	4		2	7	1	3
None	9	1		2	0	0	1

S= Stickler syndrome; TC= Treacher Collins syndrome; VCF= velo-cardio-facial syndrome; VDW= van der Woude syndrome
ns= not significant
* SA= Sagittal, CI= Circular, CO= Coronal, L= Lateral, B= Bilateral

[24]Wilcoxon Rank Sum Test

[25]Fisher's Exact Test

Table 4.5. Displacement ratios and characteristics of velopharyngeal gestures based on multi-view videofluoroscopy. A ratio of 1.0 represents maximum possible displacement.

VARIABLE Mean (N[26]) S.D. Range	NARROW PHARYNX	WIDE PHARYNX	P. NARROW X WIDE[27]	S	TC	VCF	VDW
EN FACE VIEW VELAR DISPLACEMENT	.59 (8) .31 .21, 1.0	.34 (13) .22 0, .67	ns	.46 (4) .19 .25, .7	.71 (4) .38 .21, 1.0	.26 (6) .24 0, .6	.41 (7) .19 .23, .67
EN FACE VIEW PPW DISPLACEMENT	.15 (8) .15 0, .4	.1 (12) .1 0, .3	ns	.26 (4) .1 .18, .4	.05 (4) .1 0, .21	.1 (6) .11 0, .3	.09 (6) .09 0, .24
EN FACE VIEW LEFT LPW DISPLACEMENT	.35 (9) .15 .1, .5	.3 (13) .15 0, .5	ns	.31 (5) .12 .1, .42	.39 (4) .19 .1, .5	.2 (6) .14 0, .33	.38 (7) .09 .3, .5
EN FACE VIEW RIGHT LPW DISPLACEMENT	.35 (9) .16 .05, .5	.28 (13) .13 0, .41	ns	.33 (5) .16 .05, .45	.39 (4) .18 .12, .5	.22 (6) .15 0, .36	.34 (7) .06 .22, .41
EN FACE VIEW PERCENT OF V-P CLOSURE ACHIEVED	93% (9) 10 70-100%	74% (13) 30 0-98%	.02	91% (4) 4 85-95%	94% (5) 13 70-100%	59% (6) 40 0-89%	88% (7) 7 79-98%
FRONTAL VIEW LEFT LPW DISPLACEMENT	.35 (17) .16 .05, .63	.26 (20) .17 -0.1, .53	ns	.34 (9) .14 .05, .49	.37 (8) .19 .11, .63	.19 (12) .15 -.01, .46	.36 (8) .15 .1, .53
FRONTAL VIEW RIGHT LPW DISPLACEMENT	.35 (17) .17 .05, .7	.3 (19) .17 -0.1, .51	ns	.33 (9) .14 .05, .49	.37 (8) .21 .05, .7	.25 (11) .19 -0.1, .51	.38 (8) .12 .18, .5
LATERAL VIEW VELAR DISPLACEMENT	.71 (17) .22 .23, 1.0	.57 (20) .35 0, 1.0	ns	.72 (9) .22 .4, 1.0	.69 (8) .23 .23, 1.0	.59 (12) .39 0, .9	.53 (8) .31 .15, 1.0
LATERAL VIEW PPW DISPLACEMENT	.18 (17) .16 0, .5	.09 (20) .14 -0.1, .38	ns	.14 (9) .15 0, .42	.22 (8) .16 0, .5	.03 (12) .08 -0.1, .2	.2 (8) .15 0, .38

S= Stickler syndrome; TC= Treacher Collins syndrome; VCF= velo-cardio-facial syndrome; VDW= van der Woude syndrome
ns= not significant

[26]Number of observations for each ratio is indicated.

[27]Wilcoxon Rank Sum Test

Table 4.6. Presence of velopharyngeal insufficiency (VPI) based on multi-view videofluoroscopy for pharyngeal width and syndrome groups.

N Col % Row % FLUOROSCOPIC VIEW	NARROW PHARYNX	WIDE PHARYNX	S	TC	VCF	VDH	TOTAL Percent
EN FACE VIEW NO VPI	4 44.44 100.00	0	1 20.00 25.00	3 75.00 75.00	0	0	4 18.18
EN FACE VIEW VPI	5 55.56 27.78	13 100.00 72.22	4 80.00 22.22	1 25.00 5.56	6 100.00 33.33	7 100.00 38.89	18 81.82
TOTAL EN FACE Percent	9 40.91	13 59.09	5 22.73	4 18.18	6 27.27	7 31.82	22 100.00
FRONTAL VIEW NO VPI	5 29.41 100.00	0	2 22.22 40.00	3 37.50 60.00	0	0	5 13.51
FRONTAL VIEW VPI	12 70.59 37.50	20 100.00 62.50	7 77.78 21.87	5 62.50 15.63	12 100.00 37.50	8 100.00 25.00	32 86.49
TOTAL FRONTAL Percent	17 45.95	20 54.05	9 24.32	8 21.62	12 32.43	8 21.62	37 100.00
LATERAL VIEW NO VPI	5 29.41 83.33	1 5.00 16.67	2 22.22 33.33	3 37.50 50.00	1 8.33 16.67	0	6 16.22
LATERAL VIEW VPI	12 70.59 38.71	19 95.00 61.29	7 77.78 22.58	5 62.50 16.13	11 91.67 35.48	8 100.00 25.81	31 83.78
TOTAL LATERAL Percent	17 45.95	20 54.05	9 24.32	8 21.62	12 32.43	8 21.62	37 100.00

S= Stickler syndrome; TC= Treacher Collins syndrome; VCF= velo-cardio-facial syndrome; VDH= van der Woude syndrome
ns= not significant

Presence of VPI x Pharyngeal width, Fisher's Exact Test
En face view: $p<.01$
Frontal view : $p<.01$
Lateral view: ns

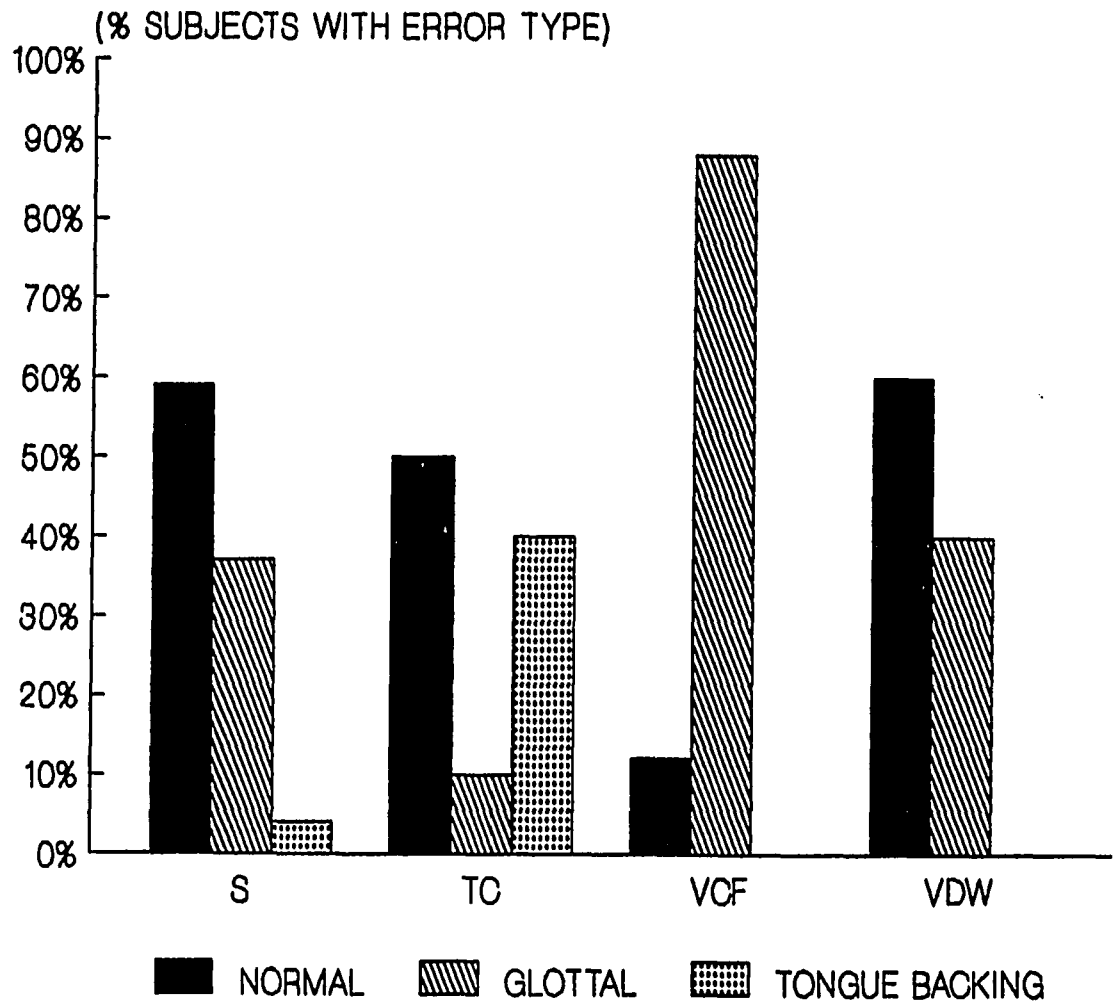


Figure 4.1. Predominant patterns of articulation development of subjects in prevalence study according to syndrome.

S= Stickler syndrome; TC= Treacher Collins syndrome; VCF= velo-cardio-facial syndrome; VDW= van der Woude syndrome

Note: developmental, phonological, and obligatory articulation errors were categorized as "normal"; all compensatory errors associated with VPI were categorized as "glottal" (Hoch et al, 1986).

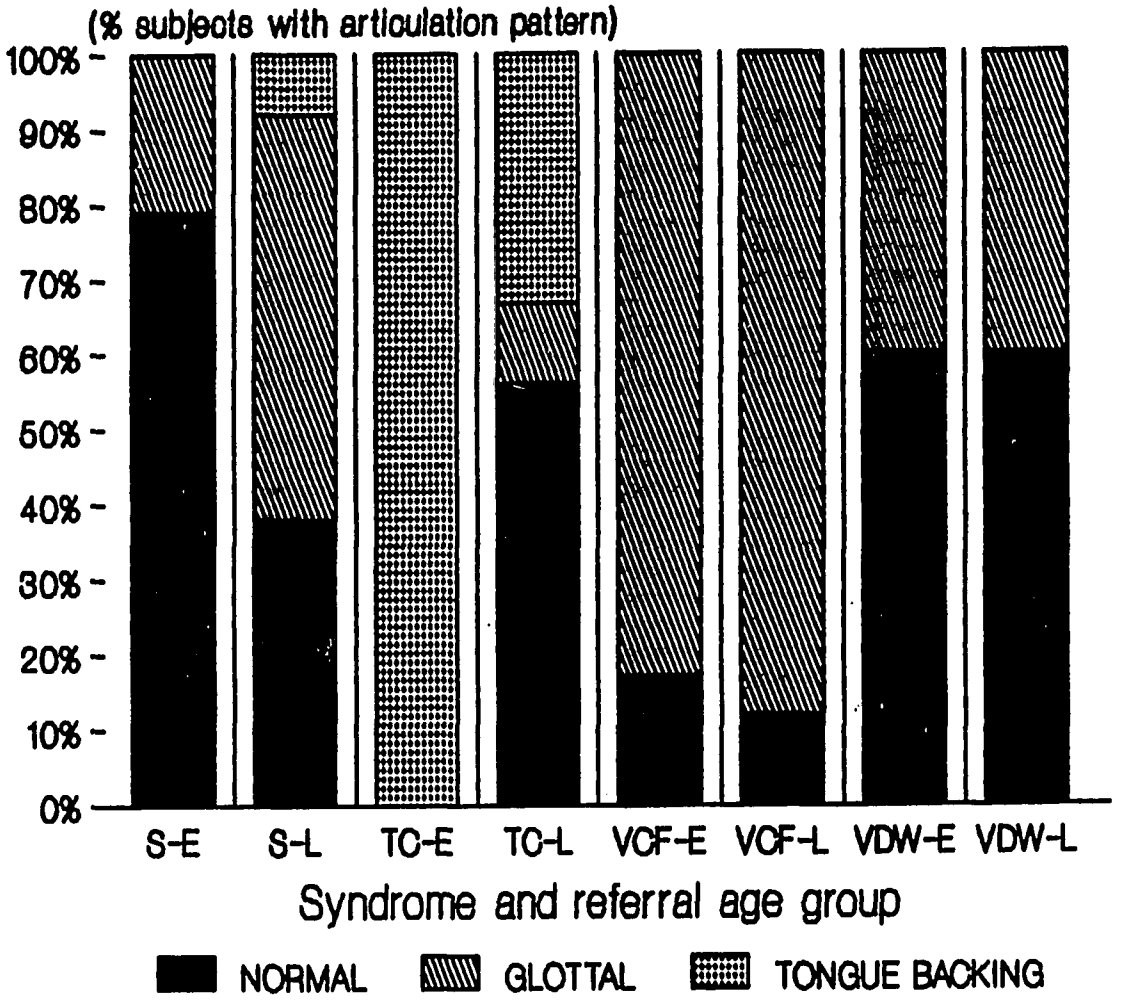


Figure 4.2. Predominant within-syndrome patterns of articulation development according to age at time of ascertainment (prevalence study). Early referrals (E) were ascertained at 2 years of age or younger; late referrals (L) were ascertained after 2 years of age.

S= Stickler syndrome; TC= Treacher Collins syndrome; VCF= velo-cardio-facial syndrome; VDW= van der Woude syndrome

Note: developmental, phonological, and obligatory articulation errors were categorized as "normal"; all compensatory errors associated with VPI were categorized as "glottal" (Hoch et al, 1986).

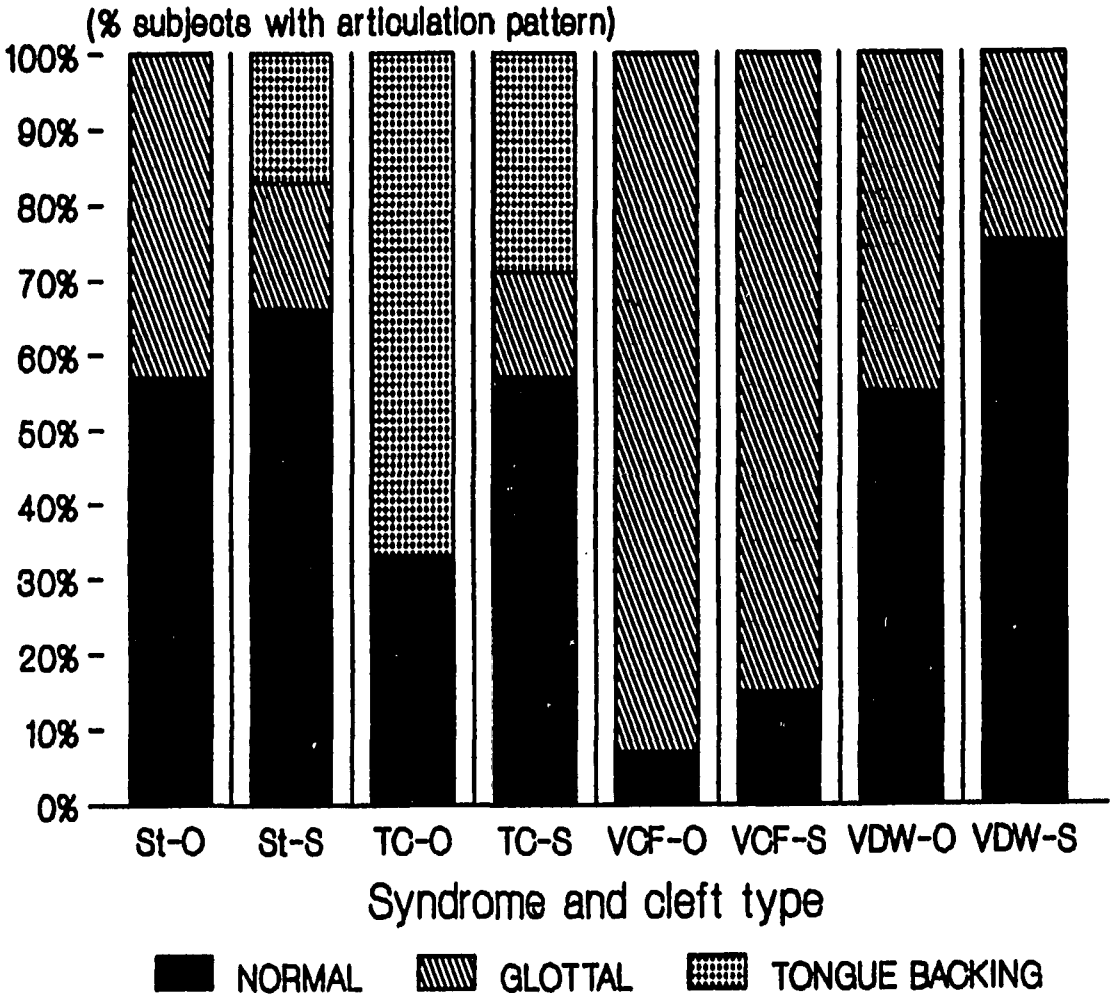
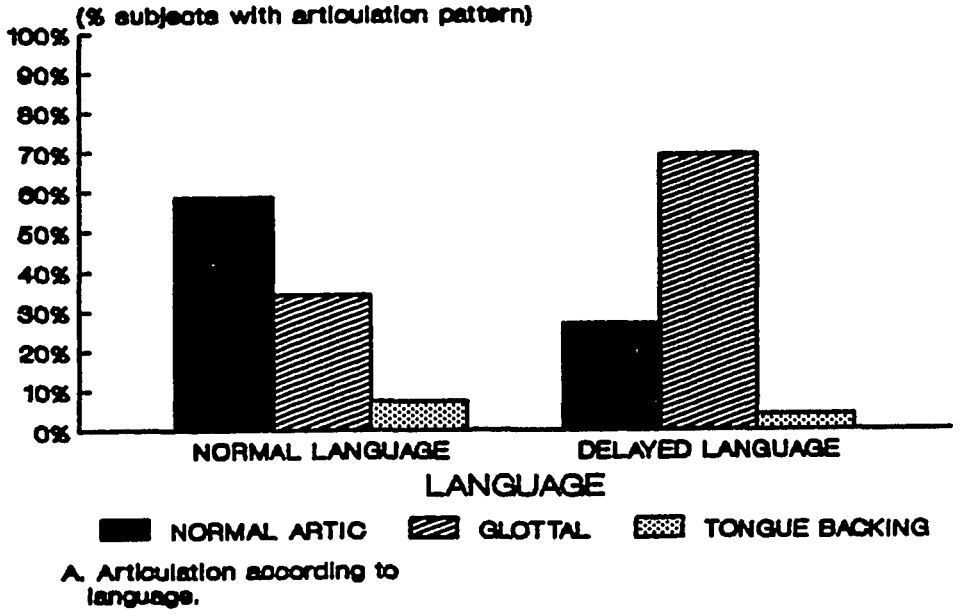


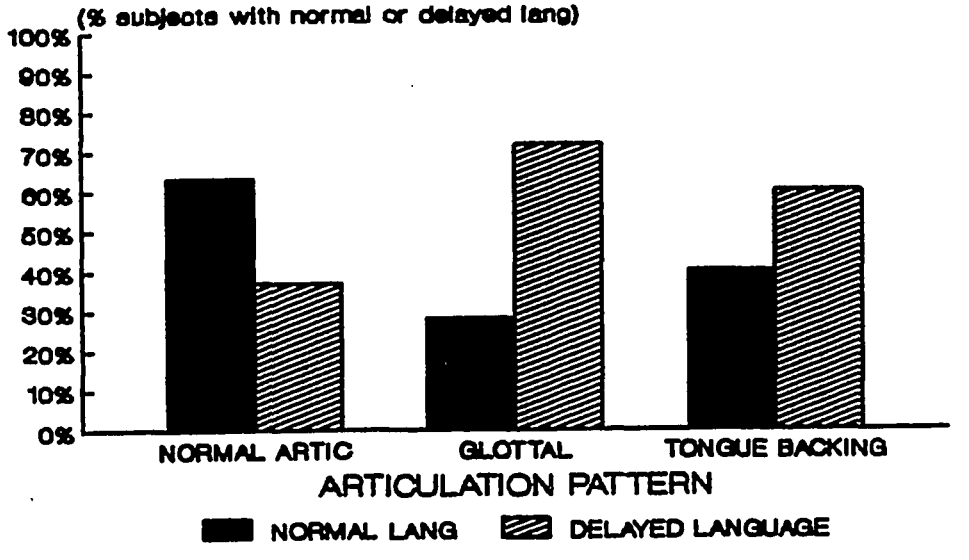
Figure 4.3. Predominant within-syndrome patterns of articulation development according to type of cleft palate (prevalence study).

St= Stickler syndrome; TC= Treacher Collins syndrome; VCF= velo-cardio-facial syndrome; VDW= van der Woude syndrome O= overt cleft palate; S= submucous and occult submucous cleft palate

Note: developmental, phonological, and obligatory articulation errors were categorized as "normal"; all compensatory errors associated with VPI were categorized as "glottal" (Hoch et al, 1986).



A. Articulation according to language.



B. Language according to articulation.

Figure 4.4. Articulation and language development of all subjects in prevalence study.

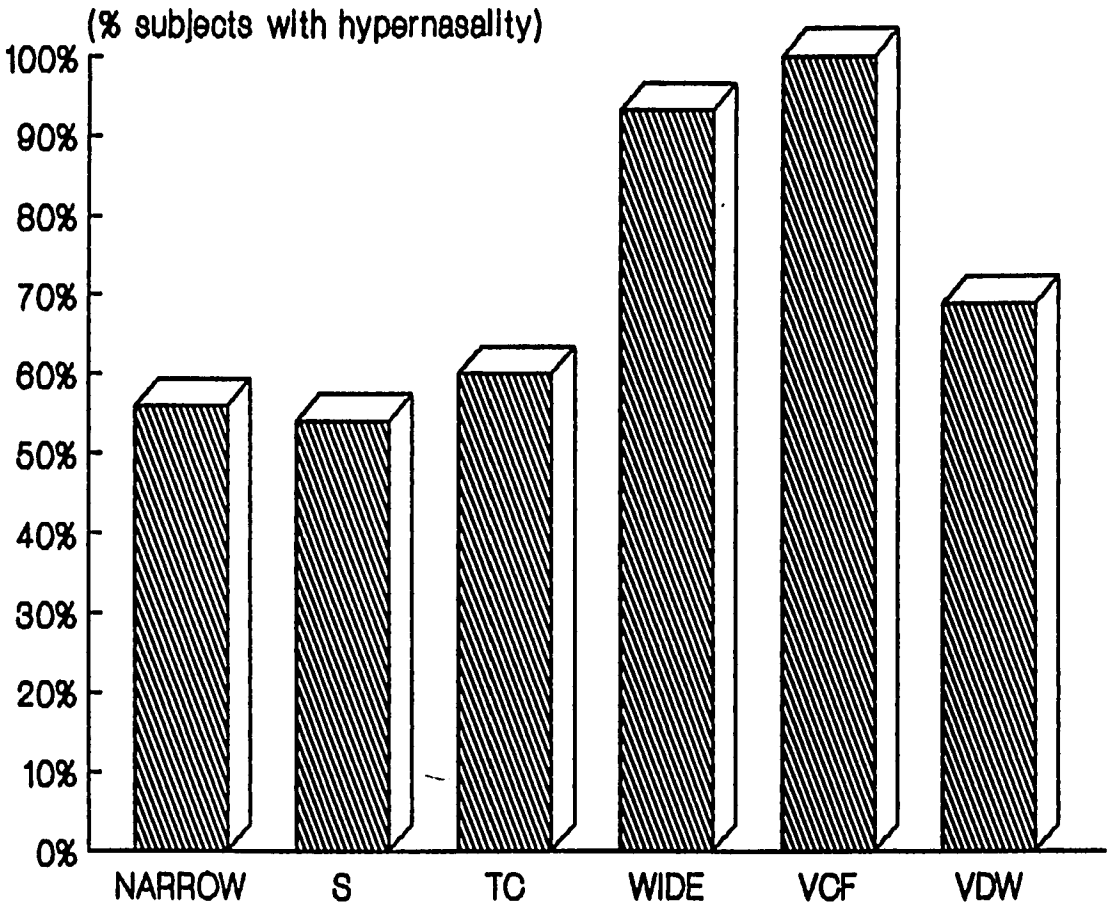


Figure 4.5. Prevalence of hypernasality according to pharyngeal width and syndrome groups.

S= Stickler syndrome; TC= Treacher Collins syndrome; VCF= velo-cardio-facial syndrome; VDW= van der Woude syndrome

NARROW pharynx: S, TC; WIDE pharynx: VCF, VDW

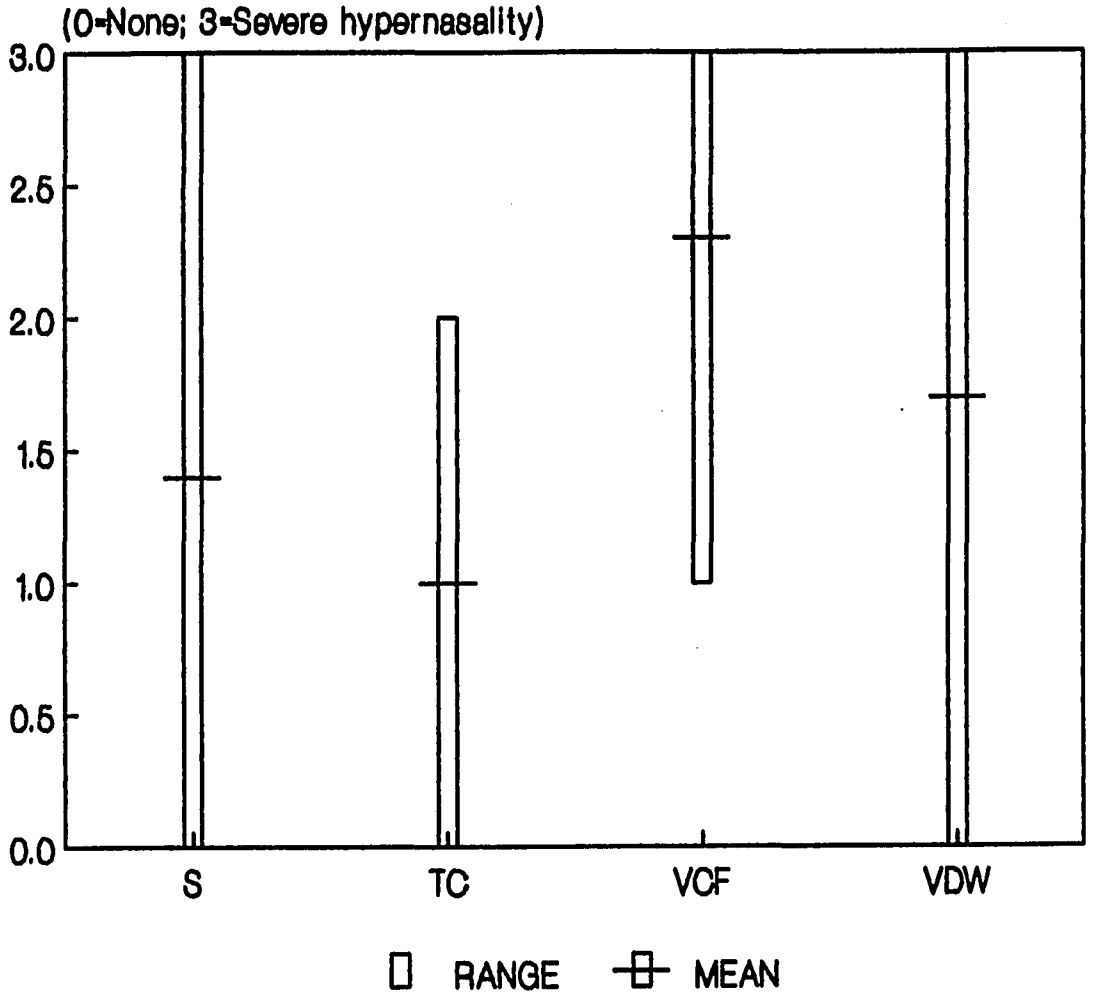


Figure 4.6. Severity of hypernasality for syndrome groups (prevalence study).

S= Stickler syndrome; TC= Treacher Collins syndrome; VCF= velo-cardio-facial syndrome; VDW= van der Woude syndrome

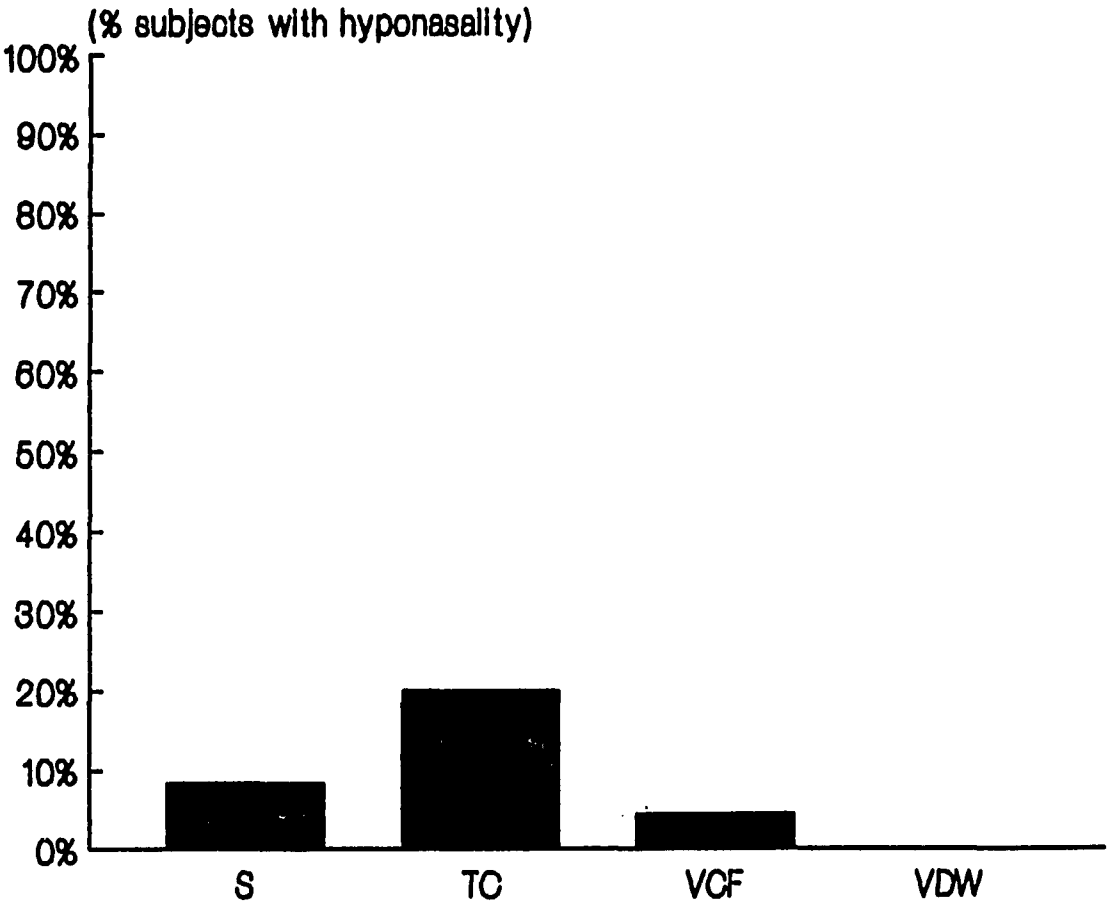


Figure 4.7. Prevalence of hyponasality according to syndrome.

S= Stickler syndrome; TC= Treacher Collins syndrome; VCF= velo-cardio-facial syndrome; VDW= van der Woude syndrome

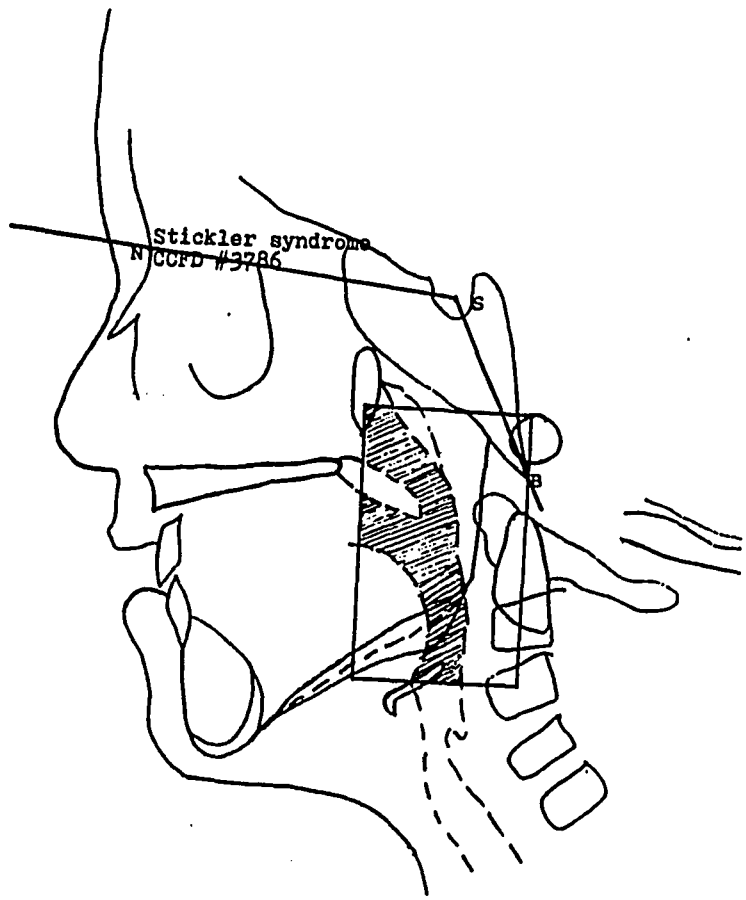


Figure 4.8. Cephalometric tracing of subject with Stickler syndrome. Cranial base angle (N-S-B) and airway frame block are drawn. Shaded area is airway.

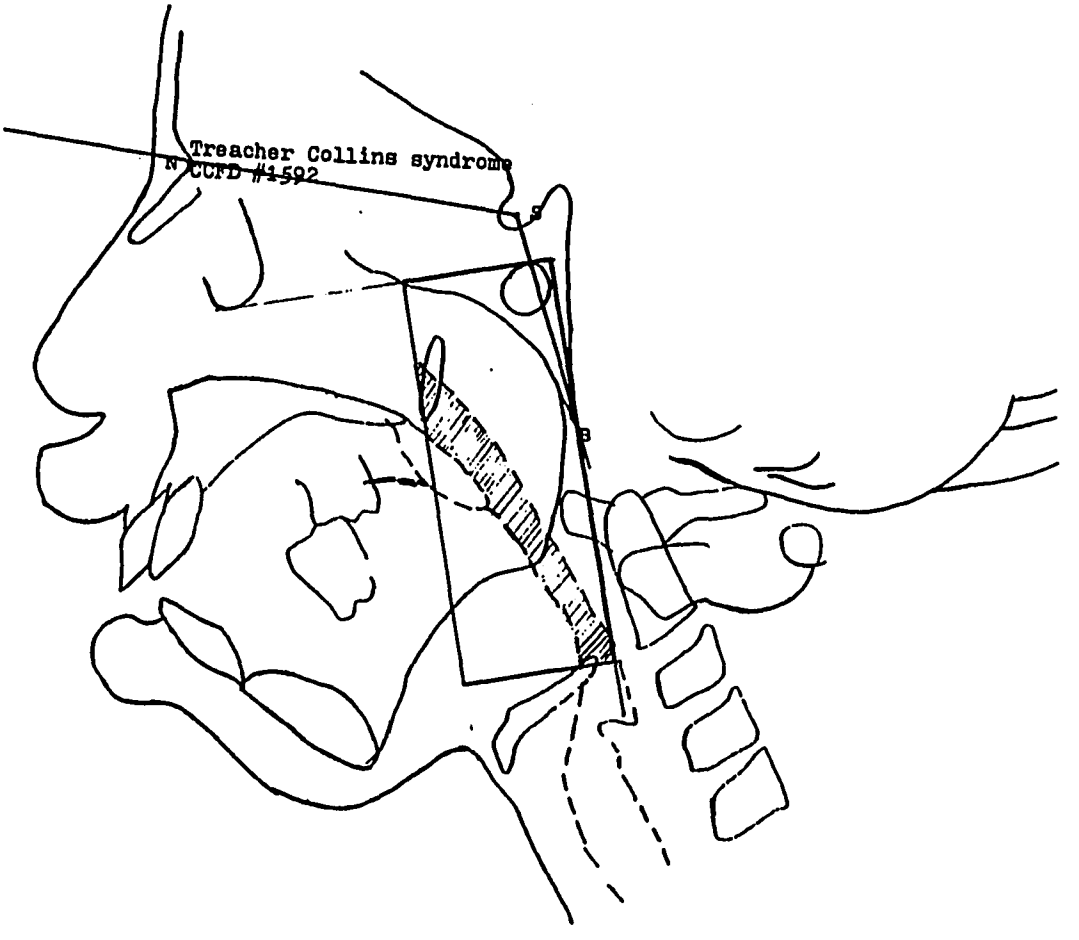


Figure 4.9. Cephalometric tracing of subject with Treacher Collins syndrome. Cranial base angle (N-S-B) and airway frame block are drawn. Shaded area is airway.

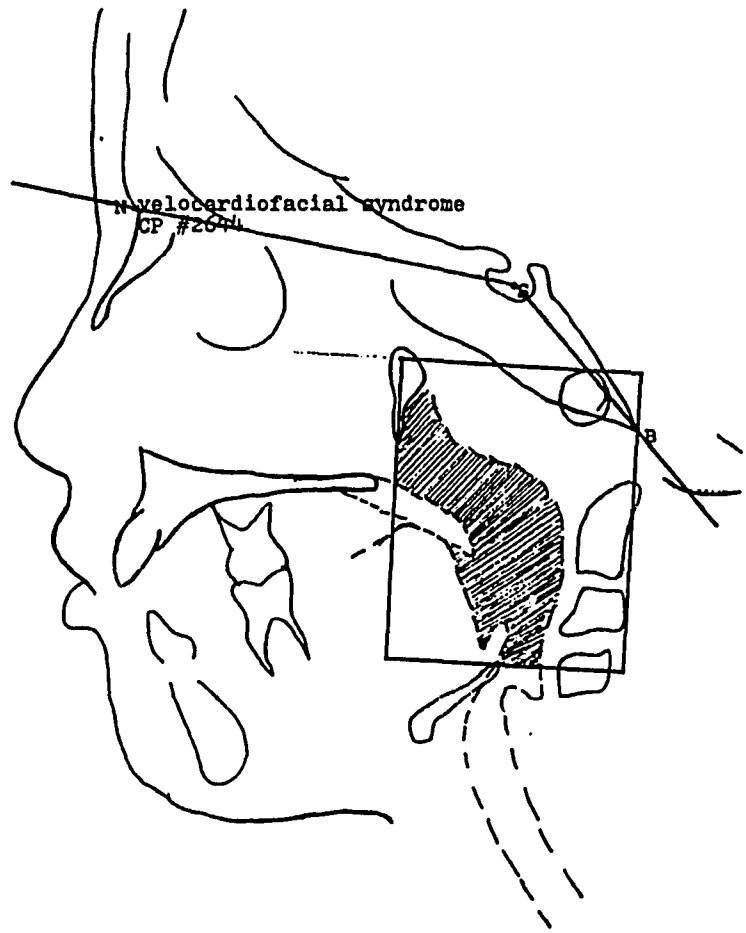


Figure 4.10. Cephalometric tracing of subject with velo-cardio-facial syndrome. Cranial base angle (N-S-B) and airway frame block are drawn. Shaded area is airway.

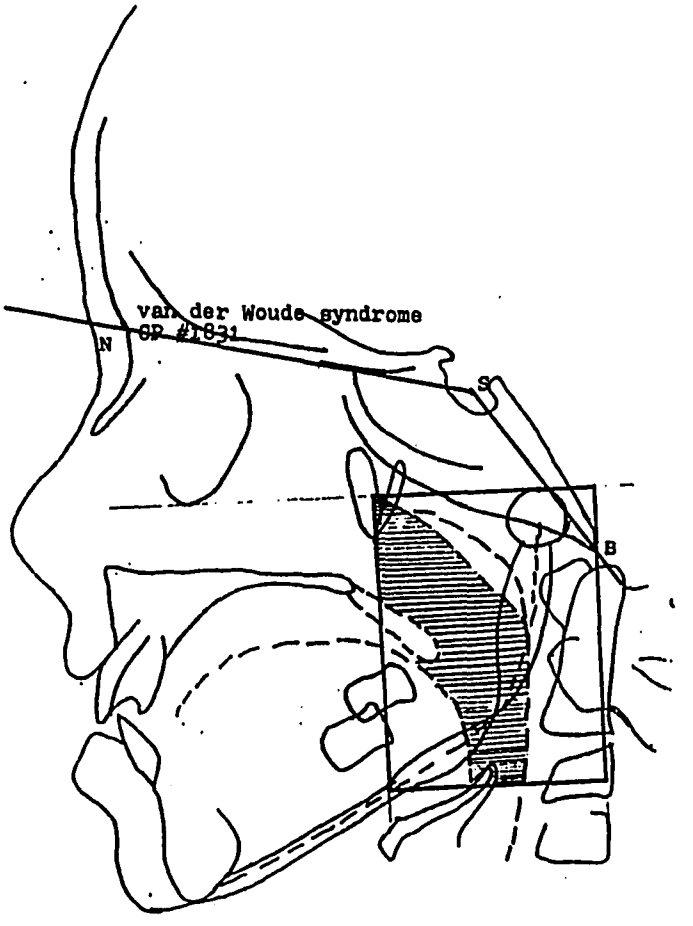


Figure 4.11. Cephalometric tracing of subject with van der Woude syndrome. Cranial base angle (N-S-B) and airway frame block are drawn. Shaded area is airway.

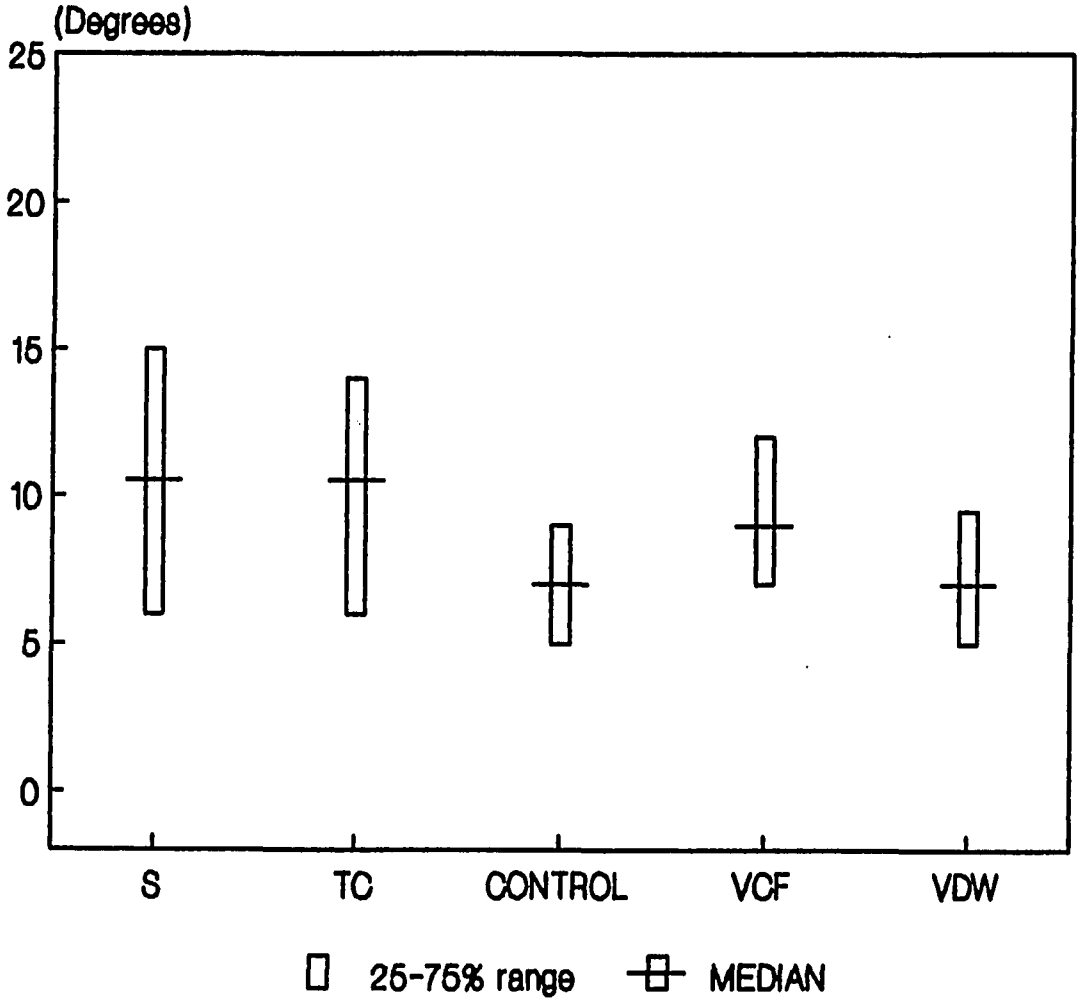


Figure 4.12. Sella height (Horizontal-Nasion-Sella). Relative height of sella turcica measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

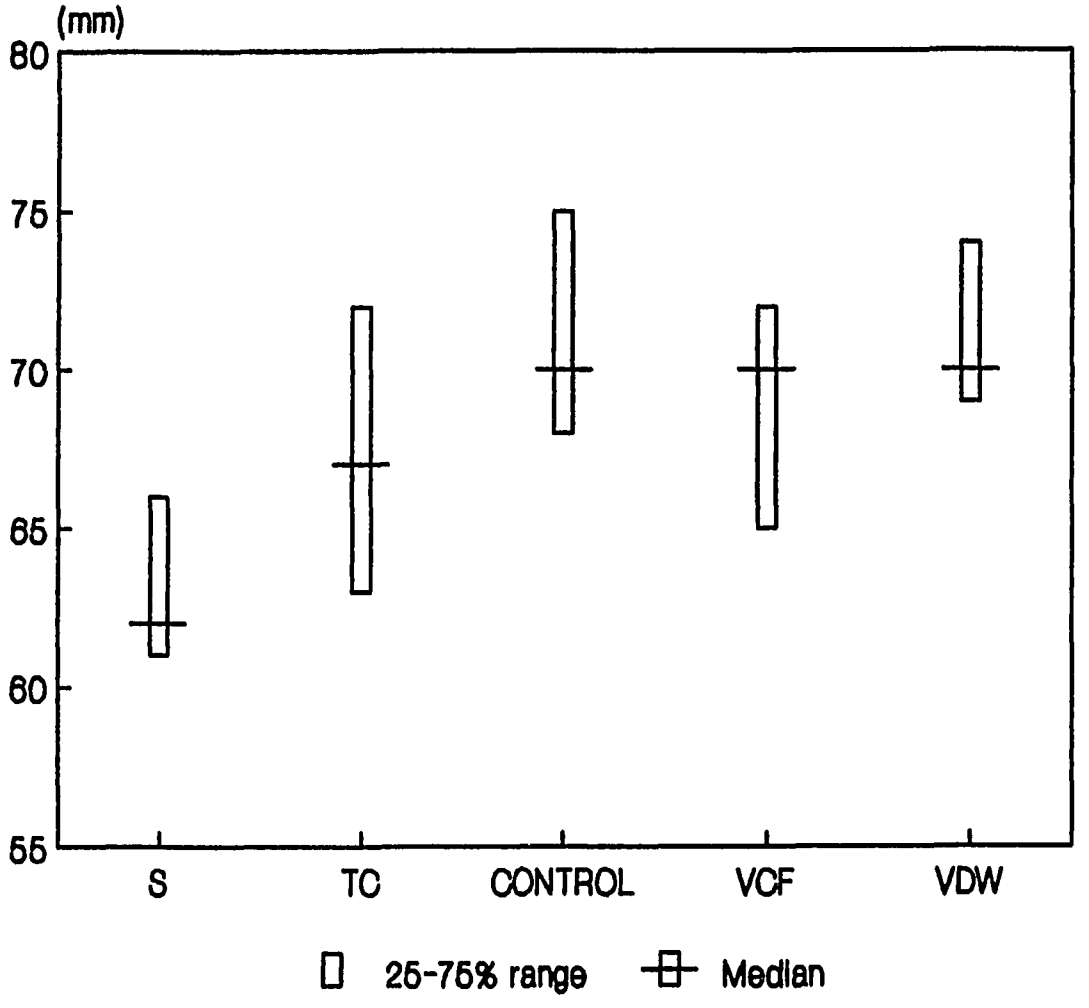


Figure 4.13. Anterior cranial base length (Nasion-Sella) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

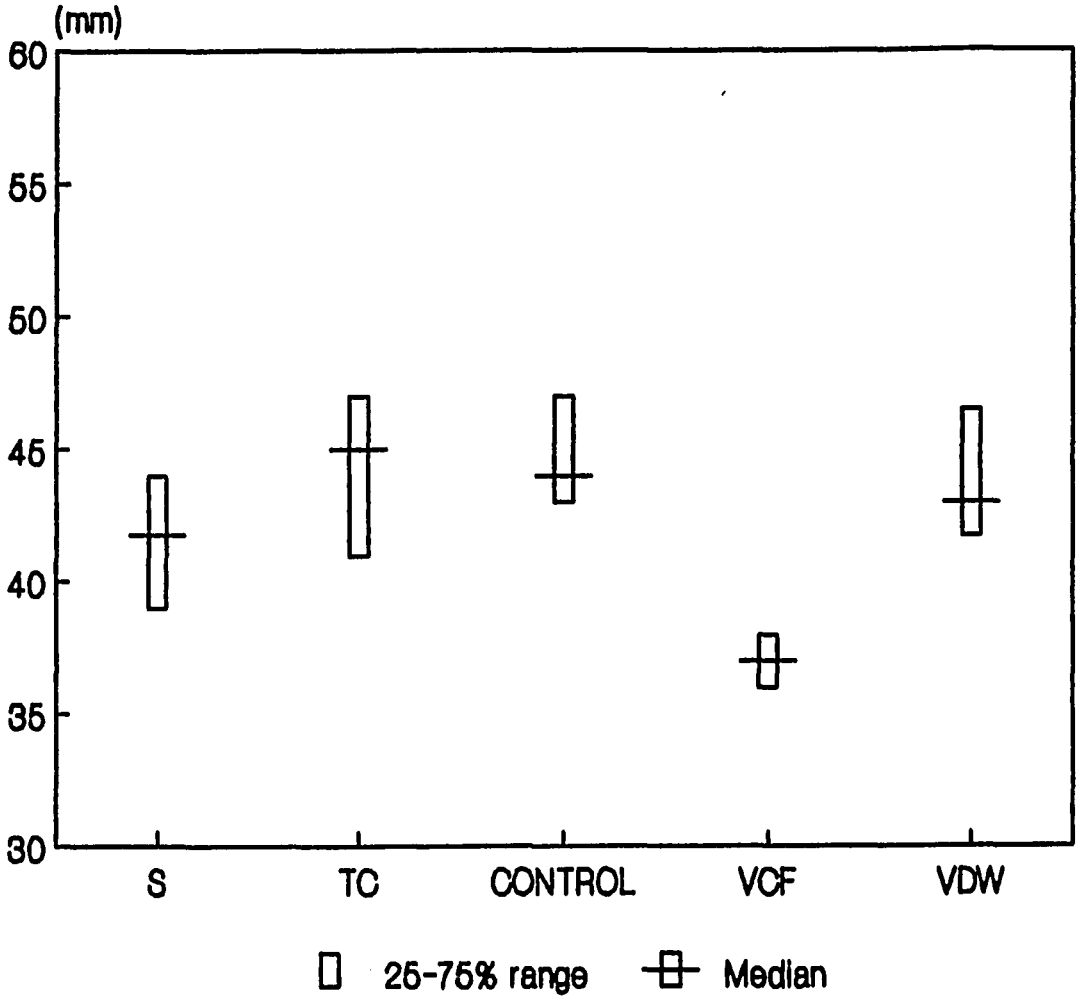


Figure 4.14. Posterior cranial base length (Sella-Basion) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

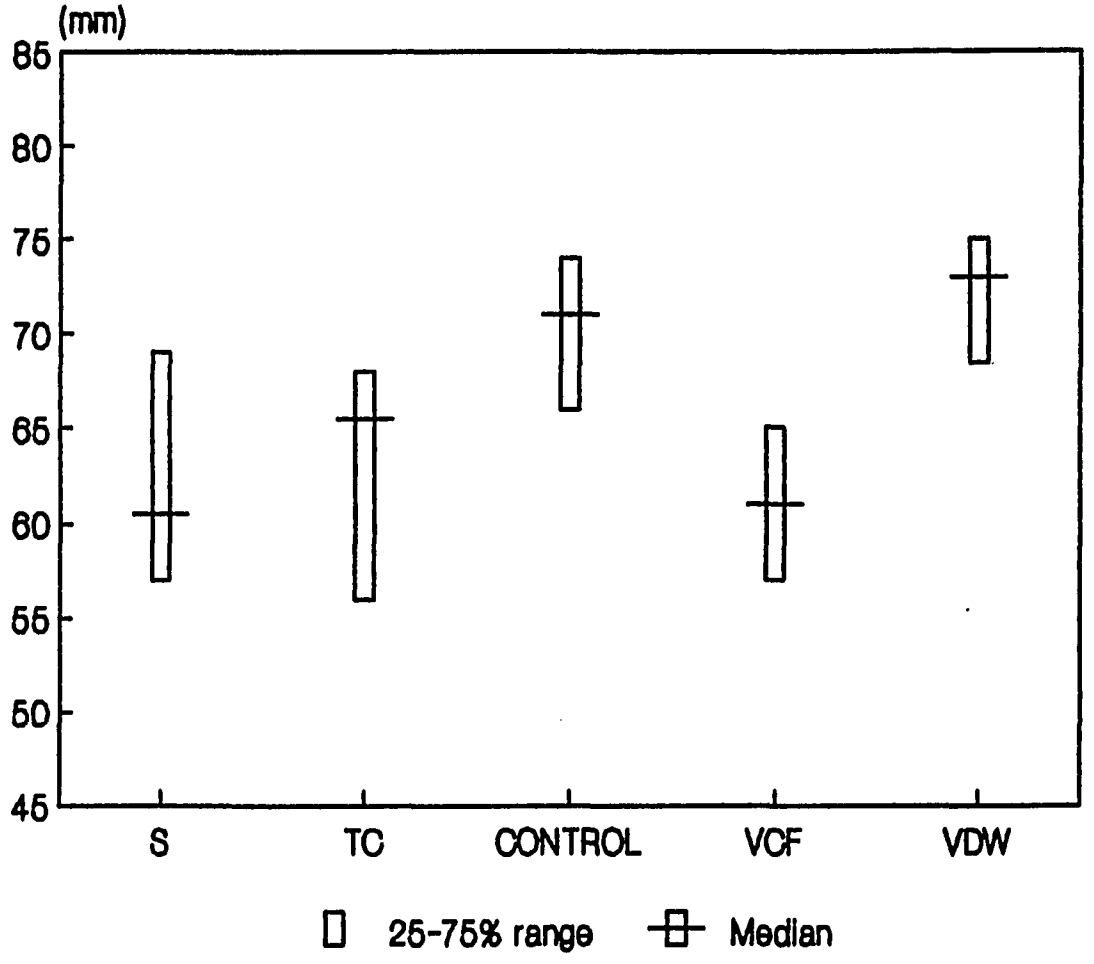


Figure 4.15. Mandibular body length (Gonion-Menton) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

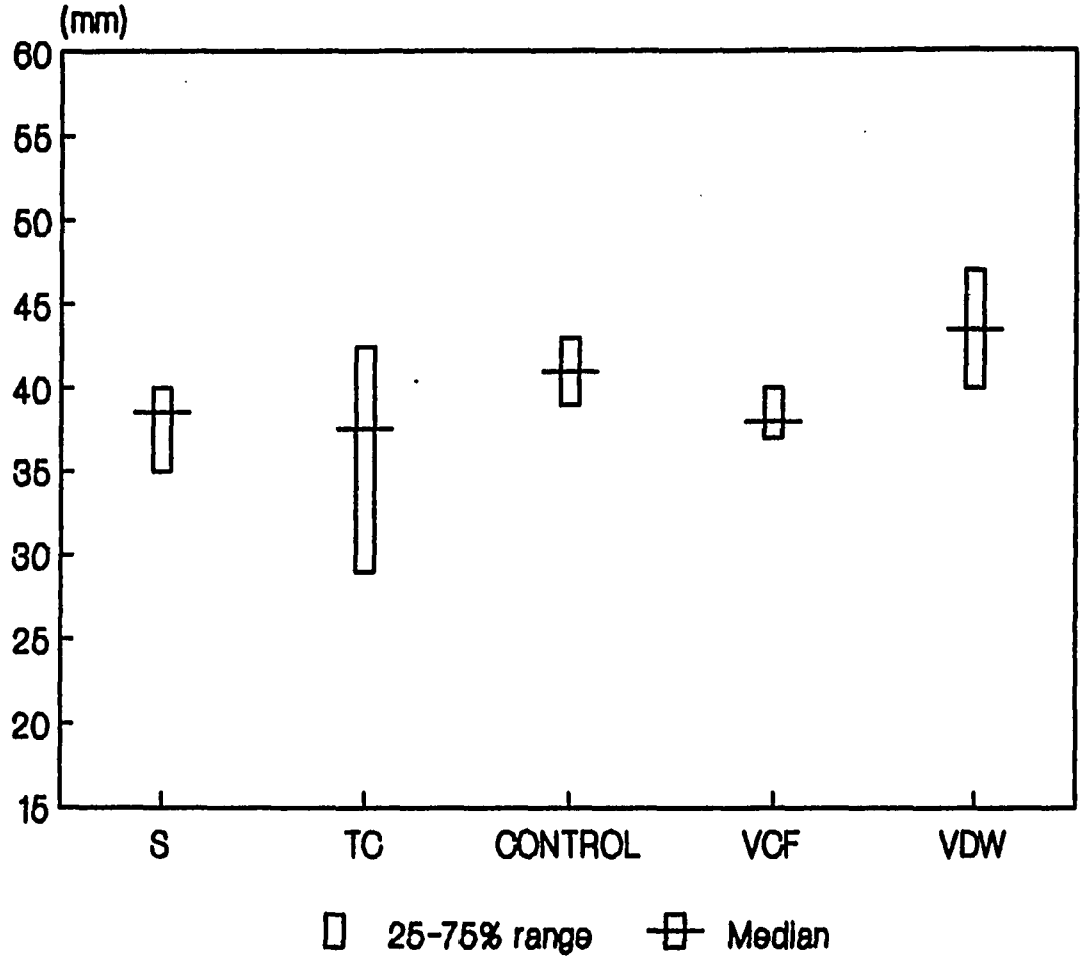


Figure 4.16. Ramus length (Articulare-Gonion) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

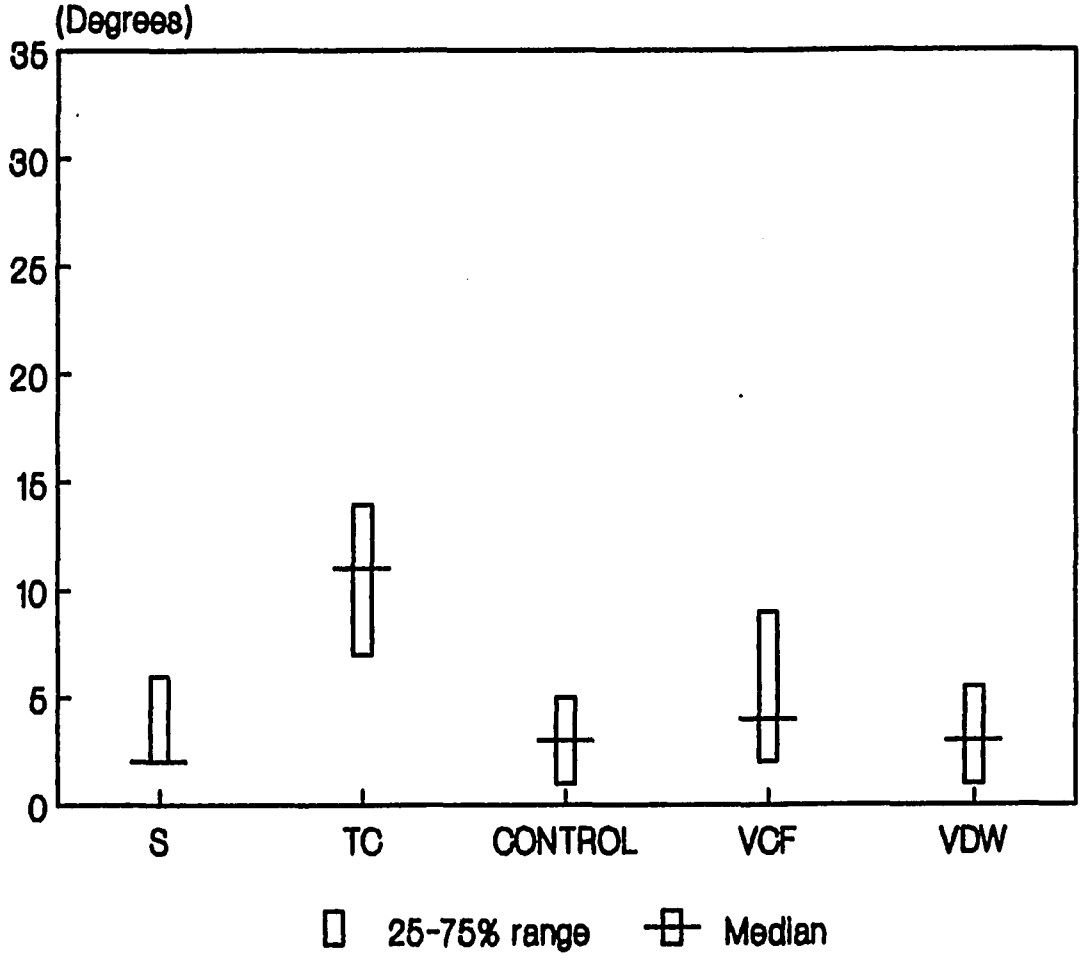


Figure 4.17. Slope of Frankfort horizontal (FH) (Horizontal-FH) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

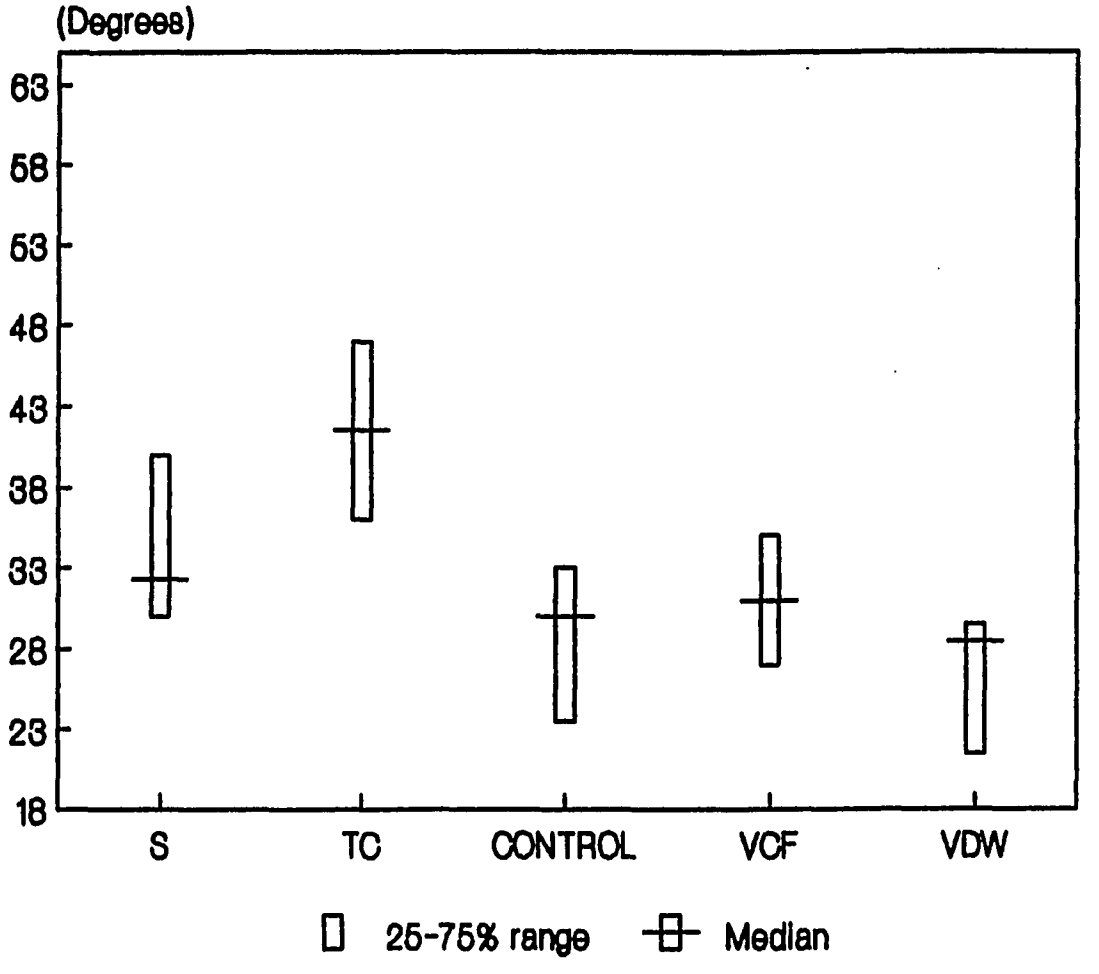


Figure 4.18. Angle formed by mandibular plane and Frankfort horizontal (FH-MPl) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

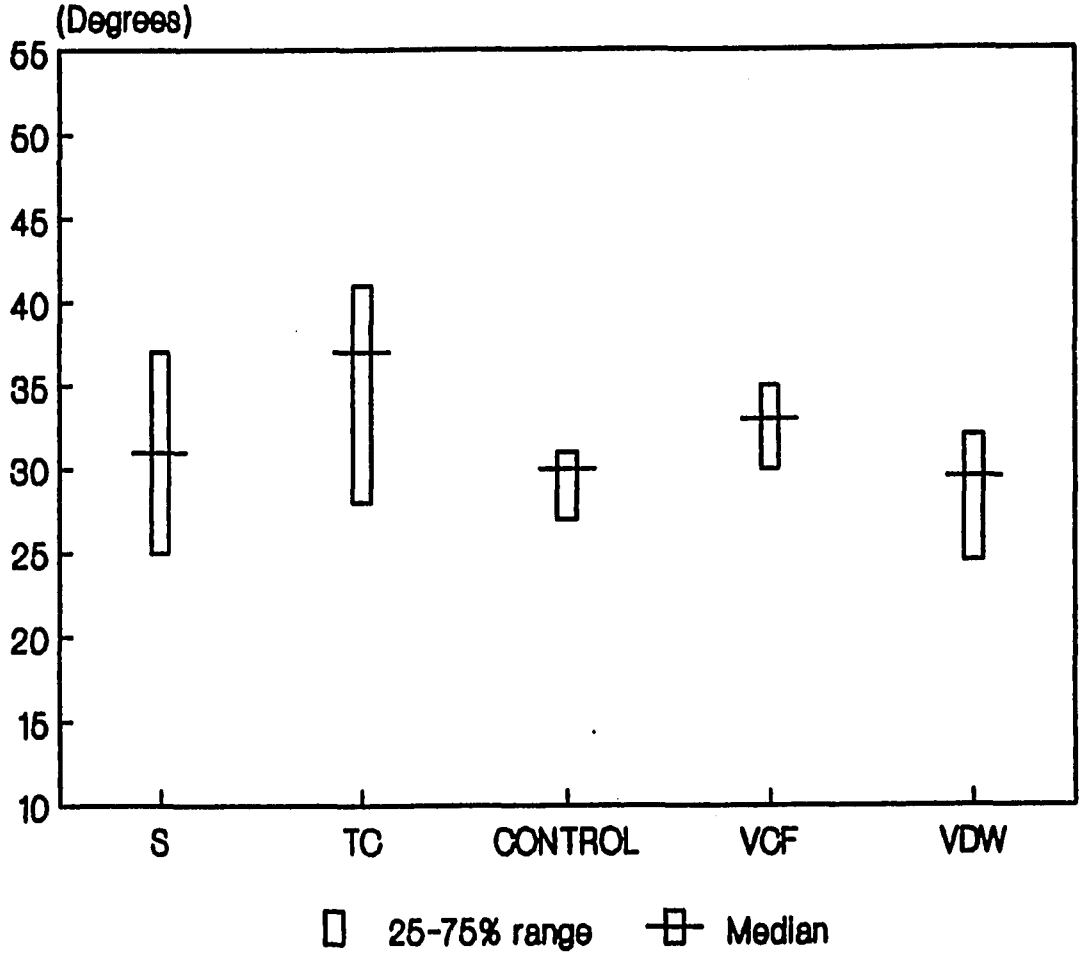


Figure 4.19. Angle formed by mandibular plane and palatal plane (MPl-PPl) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

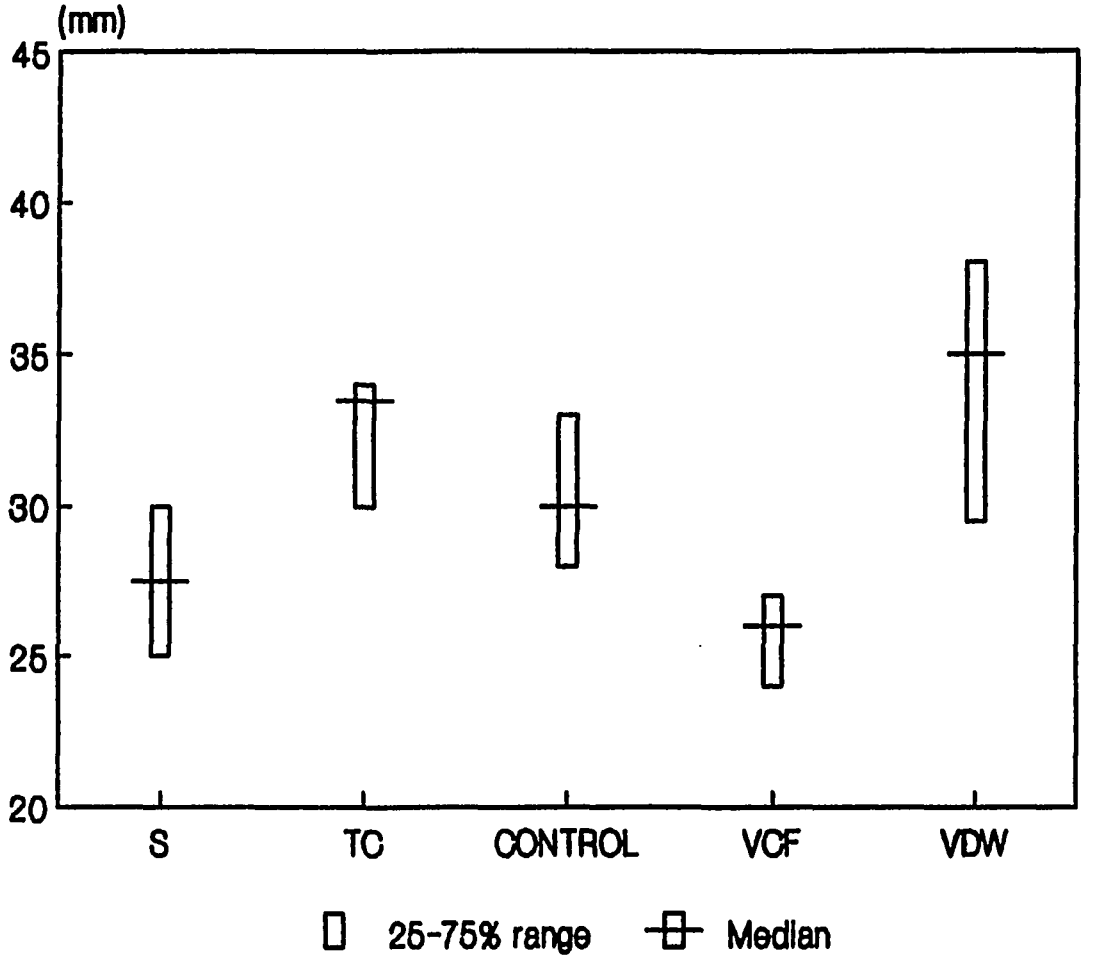


Figure 4.20. Distance from sella to intersection of ramus with posterior cranial base (Sella-Articulare) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

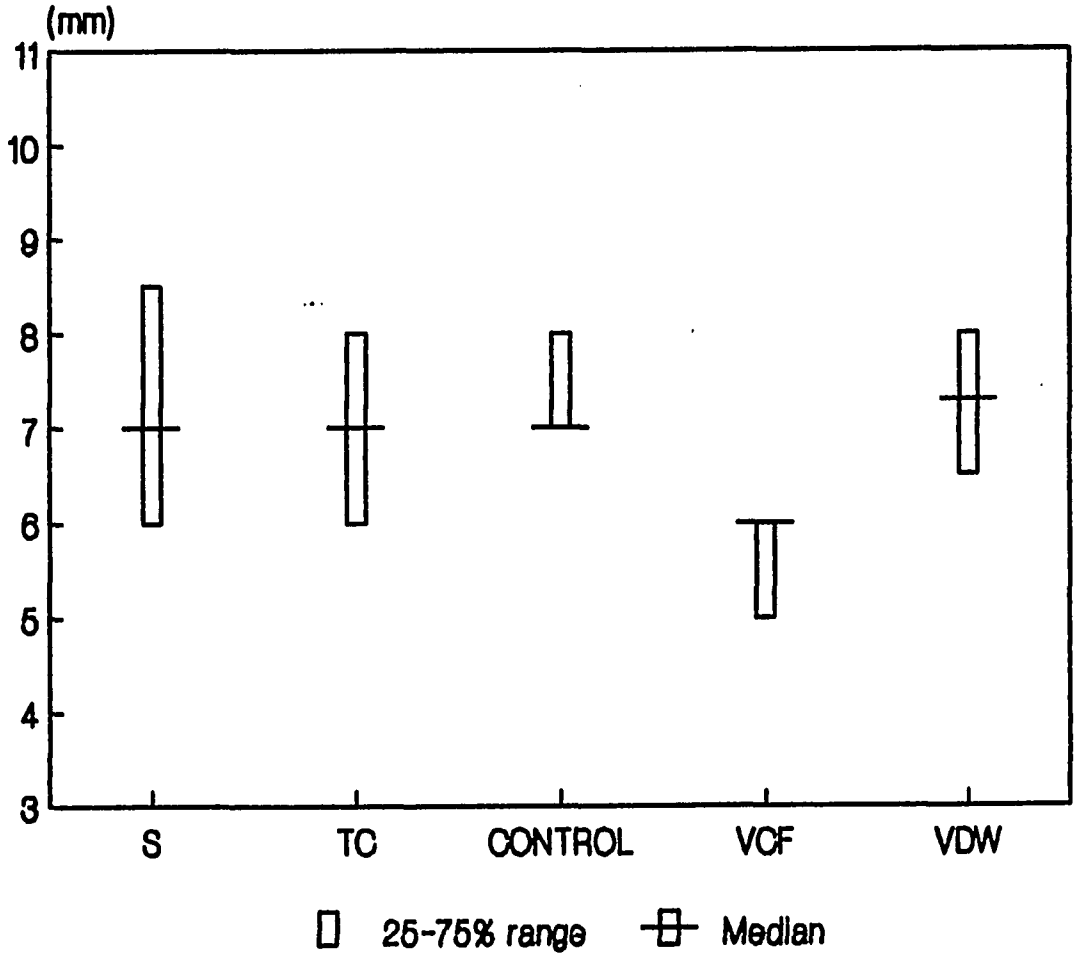


Figure 4.21. Velar thickness (V WDTH) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

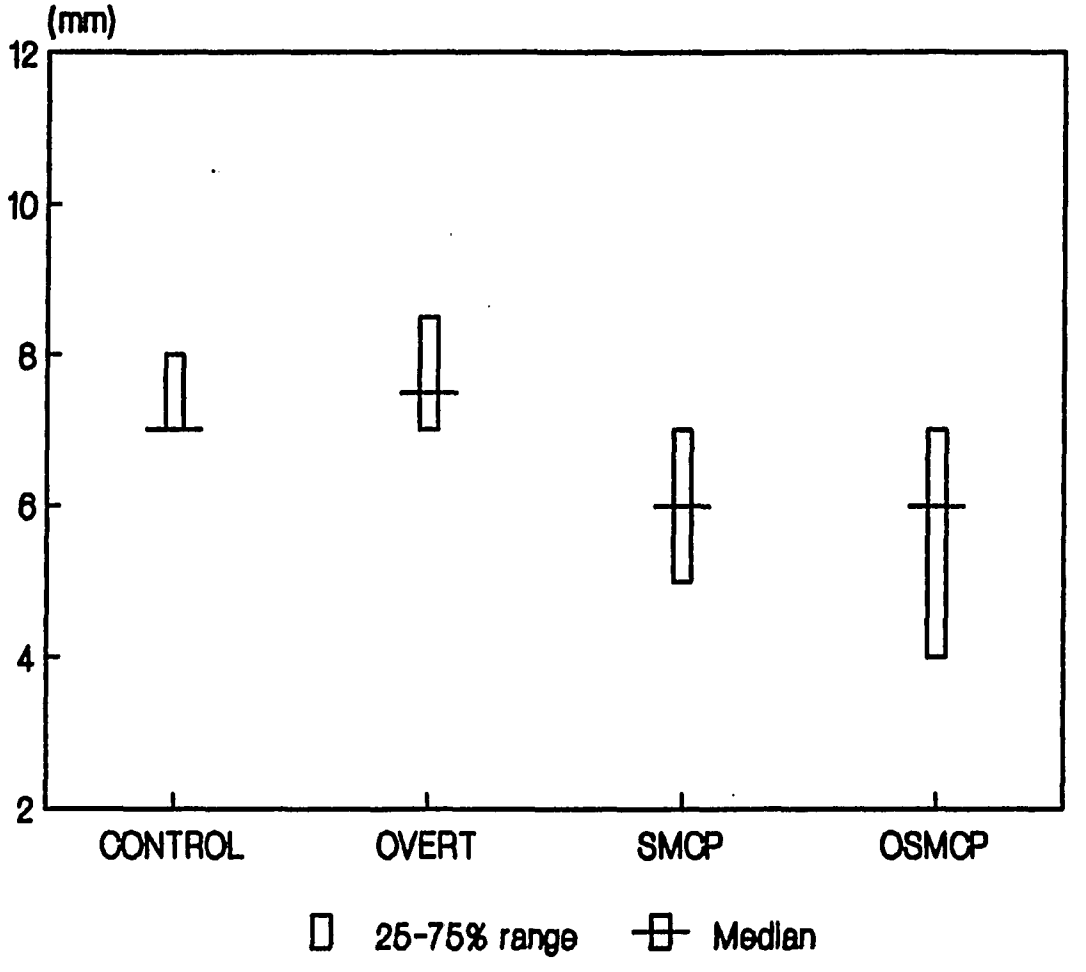


Figure 4.22. Velar thickness (**V WDTH**) measured from lateral cephalometric tracing for control group and according to type of cleft palate.

Overt= repaired overt cleft palate; SMCP= submucous cleft palate; OSMCP= occult submucous cleft palate

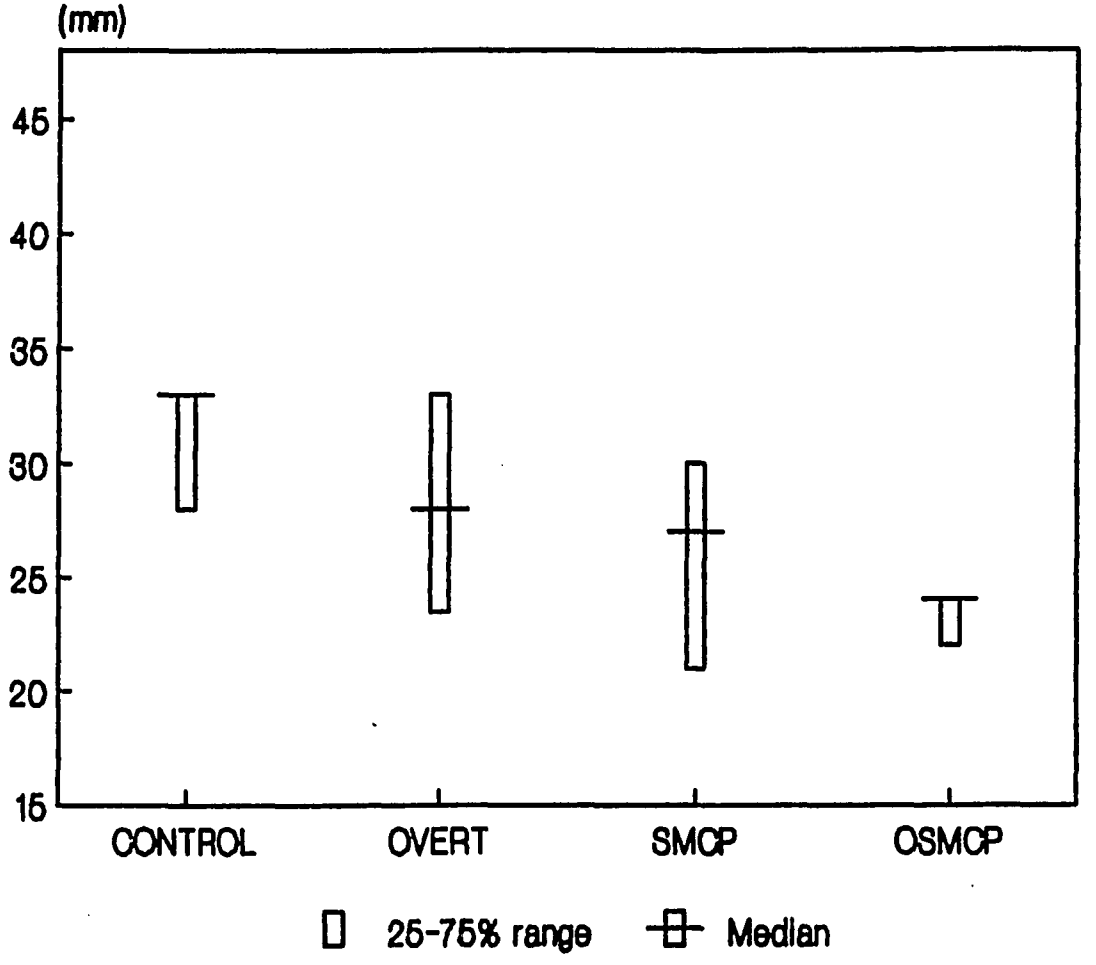


Figure 4.23. Velar length (posterior nasal spine to velar tip: PNS-V) measured from lateral cephalometric tracing for control group and according to type of cleft palate.

Overt= repaired overt cleft palate; SMCP= submucous cleft palate; OSMCP= occult submucous cleft palate

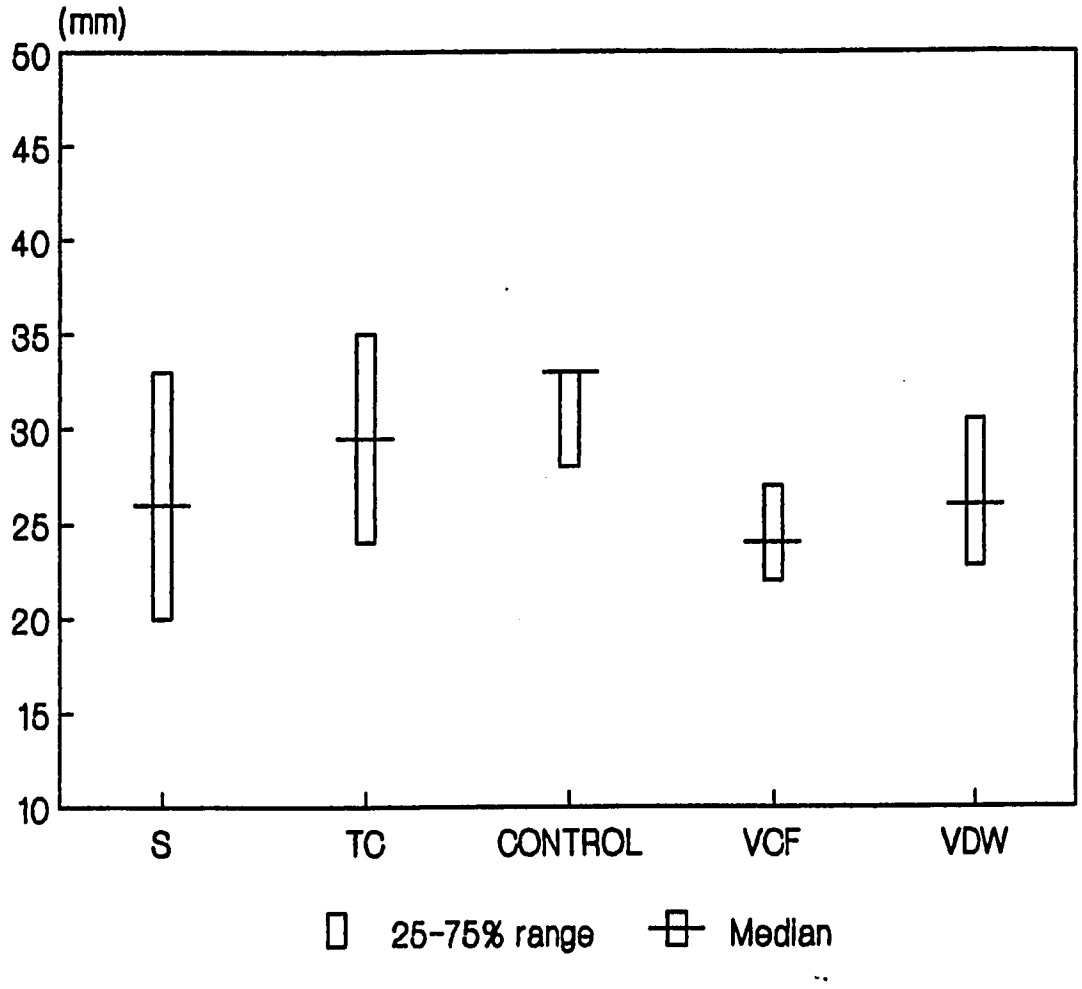


Figure 4.24. Velar length (posterior nasal spine to velar tip: PNS-V) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

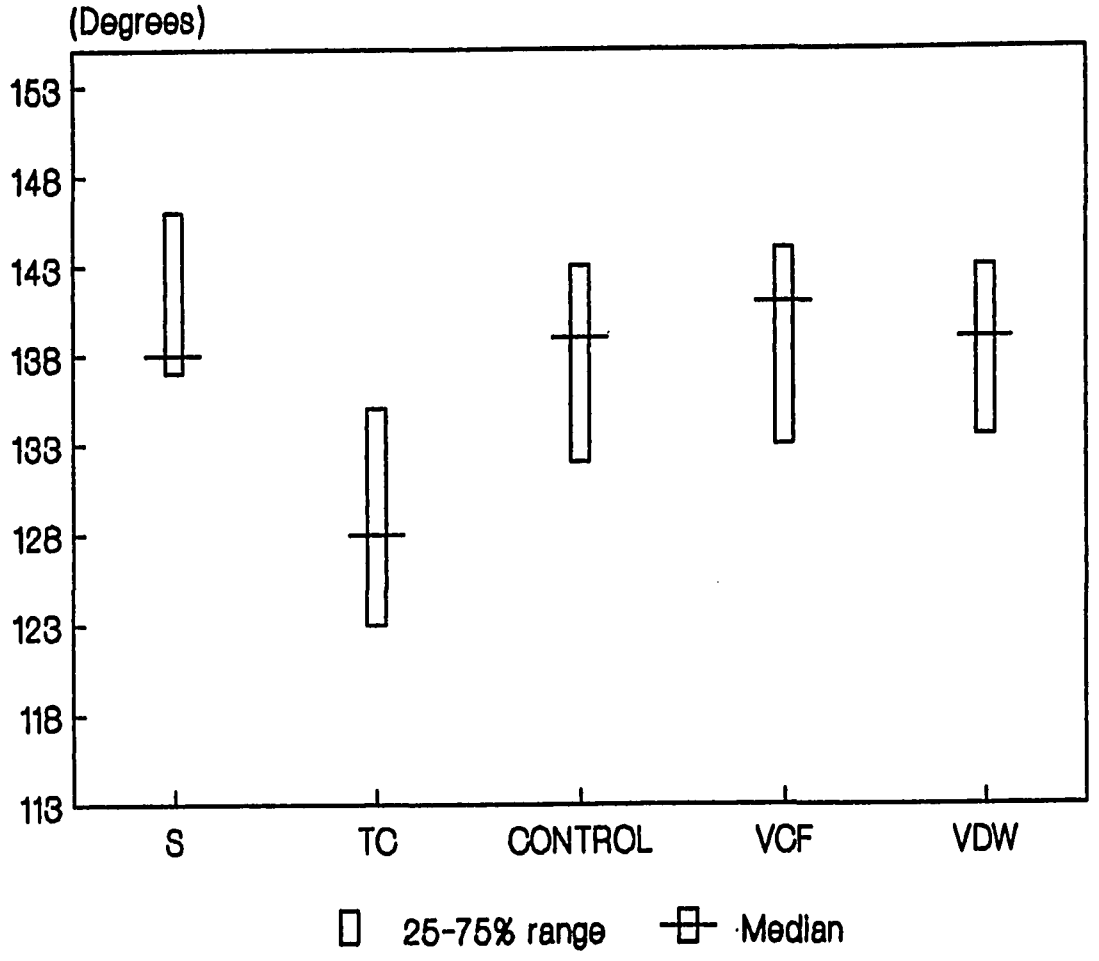


Figure 4.25. Velar drape (angle formed by lines connecting anterior nasal spine-posterior nasal spine-velar tip) (ANS-PNS-V) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

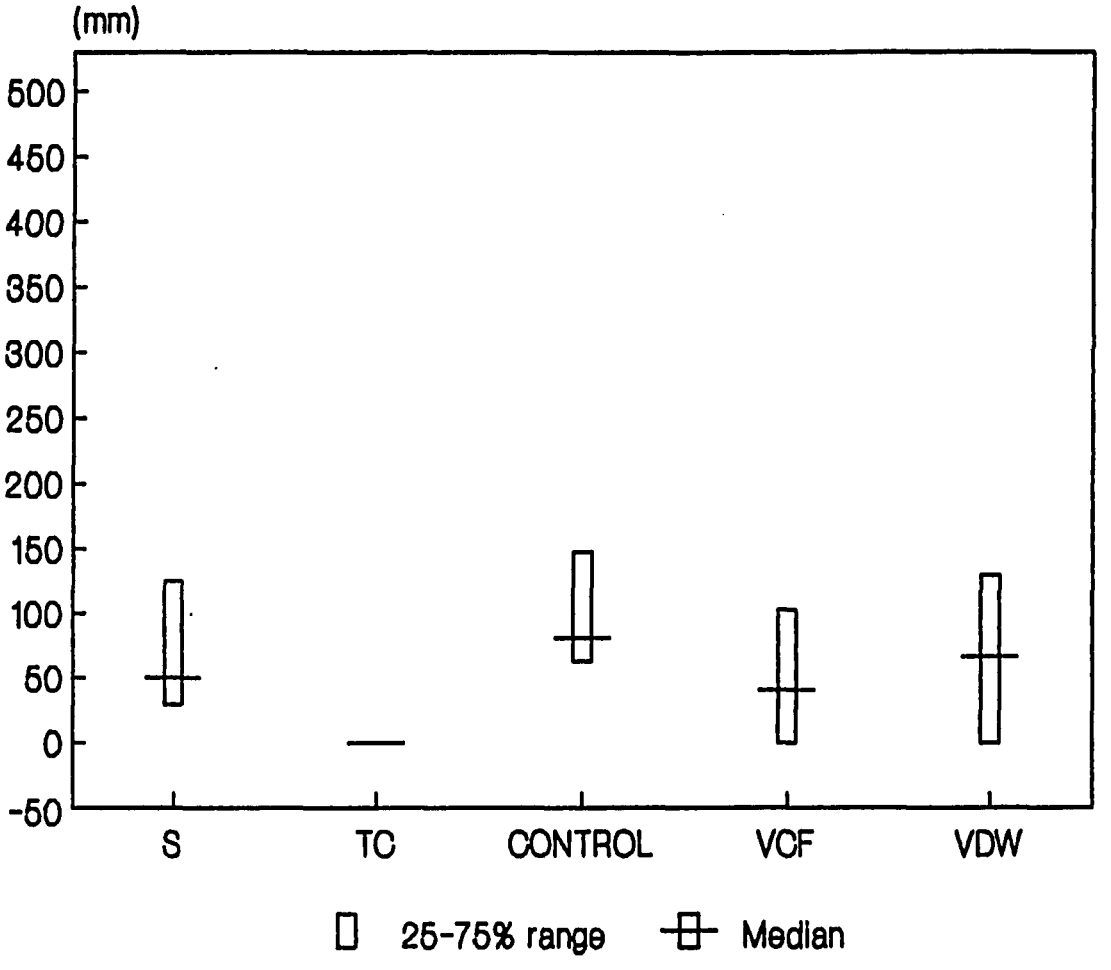


Figure 4.26. Adenoid size (Ad mm) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

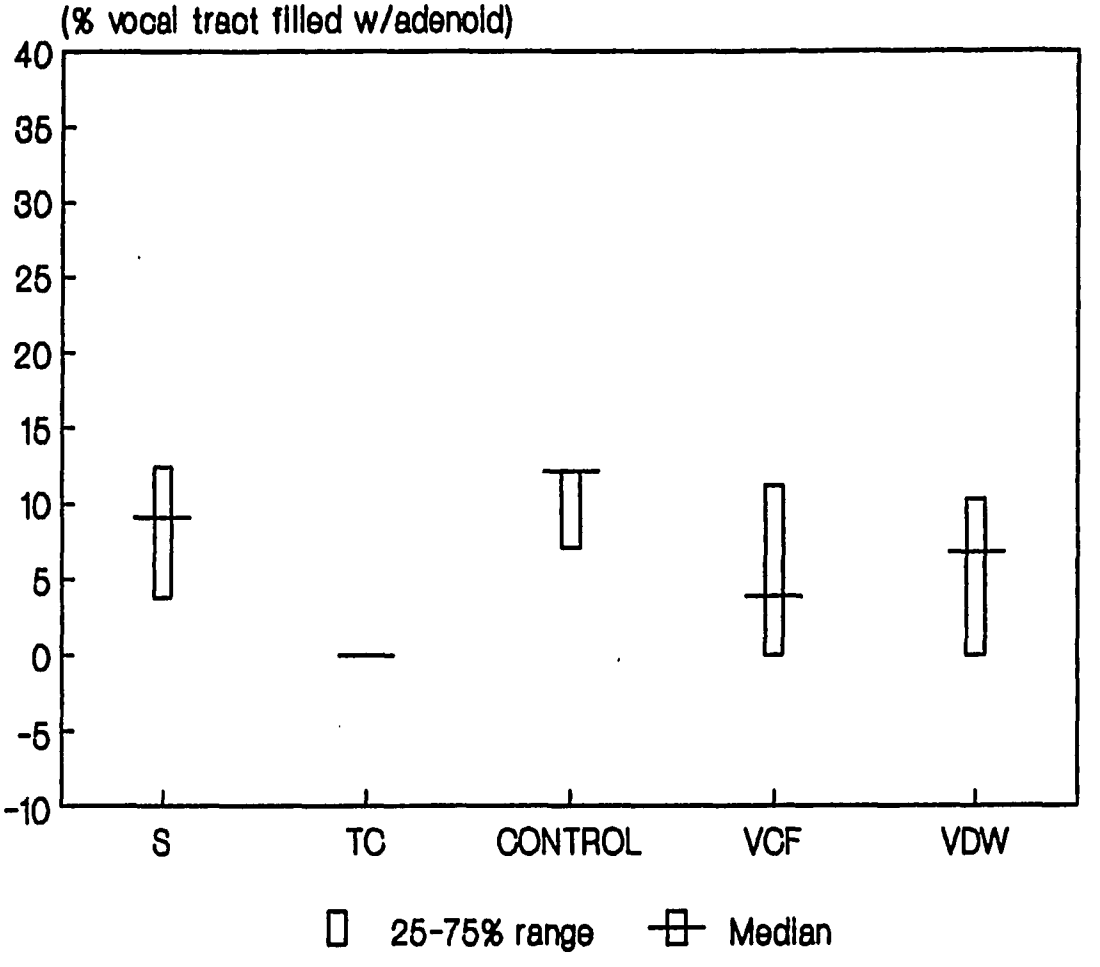
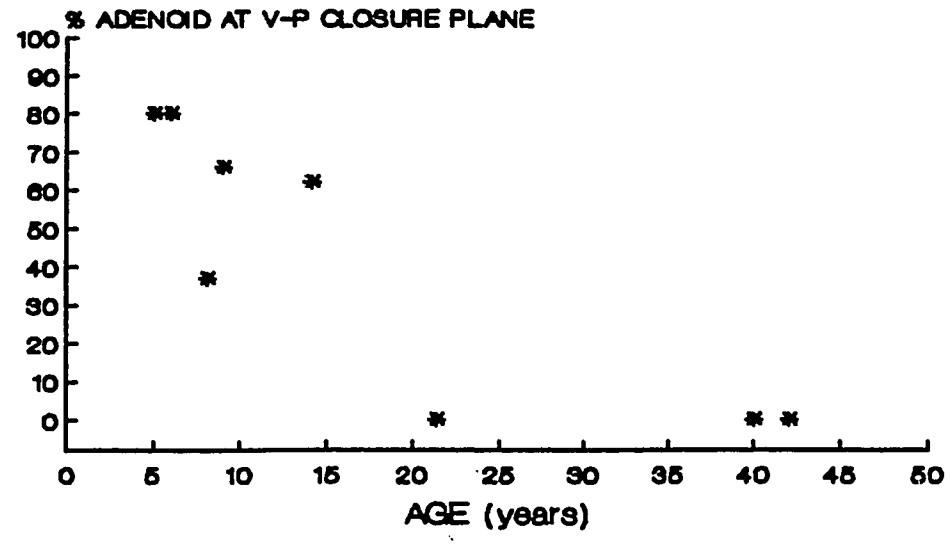
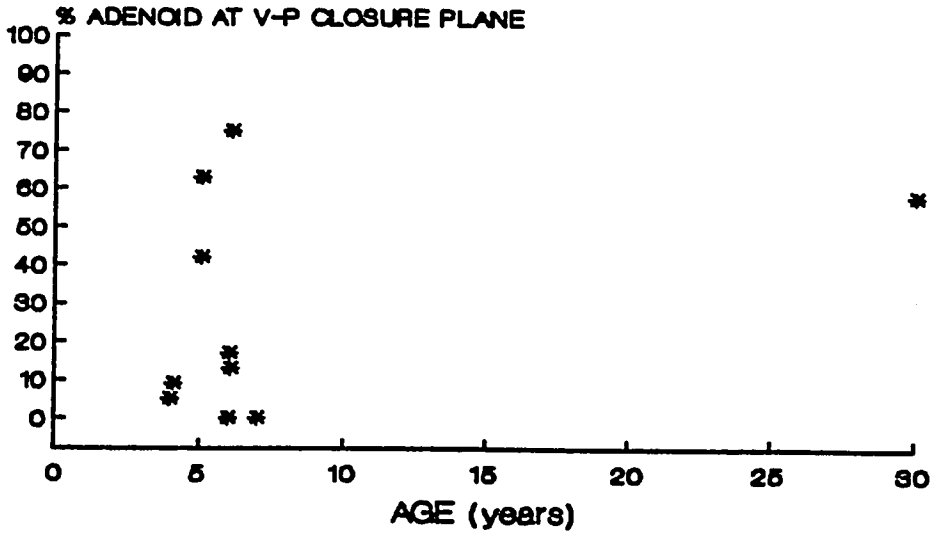


Figure 4.27. Percent of vocal tract occupied by adenoid (PCTVTAD) or relative adenoid size measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).



A. Treacher Collins syndrome



B. velo-cardio-facial syndrome

Figure 4.28. Percent of velopharyngeal closure plane occupied by adenoid measured from nasopharyngoscopic tracing according to age in A) Treacher Collins syndrome, and B) velo-cardio-facial syndrome.

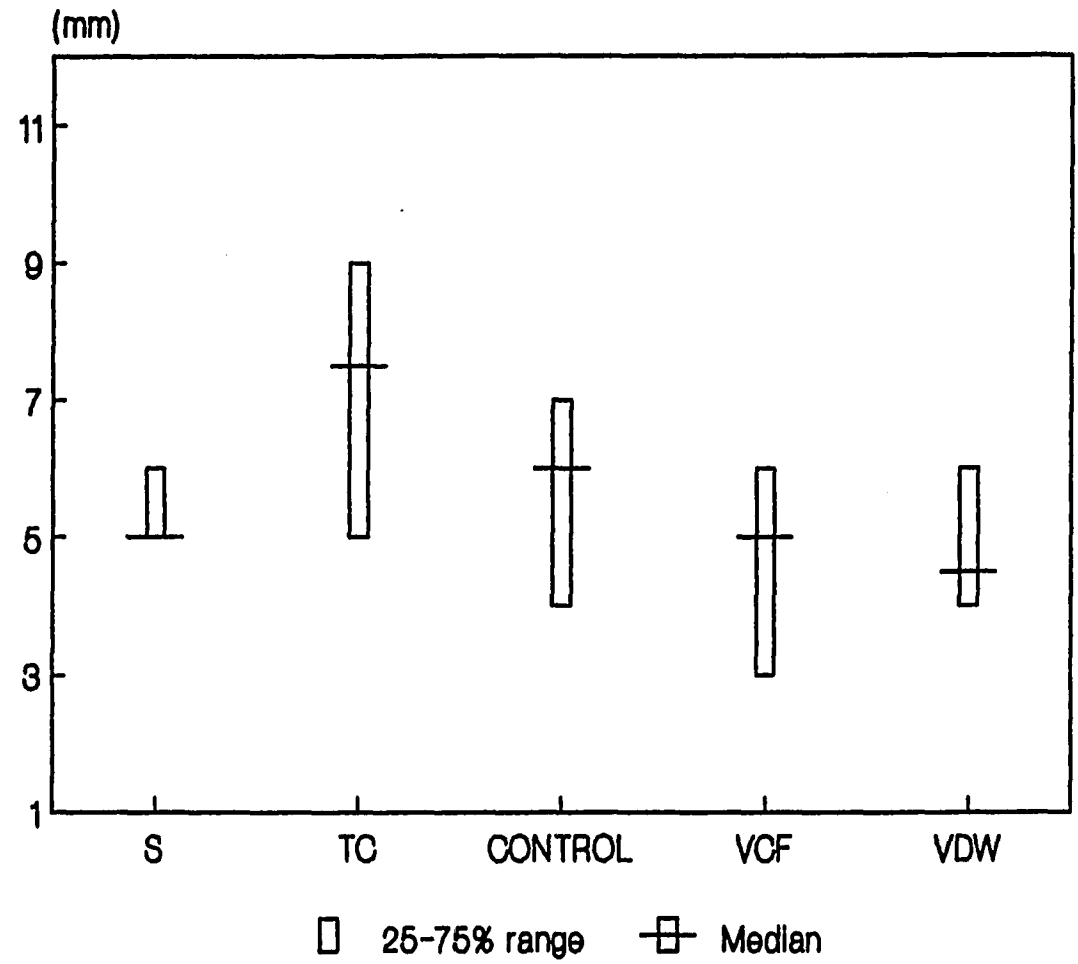


Figure 4.29. Posterior pharyngeal wall thickness at second oropharyngeal level (PPW 4) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

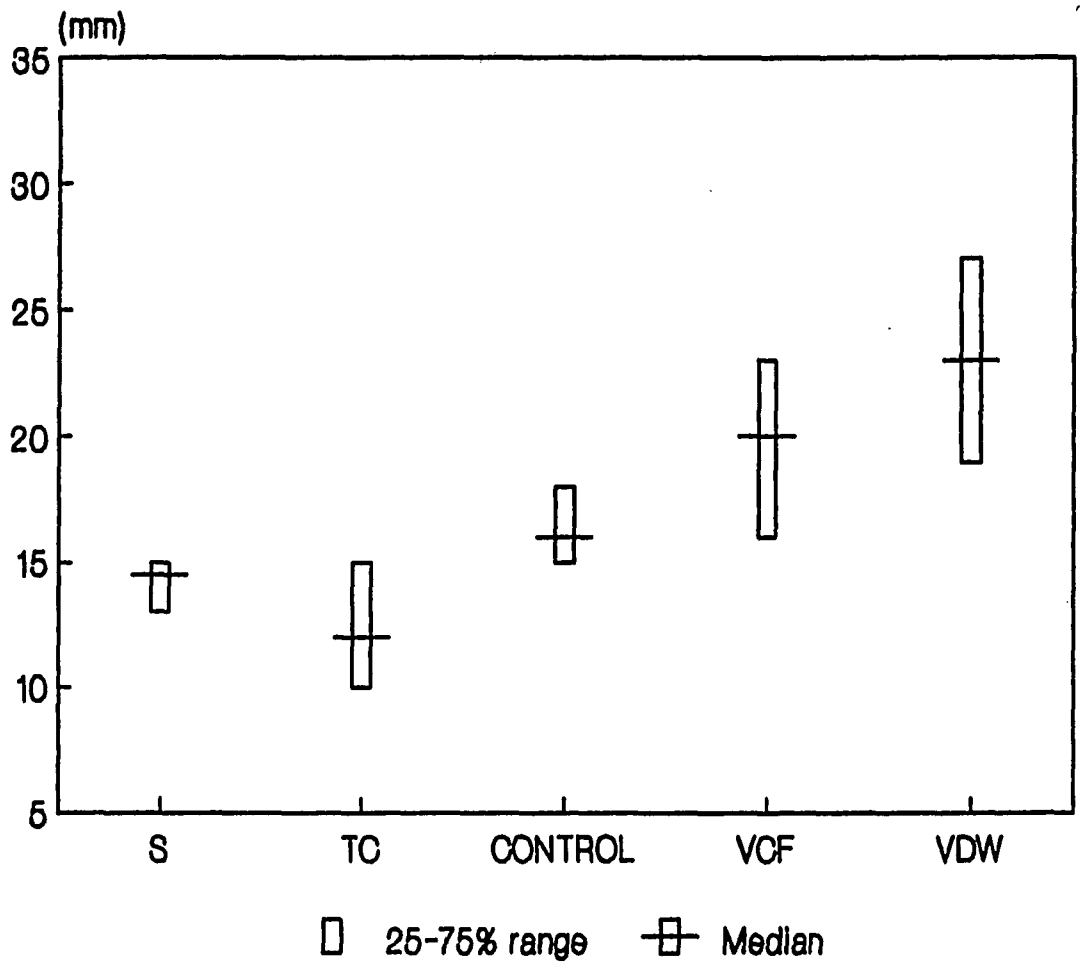


Figure 4.30. Anteroposterior depth of the vocal tract at the velopharyngeal level (Lum 1) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

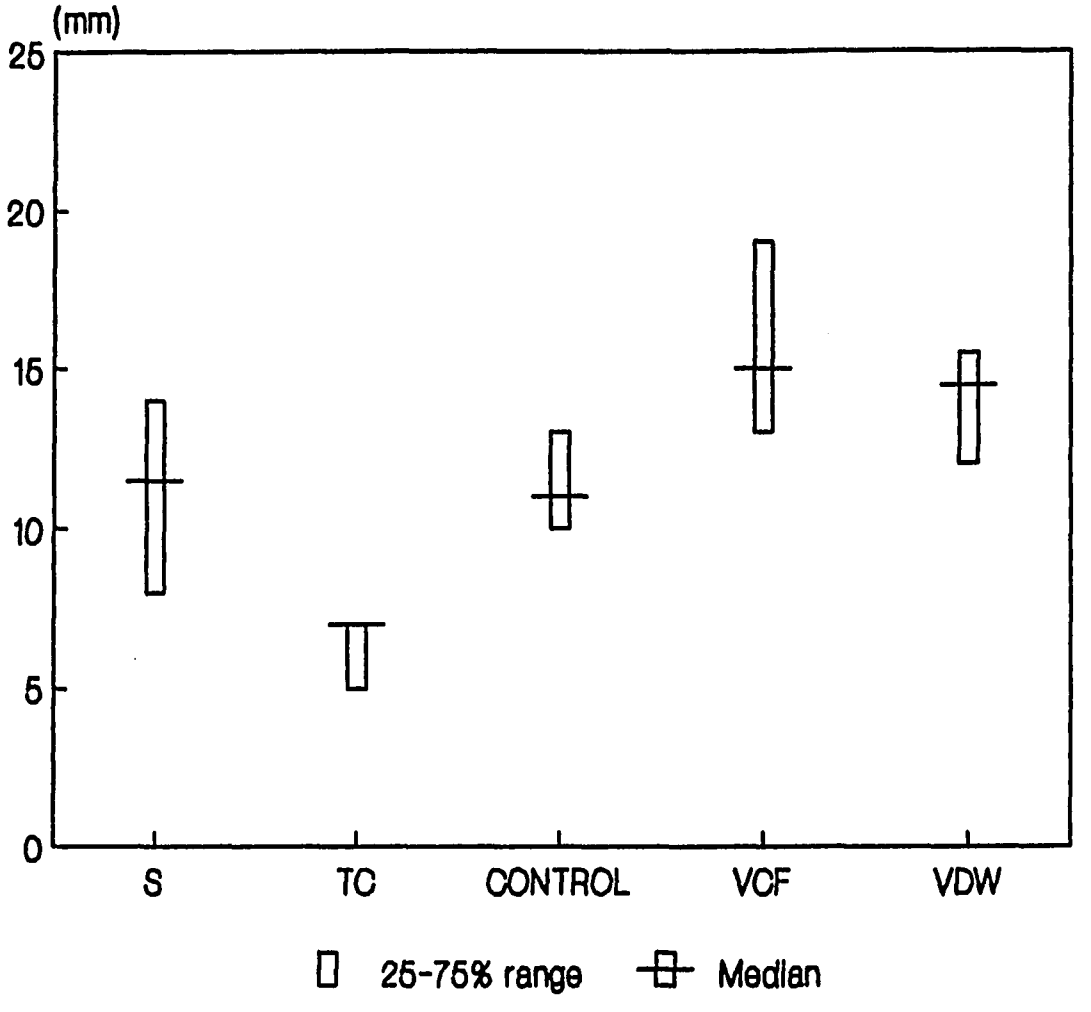


Figure 4.31. Anteroposterior depth of the vocal tract at the oropharyngeal level (Lum 4) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

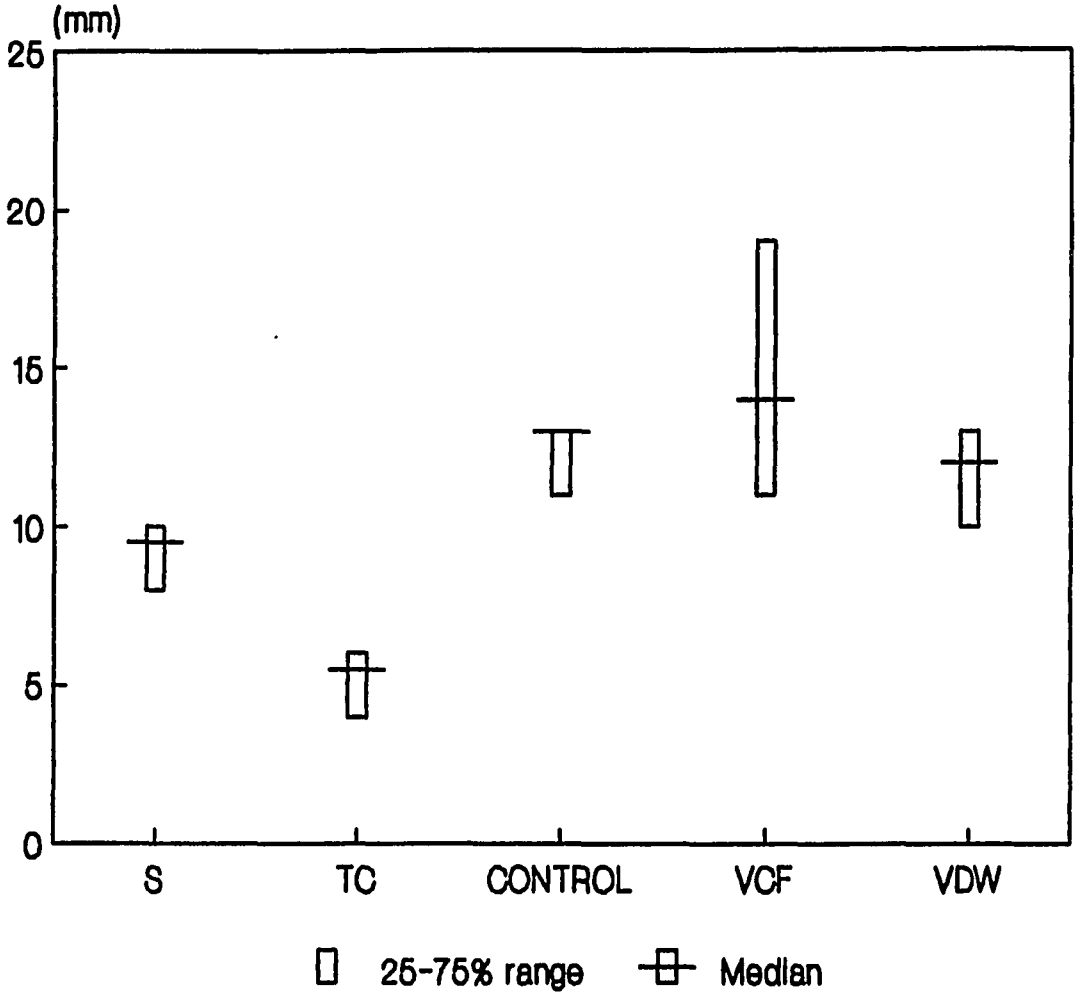


Figure 4.32. Anteroposterior depth of the vocal tract at the hypopharyngeal level (Lum 5) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

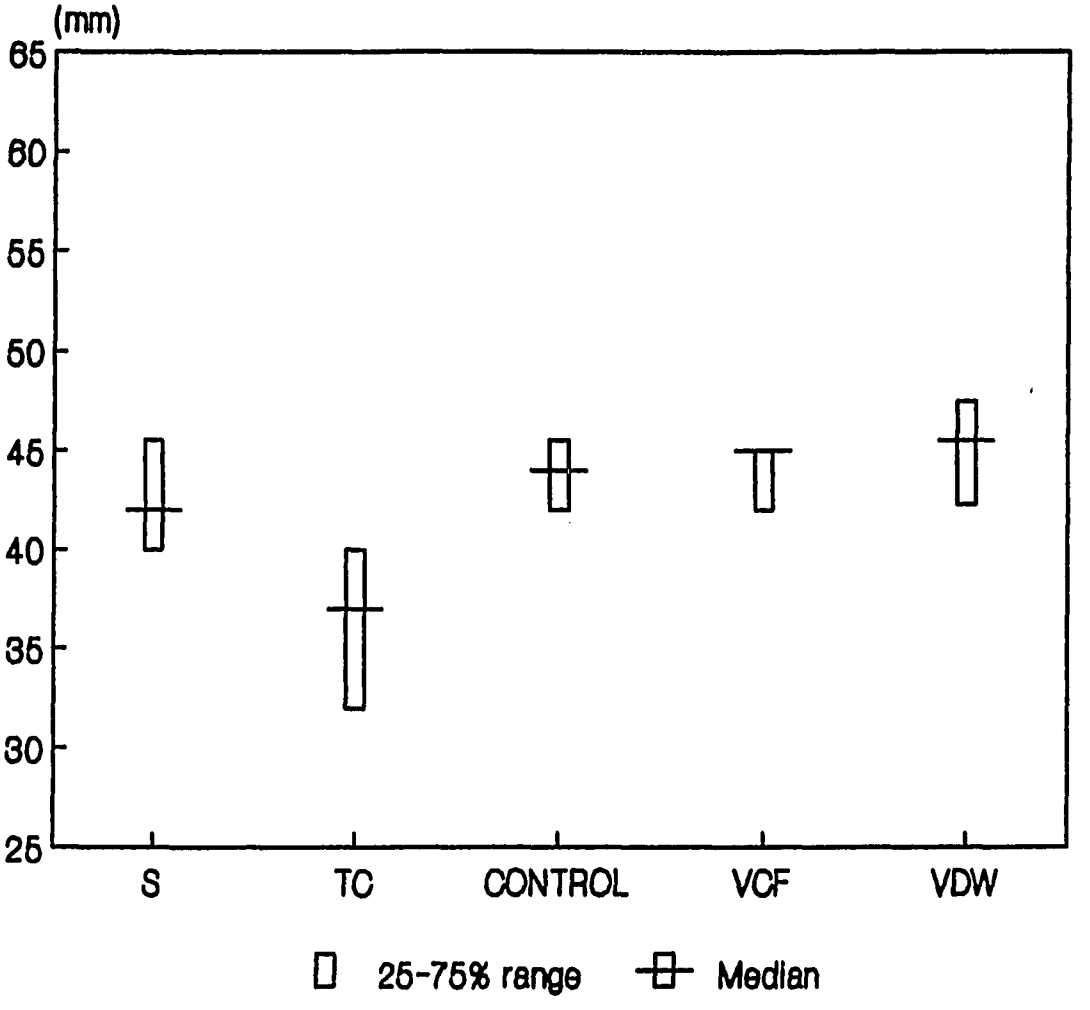


Figure 4.33. Width of the skeletal airway frame from pterygomaxillary fissure to basion (BL WDTH) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

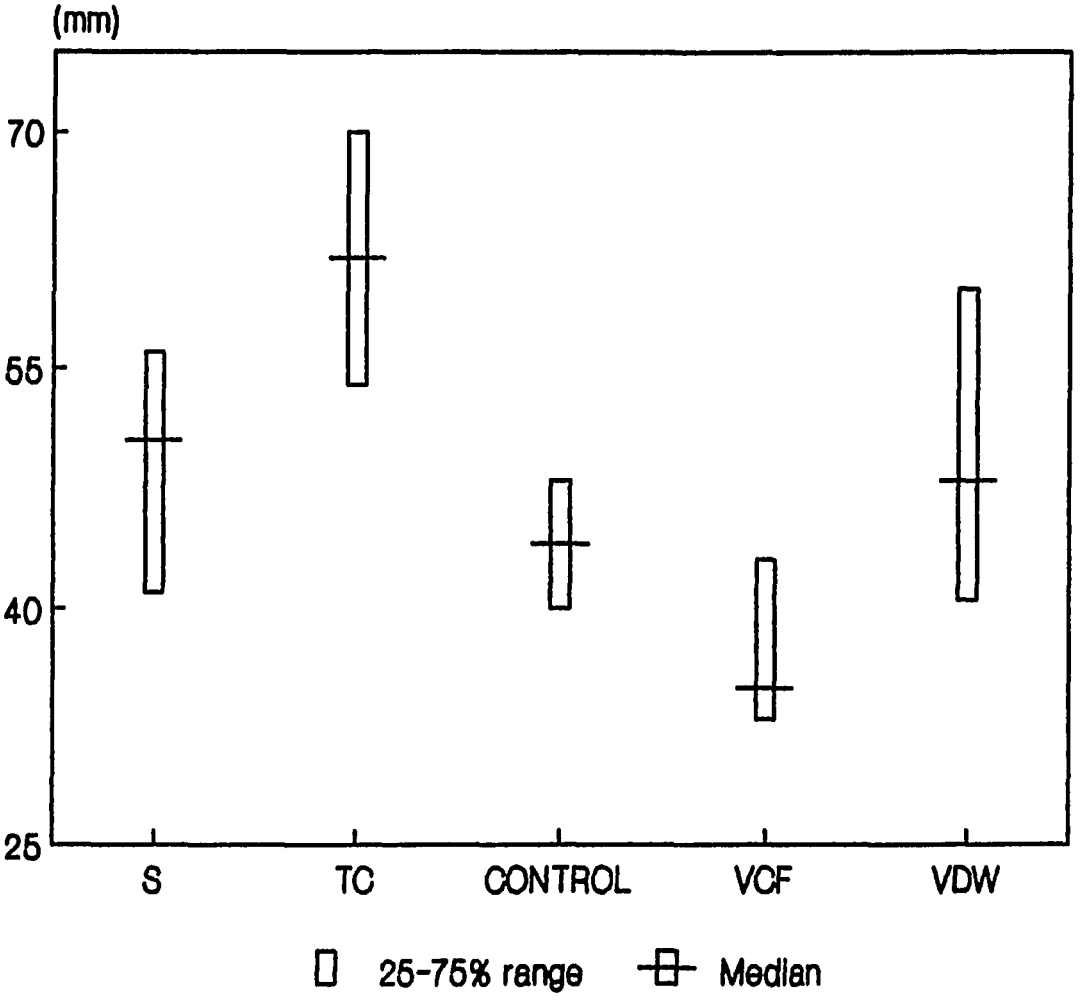


Figure 4.34. Airway height from palatal plane to hyoid plane (PPl-Hy) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

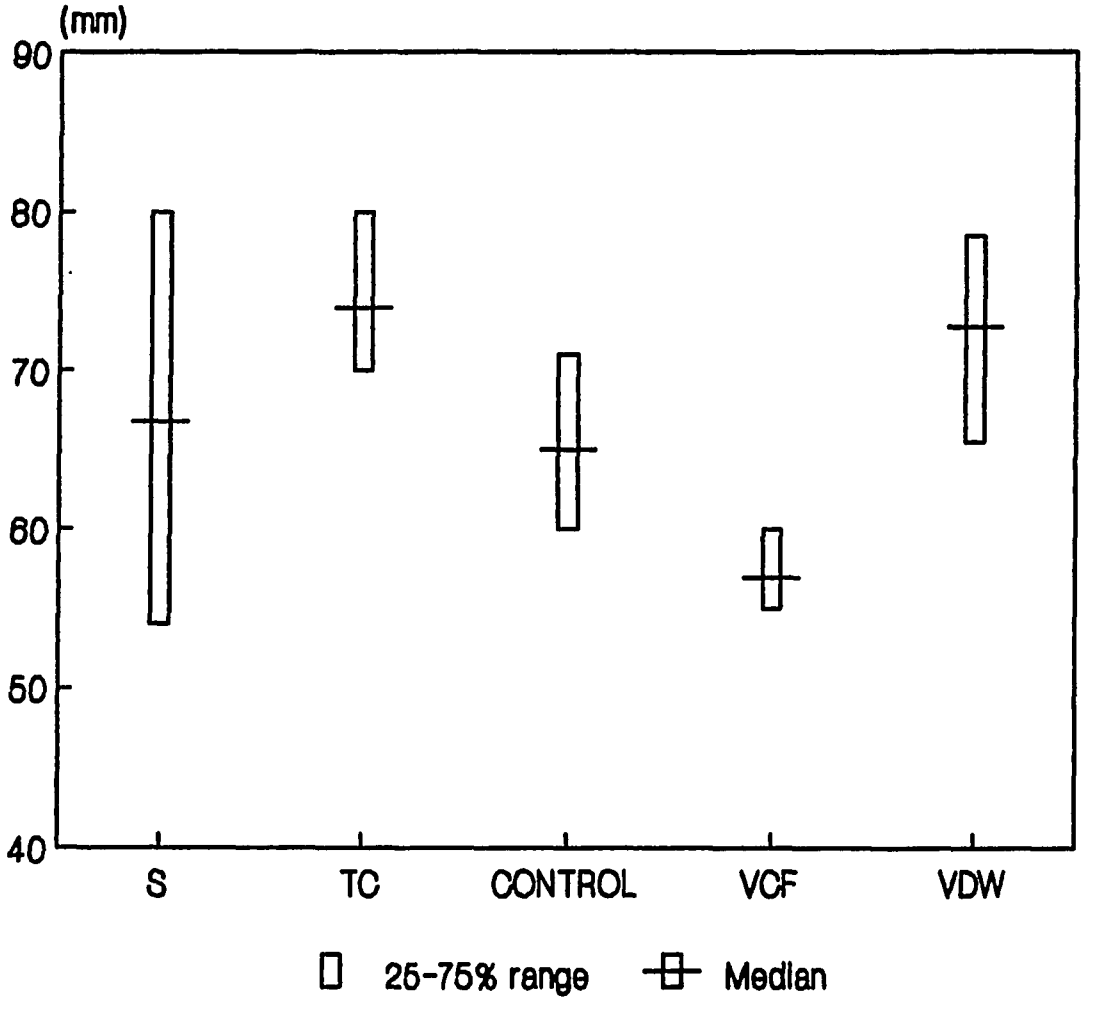


Figure 4.35. Height of the skeletal airway frame from Frankfort horizontal to hyoid plane (Bl HGHT) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

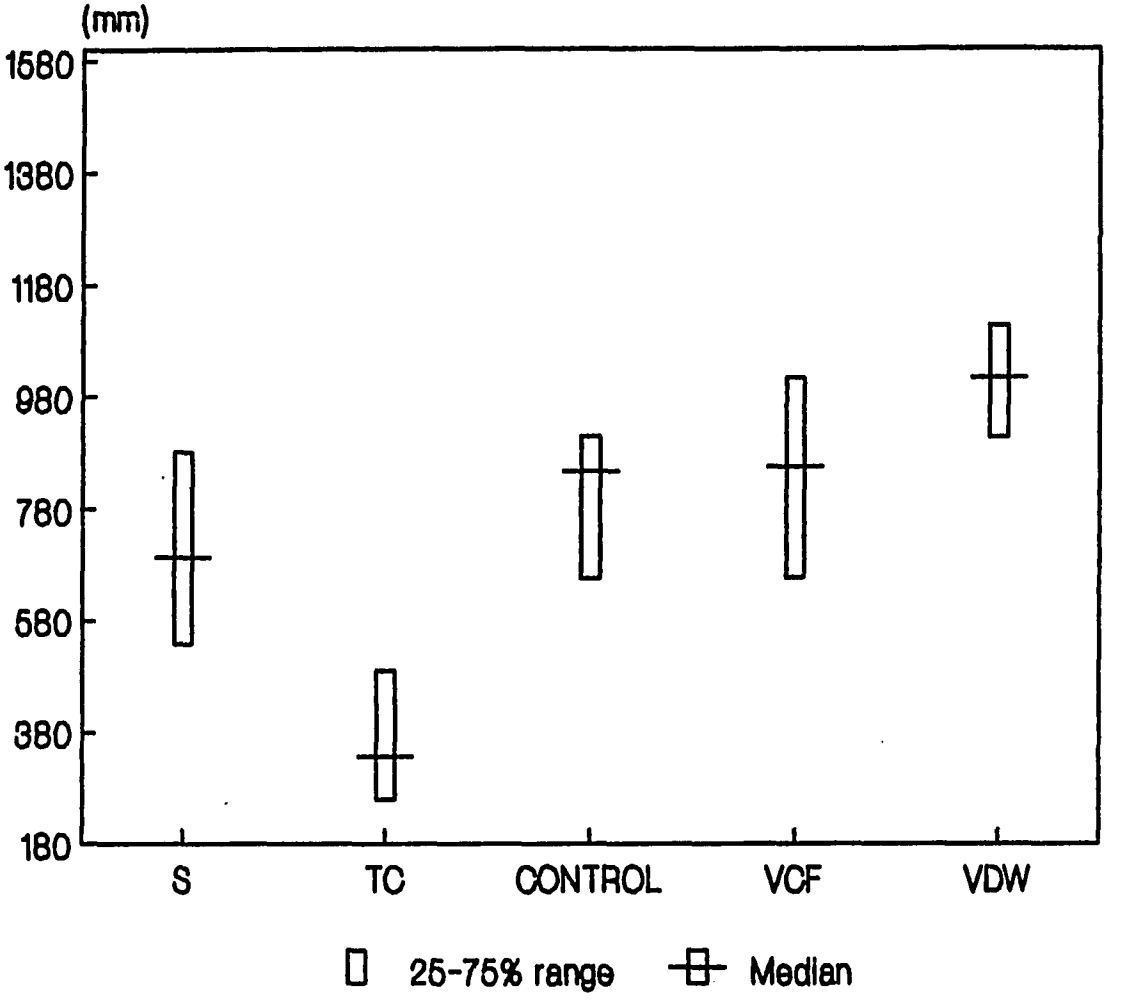


Figure 4.36. Vocal tract area (AW mm) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

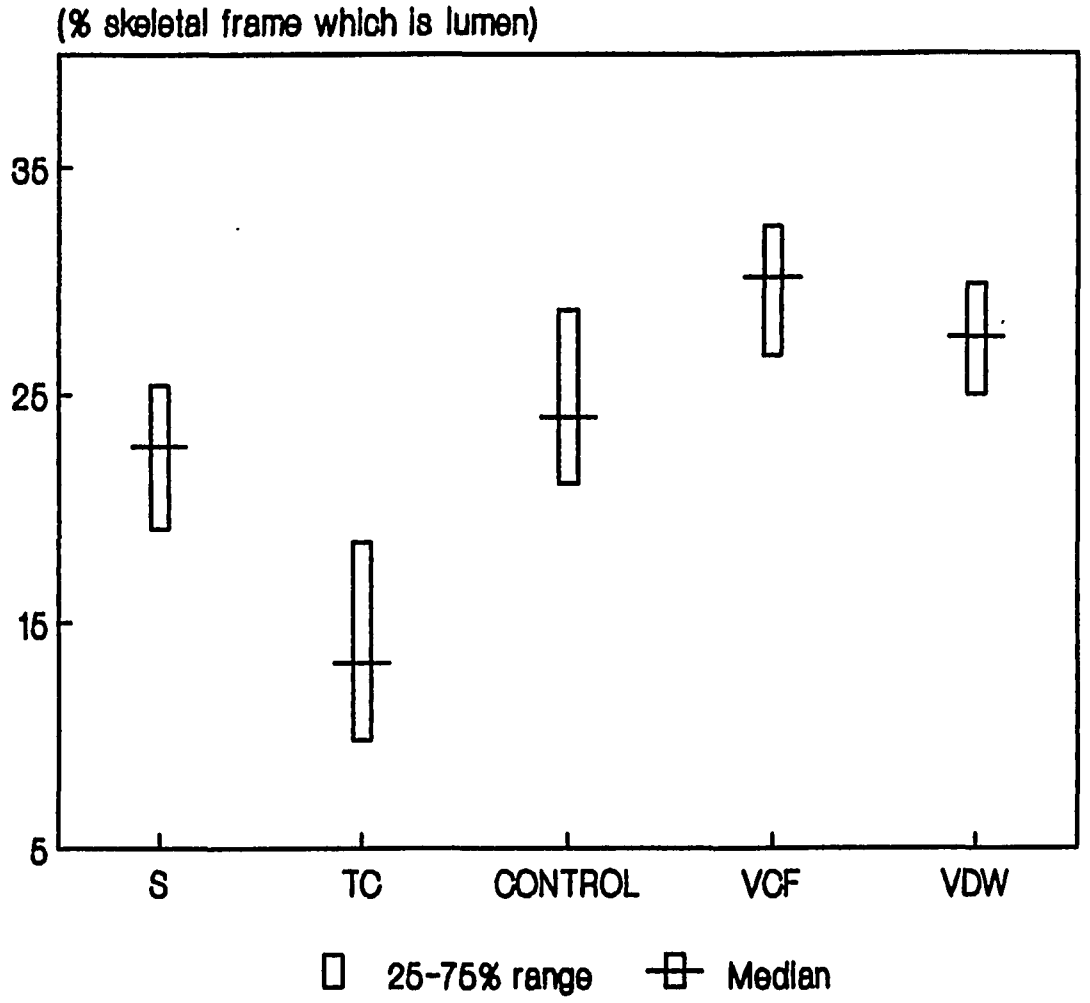


Figure 4.37. Relative vocal tract size: proportion of the airway frame block which is lumen (PCTSKAW) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

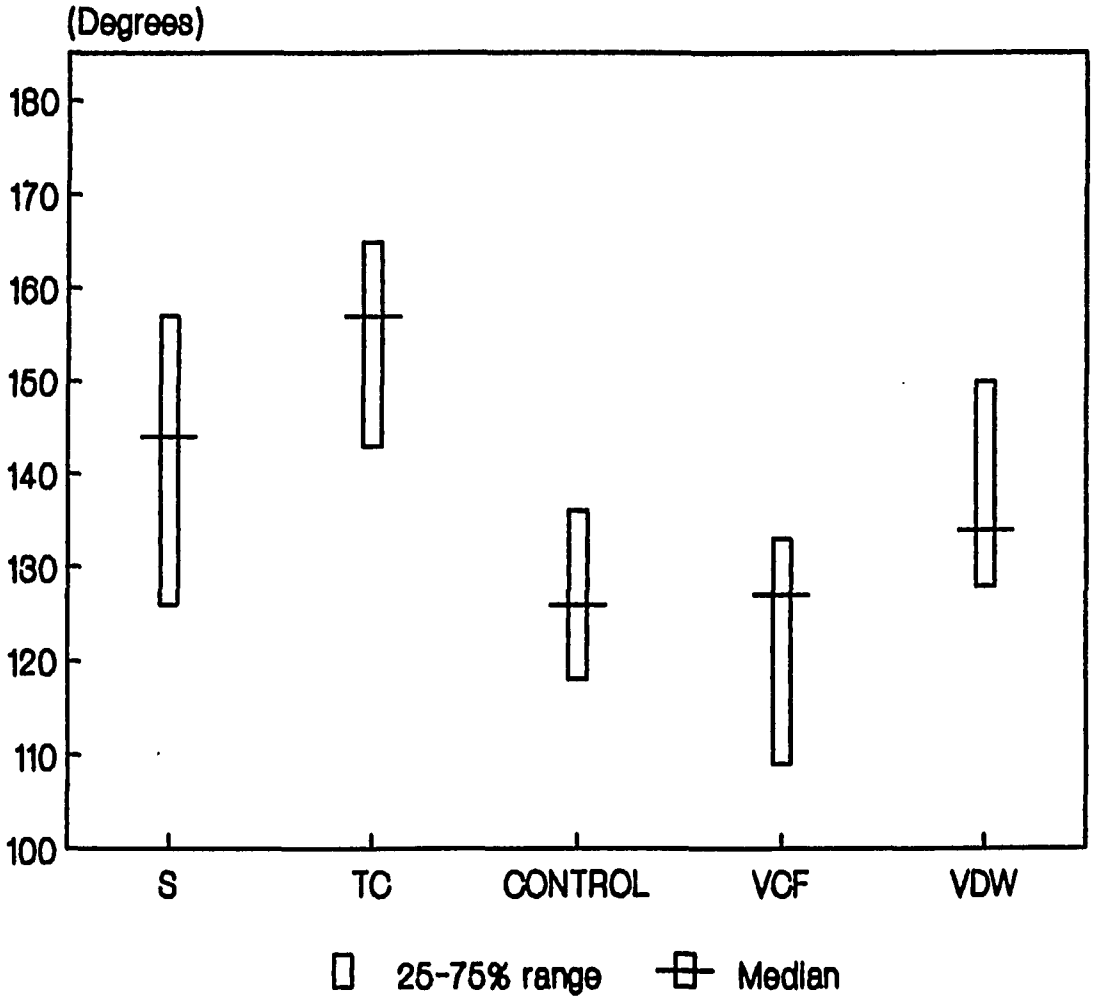


Figure 4.38. Nasopharyngeal angle: angle formed by lines tangent to adenoid and posterior pharyngeal wall (A-PPW) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

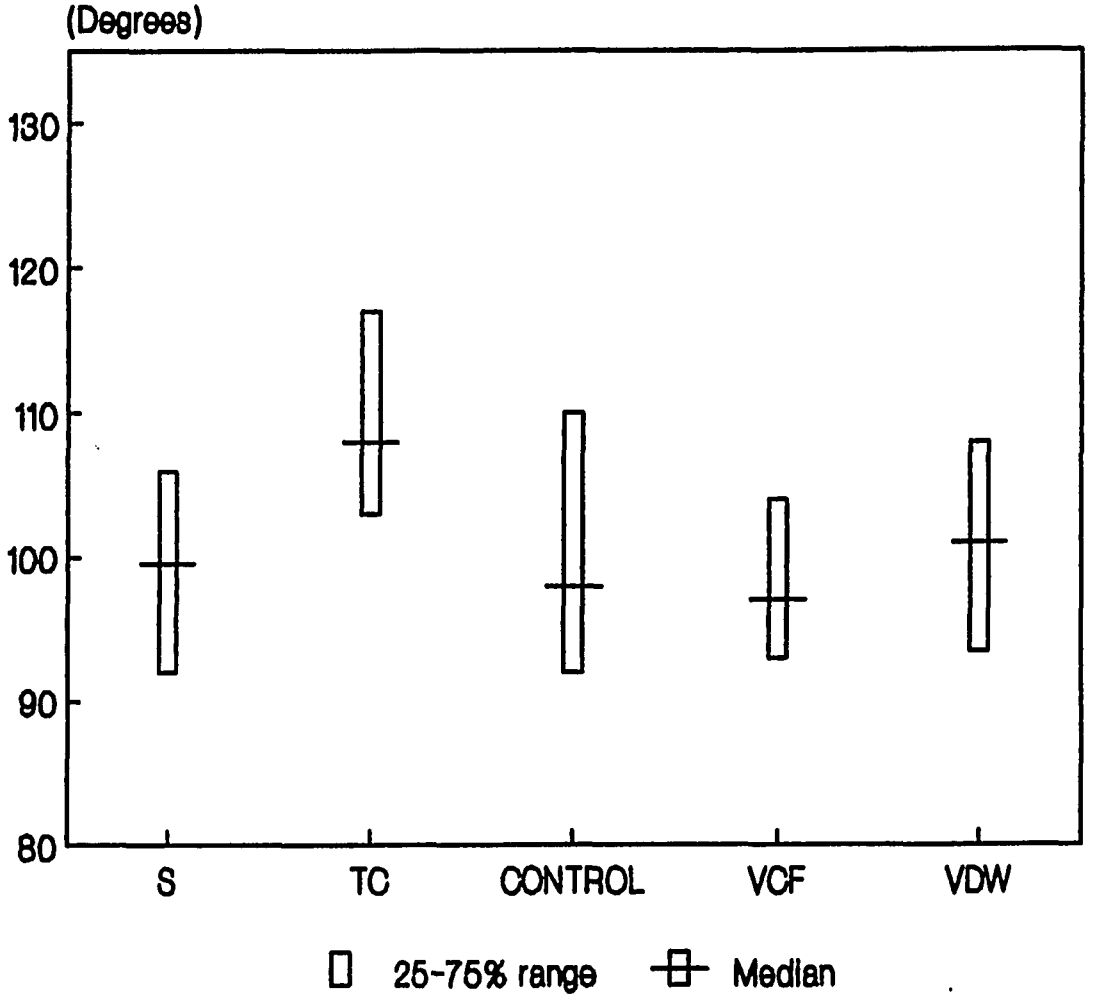


Figure 4.39. Palatopharyngeal angle: angle formed by palatal plane and line tangent to the posterior pharyngeal wall (PPl-PPW) measured from lateral cephalometric tracing for control group, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

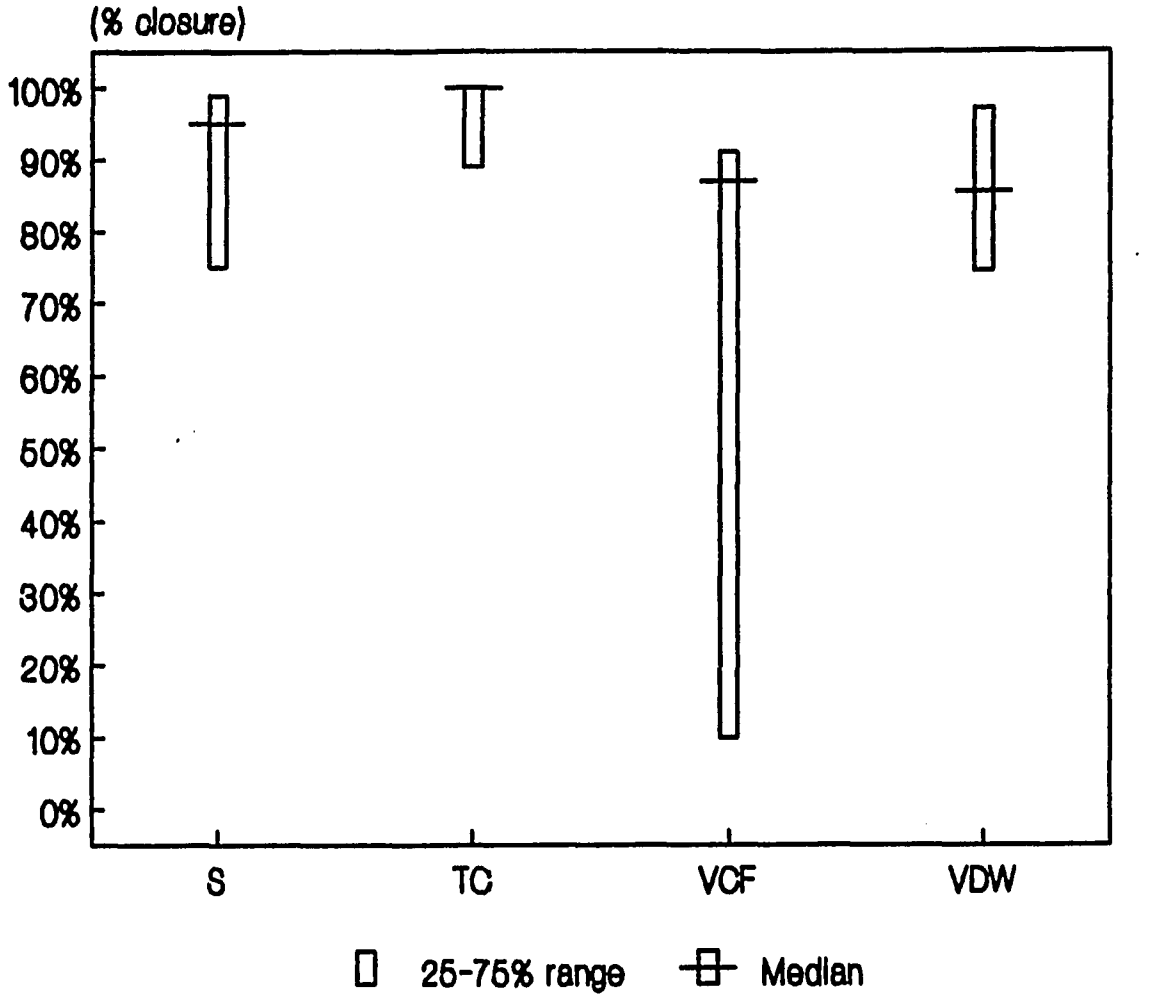


Figure 4.40. Percent velopharyngeal closure achieved measured from nasopharyngoscopic tracing for Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

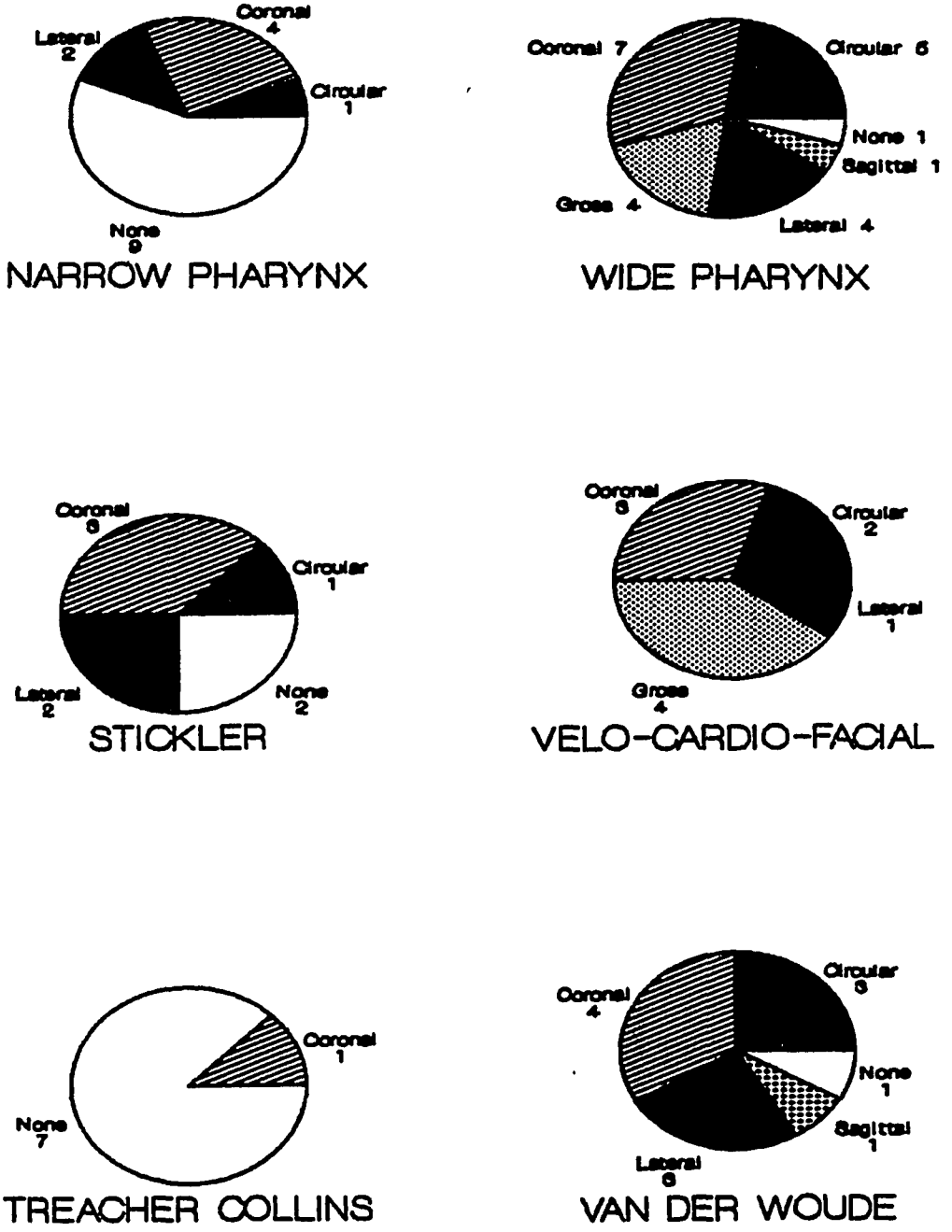


Figure 4.41. Shape of velopharyngeal gap based on nasopharyngoscopic view, according to pharyngeal width and syndrome (NARROW: Stickler, Treacher Collins; WIDE: velo-cardio-facial, van der Woude). Pie charts show number of all subjects in group with each gap shape.

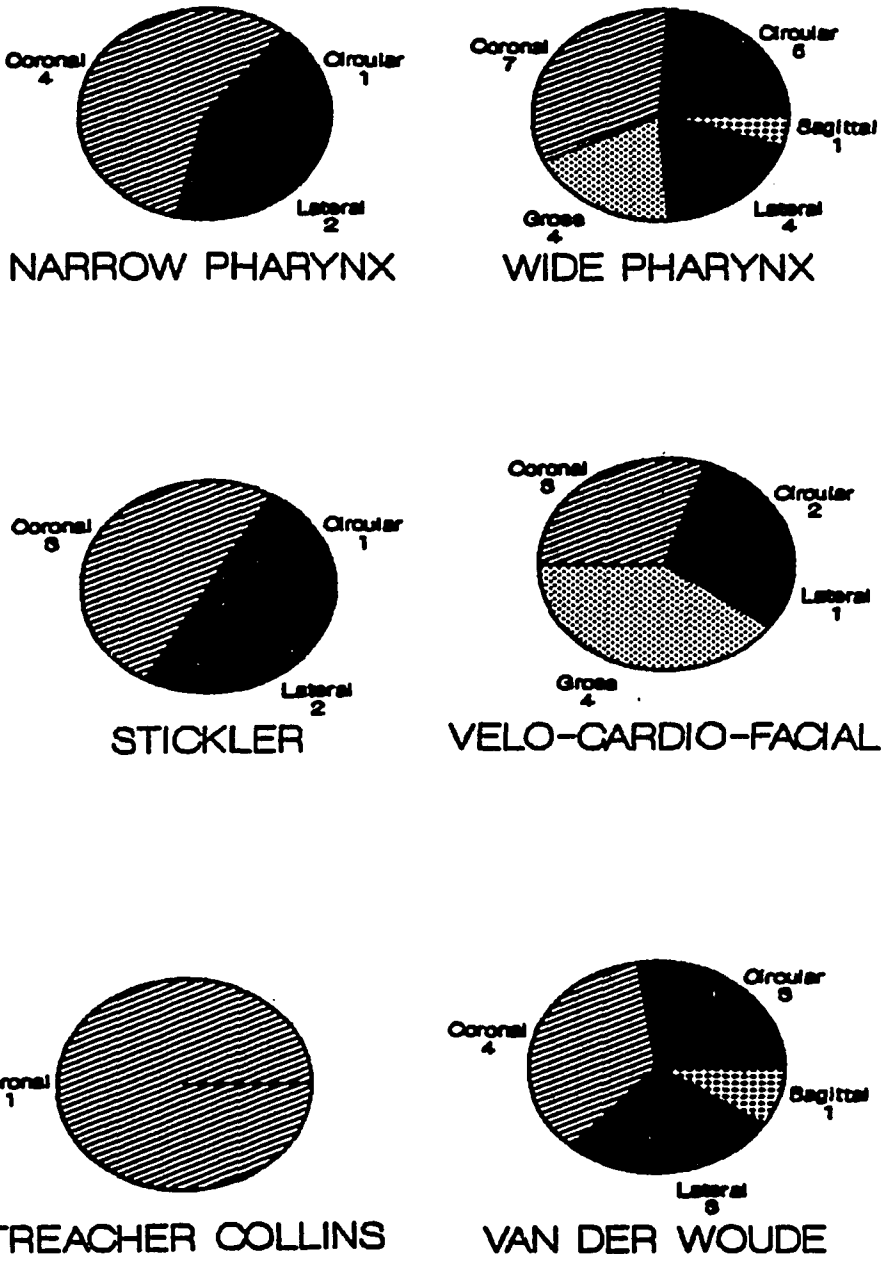


Figure 4.42. Shape of velopharyngeal gap based on nasopharyngoscopic view excluding subjects with no gap, according to pharyngeal width and syndrome (NARROW: Stickler, Treacher Collins; WIDE: velo-cardio-facial, van der Woude). Pie charts show number of all subjects with VPI in group with each gap shape.

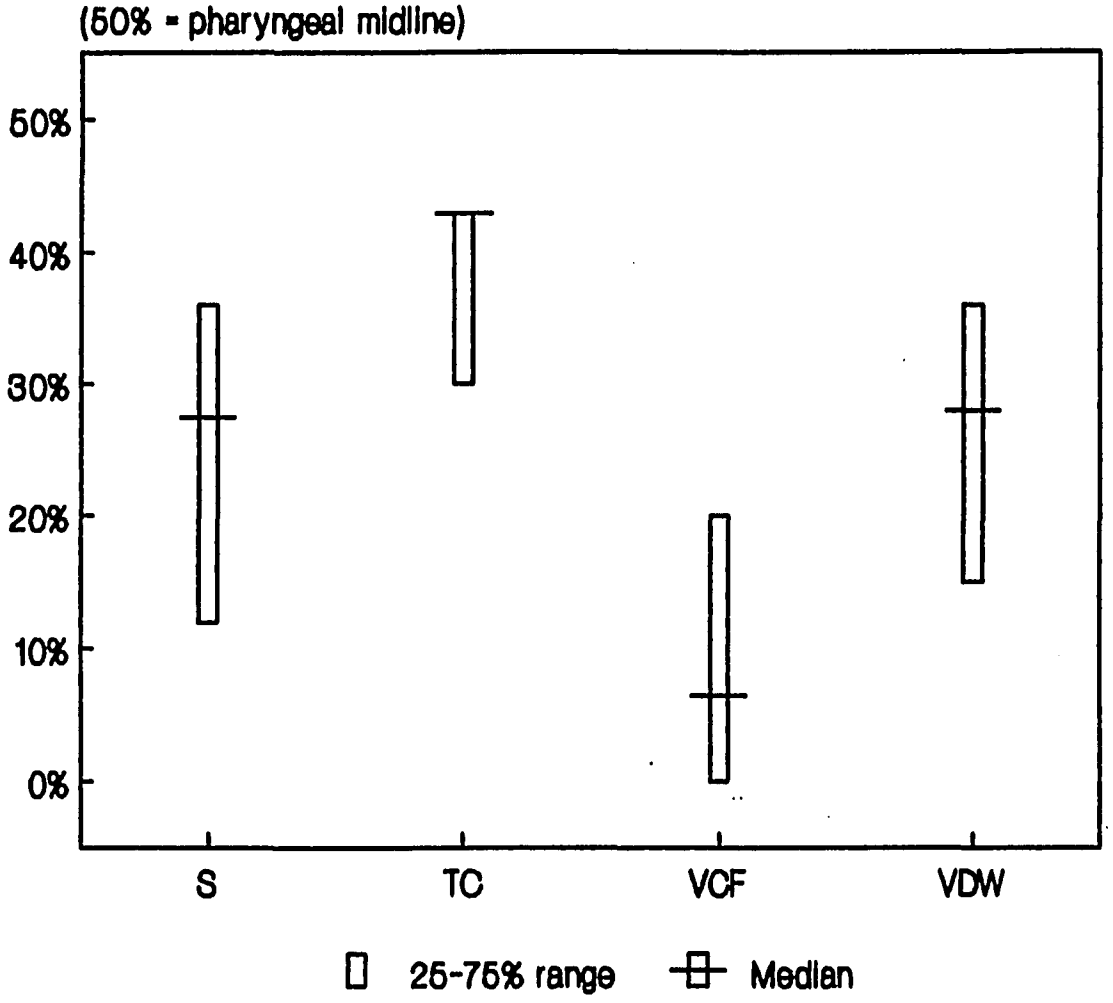


Figure 4.43. Lateral pharyngeal wall (LPW) displacement ratios measured from nasopharyngoscopic tracing for Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der woude syndrome (VDW). Ratios represent percent of pharynx traversed by right LPW

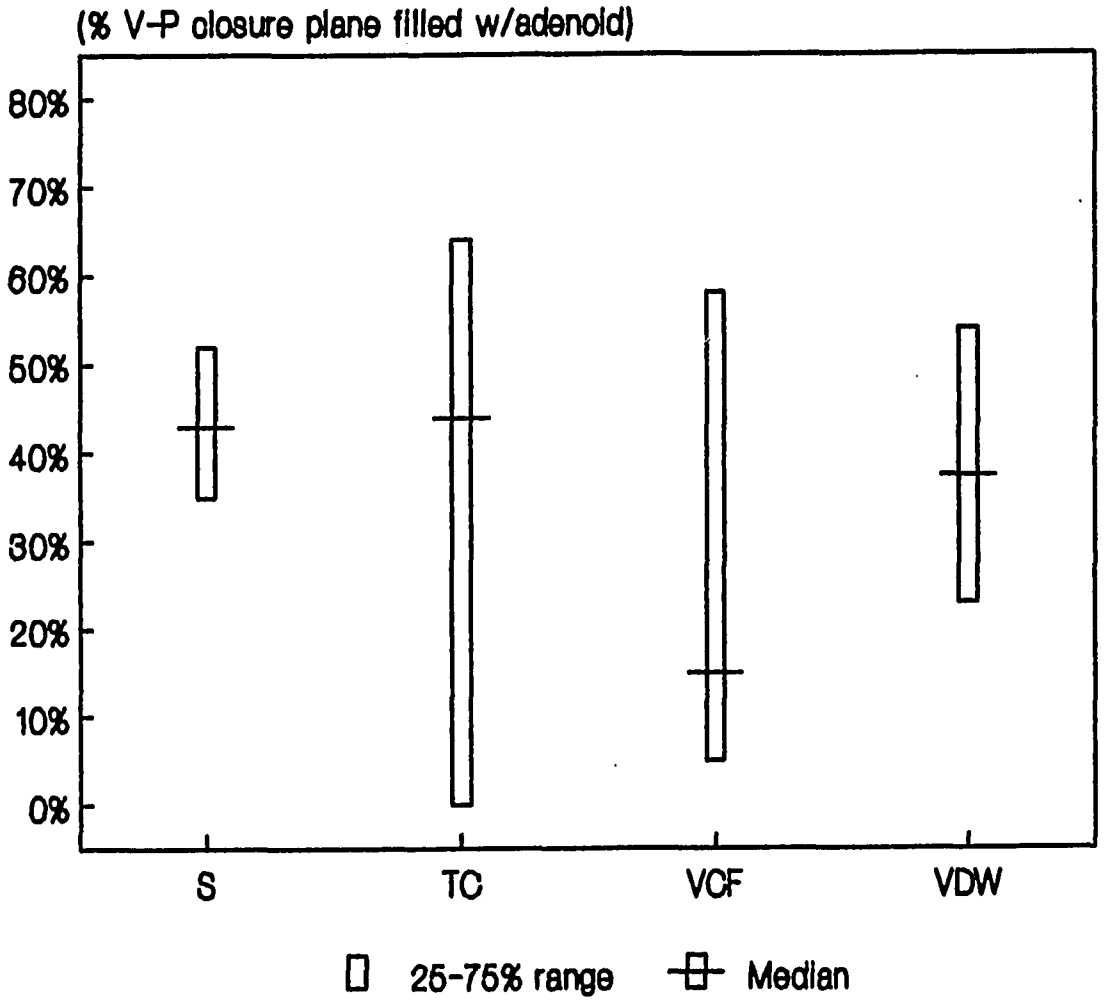


Figure 4.44. Percent of velopharyngeal closure plane occupied by adenoid measured from nasopharyngoscopic tracing for Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

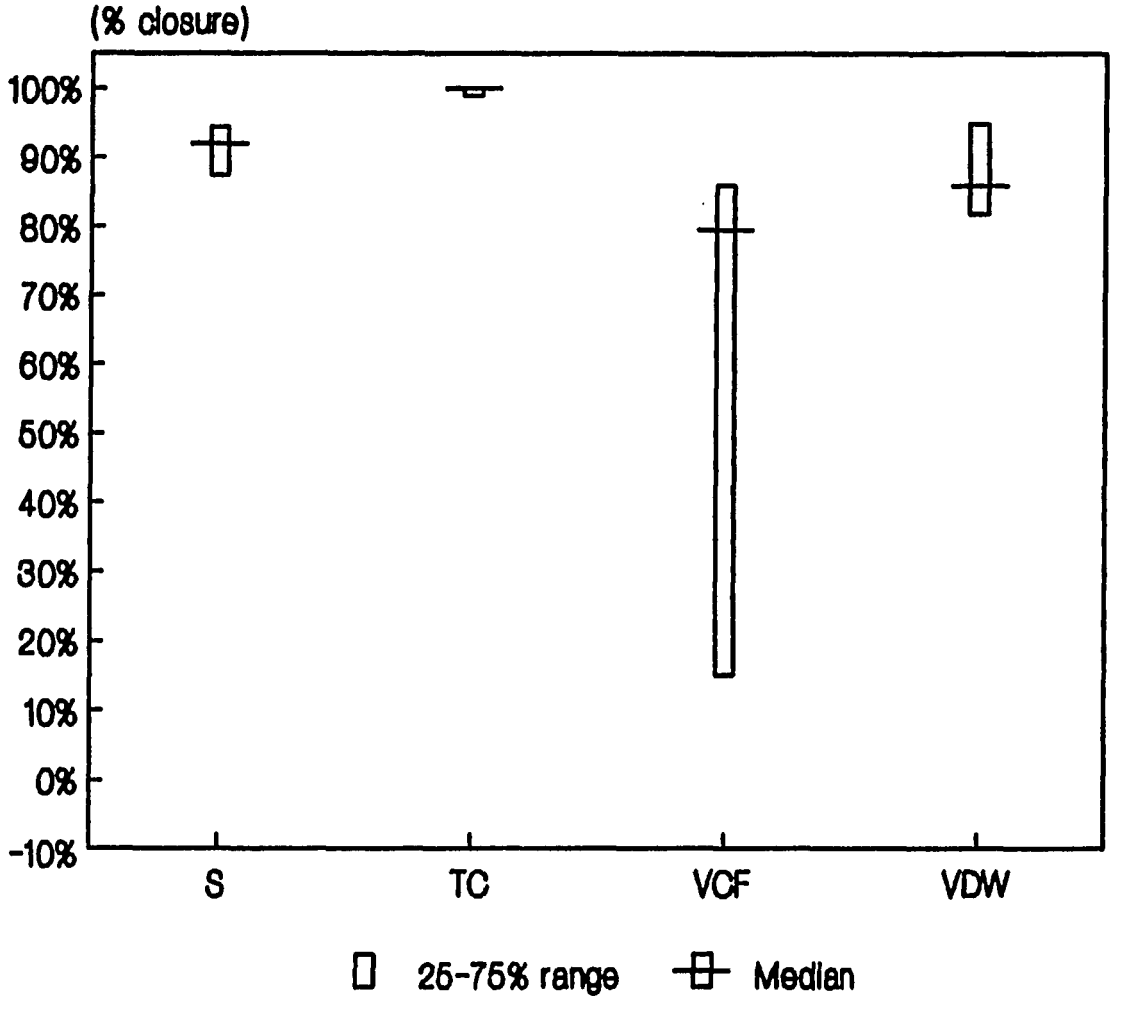


Figure 4.45. Percent velopharyngeal closure achieved measured from en face view fluoroscopic tracing for Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW).

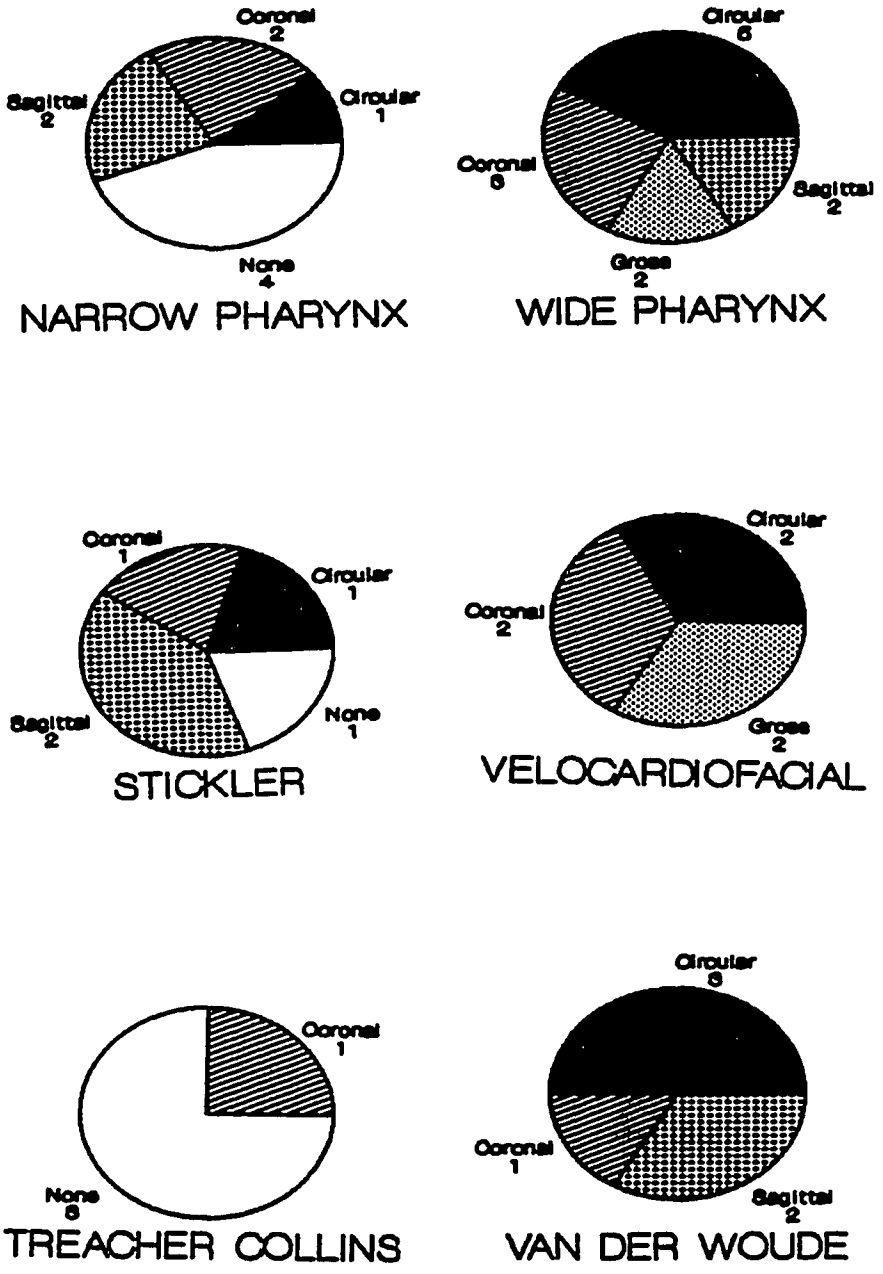


Figure 4.46. Shape of velopharyngeal gap based on en face fluoroscopic view according to pharyngeal width and syndrome (NARROW: Stickler, Treacher Collins; WIDE: velo-cardio-facial, van der Woude). Pie charts show number of subjects in group with each gap shape.

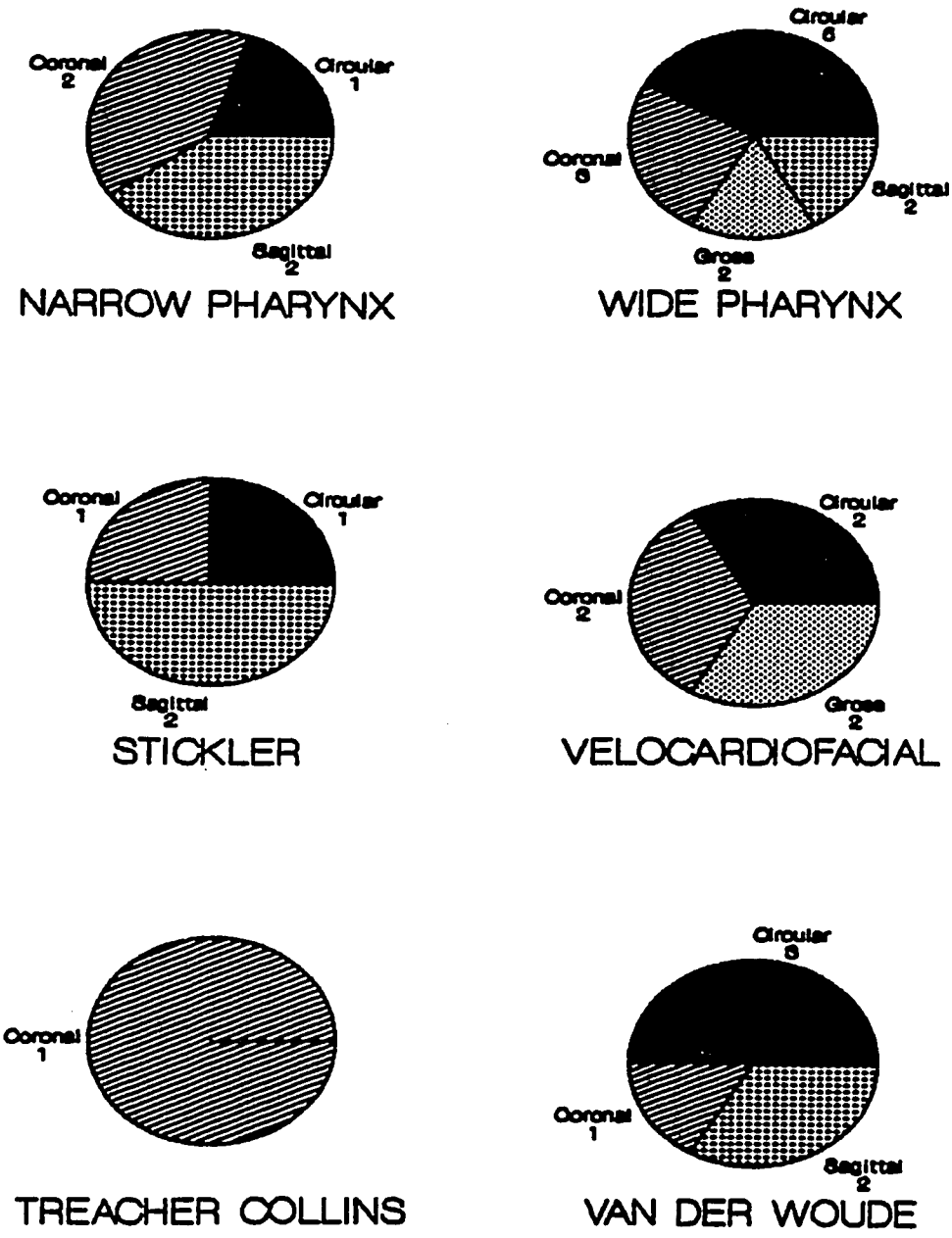


Figure 4.47. Shape of velopharyngeal gap based on en face fluoroscopic view excluding subjects with no gap, according to pharyngeal width and syndrome (NARROW: Stickler, Treacher Collins; WIDE: velo-cardio-facial, van der Woude). Pie charts show number of subjects with VPI in group with each gap shape.

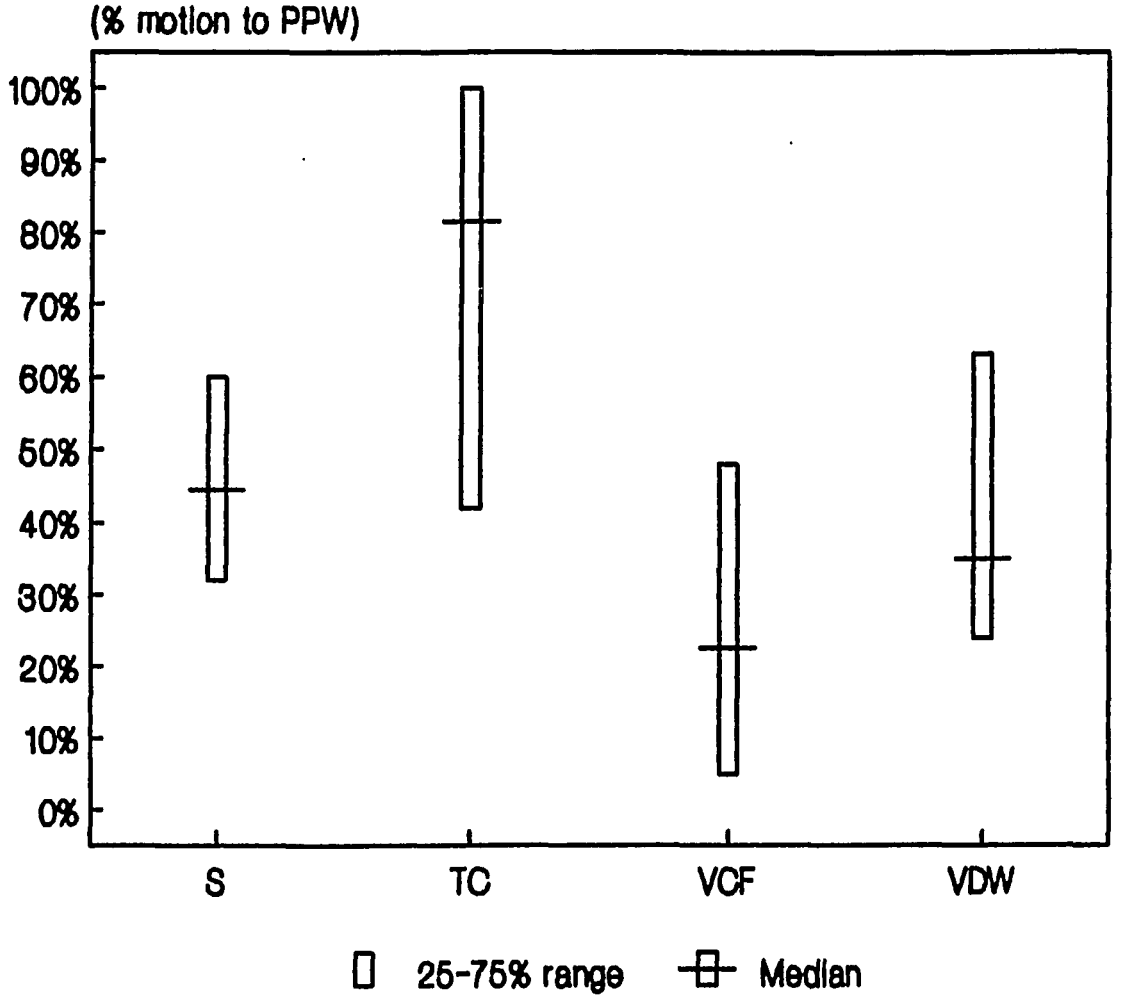


Figure 4.48. Velar displacement ratios based on en face fluoroscopic tracing for Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der woude syndrome (VDW). Ratios represent percent of velopharyngeal port traversed by velum.

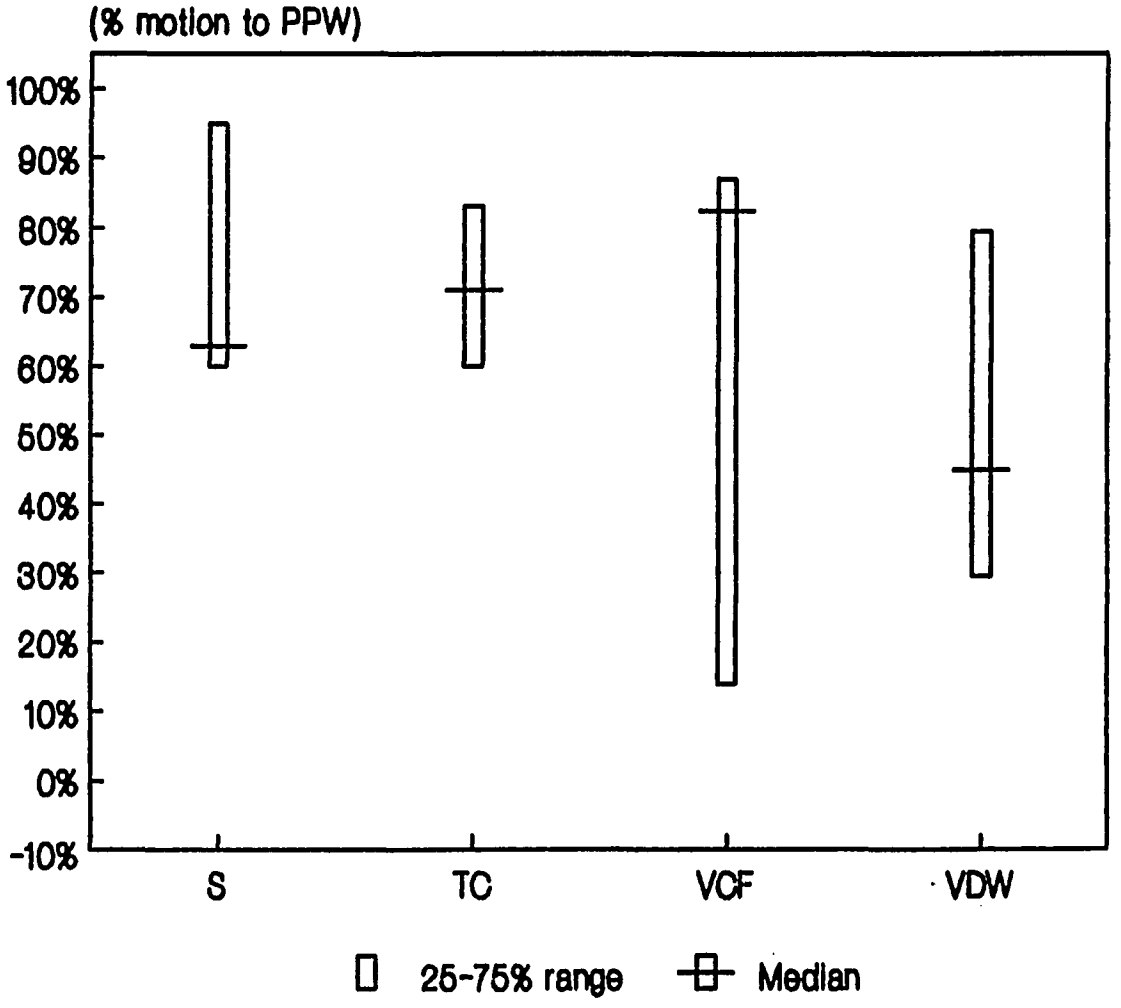


Figure 4.49. Velar displacement ratios based on lateral fluoroscopic tracing for Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der woude syndrome (VDW). Ratios represent percent of velopharyngeal port traversed by velum.

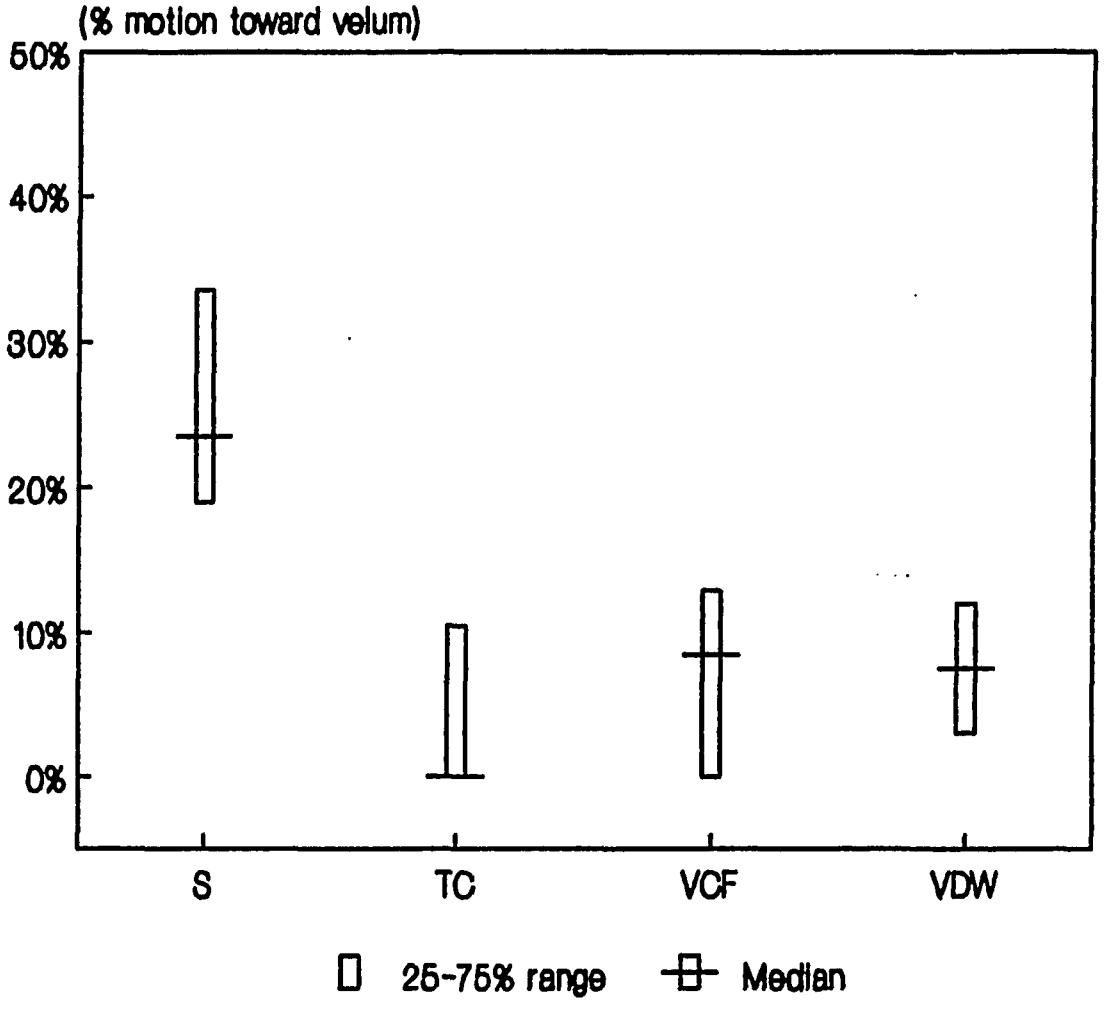


Figure 4.50. Posterior pharyngeal wall (PPW) displacement ratios based on en face fluoroscopic tracing for Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der woude syndrome (VDW). Ratios represent percent of velopharyngeal port traversed by PPW.

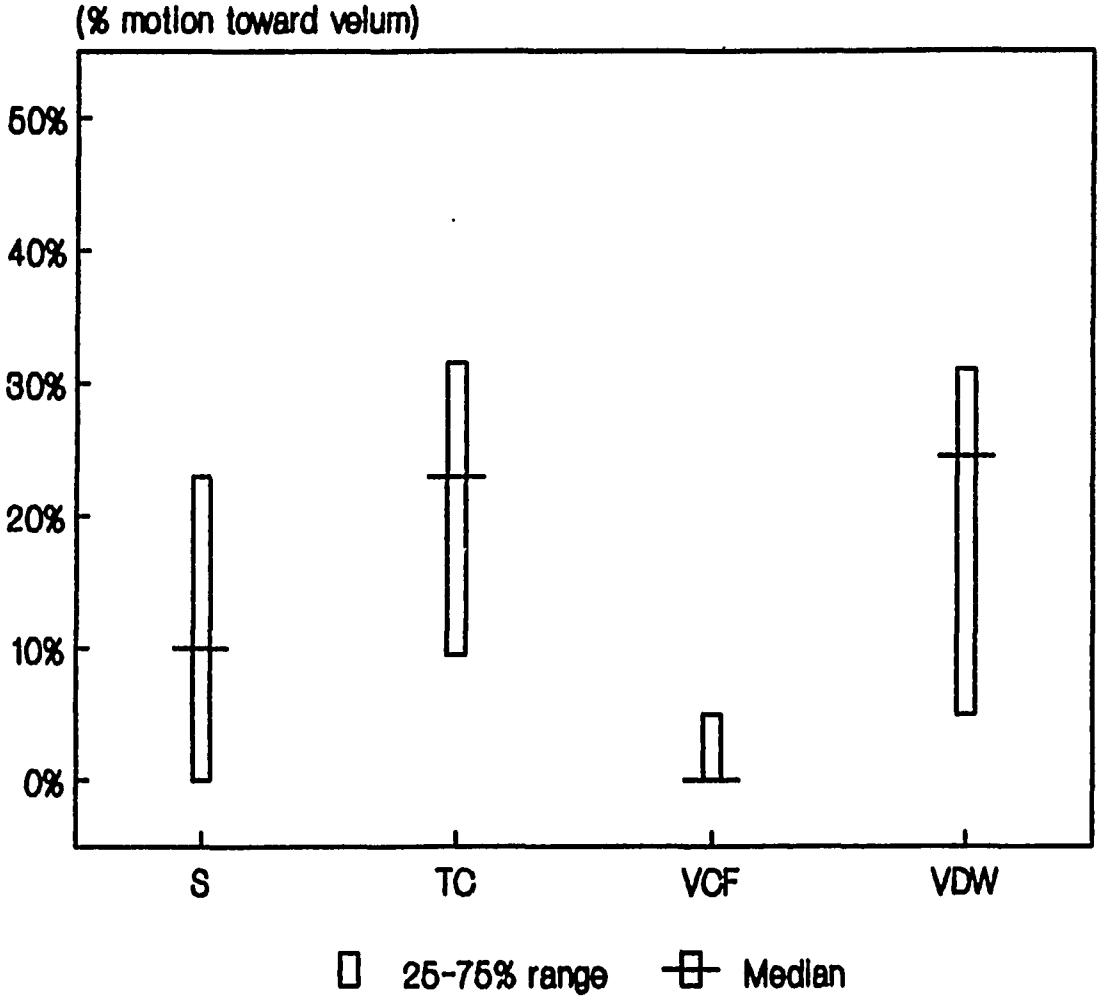


Figure 4.51. Posterior pharyngeal wall (PPW) displacement ratios based on lateral fluoroscopic tracing for Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der woude syndrome (VDW). Ratios represent percent of velopharyngeal port traversed by PPW.

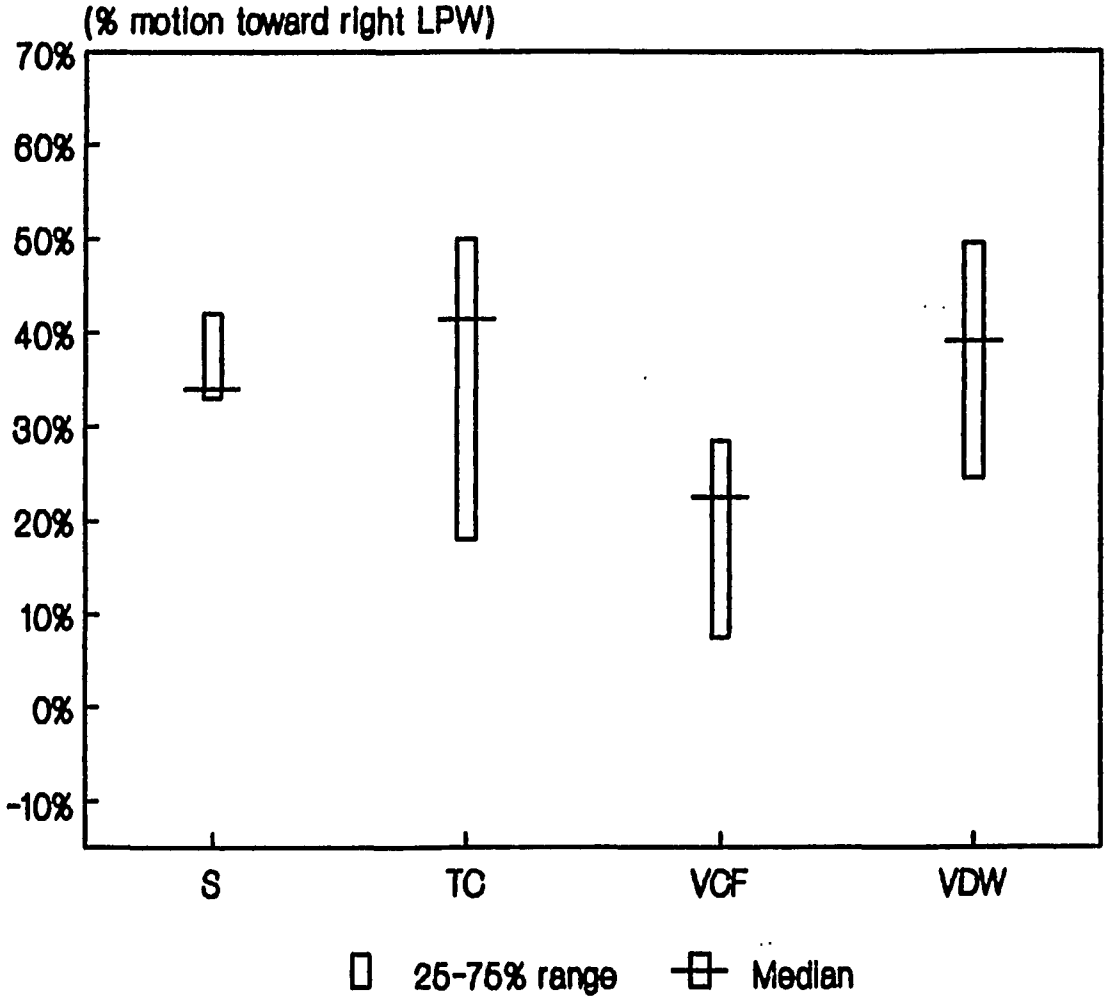


Figure 4.52. Lateral pharyngeal wall (LPW) displacement ratios based on frontal fluoroscopic tracing for Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der woude syndrome (VDW). Ratios represent percent of velopharyngeal port traversed by Left LPW.

CHAPTER 5

DISCUSSION

This project was comprised of two related studies. The purpose of the first was to identify the prevalence of resonance and articulation abnormalities in a sample of 129 subjects with cleft palate in association with four syndromes: Stickler (S), Treacher Collins (TC), velo-cardio-facial (VCF), and van der Woude (VDW) syndromes. The second part was a detailed examination of craniofacial morphology and velopharyngeal function which might contribute to the development of these speech disorders. A subset of 45 subjects with the four syndromes who were included in the prevalence study served as subjects.

Caution must be exercised in trying to correlate morphological and physiological data obtained on a small number of subjects to speech data describing a larger population. Therefore, the two parts of this study are discussed separately. When appropriate and possible, clinical data on the subgroups were compared with the larger syndrome groups from Part I to obtain a sense of the degree to which the smaller group was a representative sample.

PART I: PREVALENCE OF SPEECH DISORDERS IN FOUR SYNDROMES

Stickler syndrome

The findings that over half of the subjects with Stickler were hypernasal and that hyponasality was rare were unexpected

because of previous reports of infrequent VPI and frequent denasality in this syndrome based on observations of many of the same subjects (Siegel-Sadewitz and Shprintzen, 1982; Gereau and Shprintzen, 1988). When present, hypernasality was mild to moderate and slightly over one-third of the subjects developed a glottal stop speech pattern. Subjects with Stickler syndrome tended to present for medical treatment earlier in infancy than the other groups because of Robin-related airway problems in one-third of the subjects and a very high prevalence of overt cleft palate. The rate of both hypernasality and glottal speech was lower among subjects ascertained in early infancy prior to speech development and may suggest an ascertainment bias also supported by the frequency with which speech problems were cited as the reason for referral in subjects older than 2 years of age.

It might be expected that the subjects referred earliest who had the highest prevalence of airway obstruction because of abnormally small vocal tracts would have a lower prevalence of cleft-related speech problems such as hypernasality and glottal speech. This was the case and only 30% of the subjects who required glossopexy in infancy were subsequently hypernasal in contrast to 68% of those who did not require glossopexy.

The fact that most (80%) of the clefts in this group were overt may represent a bias because in the presence of normal speech a submucous cleft may go unnoticed, while overt clefts do not. Therefore, individuals with Stickler syndrome who are less severely affected who do not have an obvious cleft palate

or airway obstruction may be followed by other medical specialists such as ophthalmologists or orthopedists. Because of their normal speech and appearance, they may never be referred to a cleft palate or craniofacial center. Even if followed at a cleft palate center, if not subjected to careful diagnostic scrutiny because of their normal appearance, the diagnosis of Stickler syndrome may be missed, and they might be considered to have a nonsyndromic cleft palate. Stickler syndrome is a diagnosis which is frequently made retrospectively (Shprintzen et al, 1985c). If speech is normal following primary palatoplasty as is likely and there are no other obvious anomalies, subjects may not be followed long enough for the diagnosis to manifest.

Treacher Collins syndrome

Subjects with TC were either ascertained early in infancy following referral for surgical airway management or as teenagers for correction of craniofacial anomalies thus raising the median age of referral.

VPI in Treacher Collins syndrome was found to be infrequent by Gereau and Shprintzen (1988) who examined some of the subjects described here. They did not report the prevalence of hypernasality among the subjects they studied, but hypernasality is an unexpected finding in the presence of velopharyngeal closure. It was therefore surprising to find that over half of the subjects in this study were hypernasal. On the other hand, this was consistent with most other previous reports which indicated that hypernasality was common

in TC "even in the absence of cleft palate" (Beighton, 1971; Peterson-Falzone and Pruzansky, 1976; Peterson-Falzone, 1981; Sparks and Millard, 1981). The fact that there were twice as many submucous clefts as overt clefts identified in this particular group of subjects with TC reflects the practice at CCFD of specific examination for cleft palate regardless of speech quality at referral. Furthermore, the observation that all TC patients with hypernasality who were examined orally and endoscopically at CCFD were found to have a cleft palate suggests that failure to identify clefts may be related more to diagnostic procedures or the definition of "cleft palate" than to palatal morphology. The 2:1 ratio of submucous cleft palate to overt clefts may be more indicative of the cleft distribution in this population than the ratio in Stickler syndrome. Subjects with TC are so dysmorphic and distinctive in appearance that whether a cleft is apparent or not, they are more likely to be referred to a craniofacial center than mildly affected subjects with Stickler or other syndromes without severe dysmorphia (e.g. VDW). The mildest cases may not be referred or recognized, but this seems less likely in Treacher Collins than in the other syndromes because even mildly affected subjects are dysmorphic.

The severity of hypernasality in TC has not been previously described. In this sample, hypernasality was intermittent or mild, and in no case worse than moderate, probably because of the very small pharyngeal lumen. Hypernasality was more prevalent among younger subjects than among the older TC subjects and will be discussed in detail

later. Hyponasality has been described as a frequent finding in TC (Gereau and Shprintzen, 1988) and was present in 20% of this sample.

Some subjects with TC had normal articulation, but this group was likely to have articulation errors attributable to a severe open bite such as tongue fronting and interdentalization, or tongue backing errors (linguopharyngeal stops, isolated nasal snorting) as reported previously (Peterson-Falzone and Pruzansky, 1976; Vallino et al, 1991). The tendency toward tongue backing could be related to the steep mandibular plane, large anterior open bite and very small pharyngeal depth. These features could create an environment in which there is an almost unavoidable tendency for the tongue body to contact the posterior pharyngeal wall any time it moves, especially if the speaker is trying to avoid interdentalization of the tongue which often occurs in the presence of a large anterior open bite. The posterior intrusion of the tongue into the pharyngeal space (the only available position for the tongue because of the mandibular abnormalities) together with the constricted pharynx could also account for the high prevalence of muffled oral resonance which was present in half of the subjects. Limited mouth opening because of mandibular anomalies has also been cited as contributing to the muffled resonance (Peterson-Falzone and Pruzansky, 1976).

Velo-cardio-facial syndrome

There was a very high prevalence of speech and resonance abnormalities in VCF, with no difference in the frequency or severity of communication disorders between subjects seen for medical treatment in infancy and those who were referred after speech development because of them. Every subject was hypernasal and 80% of them initially developed abnormal compensatory articulation patterns such as glottal stops. The elimination of glottal stops and other VPI-related compensatory errors is usually accompanied by an increase in velopharyngeal motion and often by a concomitant decrease in hypernasality (Hoch et al, 1986; Henningsson and Isberg, 1986; Golding-Kushner, 1989). However, this did not occur in subjects with VCF, either by report or in those followed longitudinally. Even following speech therapy which was successful in eliminating abnormal compensatory articulation patterns, hypernasality in subjects with VCF was moderate to severe.

Learning and language disorders are frequent features of velo-cardio-facial syndrome (Strong, 1967; Stern et al, 1977; Shprintzen et al, 1978; Golding-Kushner et al, 1985), and 80% of the subjects in this study had delayed language. However, there was no relationship between language delay and prevalence of glottal speech in this study and all but one of the VCF subjects with normal language development had glottal speech.

Only 20% of the clefts in VCF were overt, while close to one-half were classic submucous clefts of the palate with oral

manifestations, and one-third were occult submucous clefts. The high prevalence of hypernasality resulted in a large proportion of referrals for examination following speech development and subsequent diagnosis of a large number of clefts.

Van der Woude syndrome

Over 90% of the subjects with VDW had normal hearing, language, vocal quality, and vocal pitch. Articulation problems were said to be "common" in VDW, and hypernasality "routine" by Gereau and Shprintzen (1988), who diagnosed VPI in 93% of their VDW subjects with cleft palate or cleft lip and palate. In the present study, hypernasality was present in approximately 70% of all of the subjects with VDW and in only 40% of the VDW subjects ascertained in infancy, making it a frequent finding but certainly not routine. This may be related to a difference in speech between subjects with cleft lip and palate and cleft palate only. (The only adult subject with TC who was hypernasal had bilateral cleft lip and palate as opposed to cleft palate only, supporting a possible relationship to more severe clefting with more hypernasality.) Velopharyngeal gap size was not reported by Gereau and Shprintzen, nor did they report the severity of hypernasality among their subjects. Therefore, it is possible that they identified a large number of very small velopharyngeal gaps which were asymptomatic and associated with normal resonance. In the subsample of subjects included in Part II of this study, there were three subjects with VPI but perceptually

normal resonance. When present, hypernasality in the present study was generally mild to moderate as in Stickler syndrome. The presence of glottal speech in 40% of subjects was another similarity between VDW and S which was observed in this study, and suggested that pharyngeal width was not the most important cause of glottal speech.

SPEECH PRODUCTION

Based on these clinical profiles derived from the 129 subjects in the first part of this project, it is clear that the first two hypotheses must be rejected as stated in the null form:

1. There is no difference in the prevalence of "compensatory" speech disorders (glottal stops, etc.) in different syndromes.
2. There is no difference in the prevalence of resonance disorders in different syndromes.

Resonance

The high prevalence of hypernasality in the wide pharynx syndromes was in agreement with previous reports of frequency of both VPI and hypernasality in these groups. However, there was clearly a syndrome effect for the prevalence and severity of hypernasality, and both were related more to diagnosis than to cranial base angulation. Subjects with VCF were more frequently and more severely affected than subjects with VDW. The importance of the obtuse cranial base in VDW may be inferred from the vigorous velopharyngeal movement in VDW. In

the presence of a normal cranial base or acute basicranium, those subjects might not have VPI or hypernasality.

Hypernasality was less frequent in syndromes associated with an acute cranial base, although the prevalence of hypernasality in this study was higher than expected based on previously published VPI rates. In fact, the prevalence of hypernasality in all four syndromes was higher than the prevalence of VPI in subjects with nonsyndromic clefts at the same institution (Hall and Golding-Kushner, 1989). Peterson-Falzone (1990) studied subjects at three other cleft palate centers with cleft palate only and no syndrome other than VDW. She reported that hypernasality was present in 13.3% of the subjects, also lower than in the four groups in this study. Van der Woude subjects may have a higher prevalence of hypernasality than nonsyndromic clefts and should not be included in such studies.

Severity of hypernasality was also related more to syndromic diagnosis than to classification according to pharyngeal width. Hypernasality tended to be moderate to severe in VCF, but only mild to moderate in both S and VDW. This was an unexpected finding considering vocal tract size alone, because van der Woude syndrome was characterized by pharyngeal depth measurements even larger than VCF although the cranial base angle was more obtuse in VCF and the measurements in S were all normal or slightly narrowed. Hypernasality was usually intermittent or very mild in TC and 20% of the subjects with TC were hyponasal. Four other subjects were hyponasal, two each with S and VCF. The small

number of subjects may have contributed to failure to detect a significant difference among syndromes in the prevalence of hyponasality. However, hyponasality in 2 of 10 subjects with TC suggests a trend much different than 2 hyponasal subjects of 46 in VCF.

Articulation

The tendency for subjects to exhibit various types of articulation disorders also appeared to be related to diagnosis, and articulation patterns within a syndrome were not related to whether the cleft palate was overt or submucous. Subjects within a syndrome group tended to have particular patterns of articulation development regardless of age at the time of initial referral to a craniofacial center, type of cleft, severity of hypernasality, audiometric status, or language abilities. The exception, as noted above, was that in Stickler syndrome subjects with overt cleft palate who were ascertained prior to speech development had a low glottal stop rate of 20%. A similar rate of compensatory articulation development was identified in 17.8% of subjects with nonsyndromic or VDW cleft palate- only by Peterson-Falzone (1990).

The highest prevalence of glottal stop speech disorders was in velo-cardio-facial syndrome in which 90% of the subjects had glottal speech. As a result, there was a much higher prevalence of compensatory speech disorders in the wide-pharynx syndromes regardless of age at the time of referral. Similar to the severity of hypernasality, the

articulation profiles of late-referred subjects with Stickler syndrome and van der Woude syndrome were almost indistinguishable from each other with about 40% of the subjects in each group presenting with glottal speech. That glottal speech was equally prevalent in a narrow pharynx and wide pharynx syndrome suggests that other factors were more important determinants of glottal speech than pharyngeal depth alone. This impression is strengthened by the fact that lumen depth at the velopharyngeal level was greater in VDW than in VCF, but the glottal rate in VCF was much higher. Relative lumen size was greater in VCF than in VDW, suggesting that overall vocal tract volume may be a more important factor.

Subjects with TC were most likely to have articulation errors attributable to severe open bite such as tongue fronting and interdentalization, or tongue backing errors. The tongue backing tendency could be related to the steep mandibular plane, large anterior open bite and very small pharyngeal depth, setting up an environment in which there is an almost unavoidable tendency for the tongue body to contact the posterior pharyngeal wall any time it moves, especially if the speaker is trying to avoid interdentalization of the tongue which would occur in the presence of a large anterior open bite. The posterior intrusion of the tongue into the pharyngeal space together with the constricted oropharynx could also account for the high prevalence of muffled oral resonance in TC.

Overt and Submucous Cleft Palate and Speech

Hypernasality and glottal speech were more prevalent in SMCP than in repaired overt clefts. Over 60% of the subjects with repaired clefts had normal resonance, and over 60% of the subjects with SMCP were hypernasal. Subjects with glottal stop disorders were twice as likely to have submucous clefts as they were overt clefts, and SMCP was more prevalent in wide pharynx syndromes than in narrow pharynx syndromes. Overt cleft palate occurred with equal prevalence in the narrow and wide pharynx syndromes, but SMCP was more prevalent in the wide pharynx syndromes. OSMCP occurred only in VCF in this sample, although it is known to occur in nonsyndromic patients (Kaplan, 1975; Croft et al, 1978; Lewin et al, 1980).

The proportion of overt clefts to submucous clefts in Stickler syndrome was almost identical to Herrmann's sample in which of 17 subjects with cleft palate, 76% of the clefts were overt and 24% were submucous (Herrmann et al, 1975a). In the current study, 79% of the clefts in S were overt and the other 21% were SMCP. This finding is not surprising. Subjects with SMCP were almost always referred for examination after speech had developed and was known to be abnormal and hypernasal. In those cases, the hypernasality or glottal speech prompted the examination in which the submucous cleft was diagnosed. Submucous cleft palate is most often accompanied by normal speech and resonance which has led to underreporting of cleft palate in both syndromic and nonsyndromic subjects (Weatherly-White et al, 1972; Kaplan, 1975; Shprintzen et al 1985a). Subjects with normal speech

often do not present for medical attention or, if examined, may not have careful oral and nasopharyngoscopic examination. Therefore, the higher prevalence of hypernasality and glottal speech in submucous clefts than in overt clefts, and the higher prevalence of diagnosed submucous clefts in the wide pharynx syndromes may reflect an ascertainment bias. That is, subjects with normal speech may never present to a craniofacial center, or may not have their clefts detected. Underreporting of clefts in S and TC has been suggested by some authors (Cohen et al, 1971; Hall and Herrod, 1975; Shprintzen et al, 1985a). The interesting finding is that there were so many more SMCP-hypernasal subjects referred for examination with VCF than with the other four syndromes.

There are at least two possible explanations for the large number of subjects with VCF who had obvious or occult submucous clefts of the palate. It is possible that SMCP and OSMCP occur more frequently in VCF than in other syndromes, although there is no reason to believe that this is the case. Another possibility is that subjects with VCF who have submucous cleft palate are at higher risk for speech and resonance abnormalities because of the combination of structural and, possibly, neurologic abnormalities. Conversely, the velopharyngeal movement which is so vigorous in VDW may compensate for the lack of velar bulk and result in a smaller gap, or no gap at all. The vigorous movement in VDW might result in complete velopharyngeal closure in a subject with a normal cranial base and vocal tract depth. Velopharyngeal movement may be mechanically inhibited in a

very small pharynx such as in TC so the loss of velar bulk due to a cleft may have no effect. This might, in turn, set up an anatomic and physiological environment more conducive to normal speech, and one in which a SMCP or OSMCP might go unnoticed.

There were 52 subjects in the initial prevalence study with repaired cleft palate and most underwent palate repair at Montefiore Medical Center. Palate repair in infants with Robin sequence did not incorporate a palatal lengthening procedure (to reduce the chance of airway obstruction) which was done in non-Robin cases. It was beyond the scope of this study to examine the relationship between surgical technique and speech outcome. Among these subjects, surgical technique did not appear to influence speech outcome, and palatal thickness and length were not significant factors in VPI. However, this is an area for further research.

DEMOGRAPHIC DATA

There were some interesting observations pertaining to demographic data.

Gender

Birth defects in general are more common in males than in females and sex differences have been reported in the prevalence of different types of clefts. Cleft lip with or without cleft palate is more common in males although isolated overt cleft palate has been reported as more prevalent in females, with a ratio of about 1.3 females to 1 male

(McWilliams et al, 1990). More than 50% of submucous clefts may occur in males (McWilliams et al, 1990). However, all four syndromes in this study are believed to have autosomal dominant patterns of inheritance which should result in an equal number of affected males and females (Gorlin et al, 1990). In this study of subjects with syndrome-related cleft palate only, males and females were equally distributed in S and TC, the narrow pharynx syndromes. However, there were more females than males in the two wide pharynx syndromes, a 2:1 ratio in VCF (mostly with SMCP), and a 4:1 ratio in VDW. Cleft palate without cleft lip has been reported to occur without sex differences in van der Woude syndrome (Glass et al, 1979; Janku et al, 1980; Burdick et al, 1985, 1987). One possible reason for the difference in sex distribution in the four groups was sample size. Another possibility is a difference in the timing of embryonic development of the pharynx and palate in females and males which interacts in some way with the pharyngeal width characteristic of the syndrome directing the embryonic development. Alternatively, there may be a difference in the prevalence of these four syndromes in males and females, although there is no suggestion in the literature that this is the case.

Voice quality

The prevalence of hoarseness in subjects with clefts and VPI has been the subject of much debate. Studies of the prevalence of voice disorders in childhood indicate that 6 to 9 percent of school aged children are hoarse (Johnson and

Child, 1988). The prevalence of phonatory disorders in children with cleft palate or velopharyngeal insufficiency has been reported to be as low as 0.6% and as high as 43% (McWilliams et al, 1990). In the current sample of 129 subjects with cleft palate, there was a prevalence of hoarseness of 15%. There was no significant difference in the prevalence of hoarseness in the hypernasal and normal resonance subjects, but about 20% of the S and 20% of the VCF subjects were hoarse. Only 7% of the VDW subjects were hoarse, the rate reported for normal children, and there were no hoarse TC subjects. VCF represented 57% of the total population but 70% of those subjects who were hoarse. The subset of subjects with VCF who were included in the morphological and physiological analyses had findings suggestive of laryngeal immaturity such as an elevated larynx, but voice quality in VCF is in need of further investigation. Twenty-five percent of the hoarse subjects had Stickler syndrome and S accounted for 22% of the total population.

PART II: CRANIAL AND VOCAL TRACT MORPHOLOGY AND VELOPHARYNGEAL CLOSURE

Stickler Syndrome

Stickler syndrome was characterized by acute angulation of the basicranium and shortening of the anterior cranial base, hard palate, and mandibular body. Basicranial kyphosis was not found by Glander (1990), who examined 20 Stickler

cephalographs of 17 subjects, including five of the subjects in this study. He reported a mean N-S-B of 129^{0} (median 129.5^{0}), in contrast to a mean and median of 124^{0} in this study. The reason for this difference is not clear, but sample and age may have been factors. Glander's sample included multiple measurements on a single female subject who had yearly cephalographs taken at ages 16, 17, and 19 years. Her cranial base angle showed an increase in obtuseness by 1^{0} each year. Riolo et al (1974) reported that the cranial base angle in females shows increased flatness between ages 6 and 16 years of about 1.5^{0}. Glander's data suggest that this trend may continue beyond age 16 years and may be of greater magnitude. Indeed, the oldest subject with Stickler syndrome in this study was also the only one in the group with an obtuse cranial base angle (Figure 5.2). These observations suggest that there may be a tendency for the cranial base angle to become more obtuse into adulthood in S. Because the mean age of Glander's sample was 16.5 years (median 8.5 years) in contrast to a median of 5.5 years in this sample, age may have been a factor in the disagreement.

A shortened posterior cranial base which was observed by Saksena et al (1983) was not found. The shortened hard palate may have been related to the prevalence of overt clefts[28] in

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[28]The fact that the hard palate was shorter in overt cleft palate than in submucous clefts may be a radiographic half-truth. The shortened central portion of the hard palate which is palpable as a notch in overt SMCP is not detected radiographically on a lateral cephalograph because it is overlaid in the radiographic field by the longer lateral edges of the bone. Shortening of the central part of the hard palate may affect the position of the velum relative to the

this group and may also be consistent with published descriptions of the Stickler phenotype which is characterized by midface deficiency. Consistent with the categorization of S as a narrow pharynx syndrome, lumen depth was slightly constricted at the level of the velar midpoint and at the larynx. However, lumen depth was otherwise fairly normal in this group. The shorter ANS-PNS length may have resulted in increased lumen depth at the velopharyngeal level reducing the likelihood of airway obstruction, but increasing the likelihood of VPI. As noted previously, only one-third of the Stickler subjects who required glossopexy in infancy were subsequently hypernasal in contrast to two-thirds of those who did not require glossopexy. (Statistical analysis did not show a significant relationship between hypernasality and history of airway obstruction, possibly because of small sample size.) There was only slight reduction in the absolute area of the airway in Stickler and airway height was normal. Glander (1990) reported increased airway height in Stickler syndrome, but was comparing his Stickler subjects to his VCF subjects, and not to normals. The data in the current study suggest that airway height in VCF is short. The relative size of the airway (proportion of the skeletal boundary of the airway actually occupied by lumen) was also similar to normal.

Biases related to ascertainment of subjects may have influenced the results of both parts of this project. Only

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posterior pharyngeal wall.

subjects with cleft palate were included. Cleft palate is associated with a larger than normal pharyngeal width (Maue-Dickson et al, 1976), and it is possible that subjects with Stickler syndrome who have clefts have larger pharyngeal widths than non-cleft Stickler subjects, although this has not been studied. Of greater relevance to this study, the subset of subjects who were included in Part II were specifically selected based on the availability of clinical records including cephalometry and at least one physiologic study of velopharyngeal closure. Thus, this subset of subjects may have the largest vocal tracts and be closer to normal in their skeletal morphology. There were at least two types of subjects on whom no data were available: those who did not survive infancy, and those with normal speech after palate repair who were lost to follow-up. The subjects who had the most severe airway obstruction and succumbed during infancy may have had the smallest vocal tracts. Those with moderate narrowing may have had normal speech, leaving those subjects with Stickler who had the largest airways, which measured as slightly narrowed or normal. On the other hand, the subjects with VDW and cleft palate who were so similar in speech characteristics to Stickler may represent the mild end of the VDW spectrum, with unilateral and bilateral clefts representing the more severe cases.

Even with lumen narrowing at the velopharyngeal level, 8 of the 10 subjects in the Stickler subgroup were hypernasal, but all 10 had VPI noted at least occasionally in at least one view. Velopharyngeal gaps tended to be small, with at least

75% of the V-P port closed during phonation. En face fluoroscopy generally underestimated the amount of velar motion in the few subjects examined in this view, possibly because of tonsils or adenoids compromising accuracy of the head position and view. However, nasopharyngoscopy and lateral fluoroscopy indicated good velar motion with the velum approaching 70% to 80% of the distance toward the posterior pharyngeal wall and normal adenoid. The PPW moved anteriorly as much as 20% of the distance toward the velum, and LPW motion was active in most subjects such that most of the velopharyngeal gaps were oriented in the sagittal plane or were circular.

Treacher Collins Syndrome

The cranial and vocal tract morphology of TC was distinctive and the most abnormal of the four syndromes. Consistent with published cephalometric reports, TC was characterized by an acute cranial base angle and steep mandibular plane. Severe anteroposterior shortening of the airway throughout its entire length from the palatal plane to hyoid plane has also been reported previously (Shprintzen et al, 1979; Shprintzen, 1982). Lumen size was much more severely diminished than in Stickler syndrome, although the median cranial base angle was the same for each group. As already noted, lumen space at the velopharyngeal level in subjects under 15 years of age was further reduced by adenoid tissue which was relatively large and occupied more than 60% of the space in 4 of 5 subjects.

The palate in TC was of normal length and thickness, but hung almost vertically into the pharynx and was draped along the body of the tongue as a result of a downslanting palatal plane, posterior tongue position, and sloped vocal tract. The body and root of the tongue were positioned posteriorly in the oro- and hypopharyngeal spaces and the soft tissue of the posterior pharyngeal wall was slightly thickened at the oropharyngeal level constricting the airway even further.

The lumen occupied proportionately less space within the skeletal airway frame than normal at least partially because of the tongue position. The hyoid was inferiorly displaced in relation to the palatal plane, mandibular plane, and velum, elongating the oropharyngeal and hypopharyngeal airway[29]. This may also have occurred as a compensation for the position of the tongue, with the tongue pushing the hyoid down.

The epiglottis was noted radiographically and on endoscopy to be curled forward toward the tongue root in six of seven subjects with TC in whom the epiglottis was visualized (Figure 5.1). This was present in every adult with TC, suggesting that it might be a deformation resulting from long term downward pressure of the tongue against the larynx, though it was also present in an 8 year old subject. When this was observed during lateral view videofluoroscopy, it looked as if the tongue root was cradled in the anterior

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[29]As noted previously, the term hypopharyngeal usually refers to the subglottic or lower airway. It is used here to refer to the lowest one-third of the supraglottal vocal tract. The larynx itself and the subglottal vocal tract were not examined.

surface of the epiglottis. In most of the subjects younger than 18 years, the epiglottis curled upward as it contacted the posterior pharyngeal wall, again suggesting that the forward curvature may be a deformation which worsens over time. Voice quality of the subjects with TC was unaffected, but the anterior curvature of the epiglottis may contribute to the abnormal oral resonance described as "muffled." In normal subjects, curvature of the epiglottis increases between birth and 3 years of age at which time it increases in the transverse dimension and flattens to the adult configuration (Bosma, 1986). Growth in the transverse dimension of the epiglottis in TC would be constricted by the severe reduction in transverse pharyngeal width which was reported by Shprintzen et al (1979). However, longitudinal observation of individuals with TC is needed to determine if the configuration of the epiglottis is a diagnostic feature of TC or a secondary deformation which occurs over time as the cranial base angle becomes more acute, possibly leading to further anteroposterior shortening and elongation of the vocal tract.

Cranial base angle in TC. Treacher Collins was the only syndrome of the four studied in which the cranial base angle was much more acute in older subjects than in younger subjects (Figure 5.2). In fact, as discussed above, the oldest subject with Stickler syndrome had the most obtuse cranial base angle in that group. The tendency for a significant increase in kyphosis of the cranial base in TC was observed in a

longitudinal study of TC by Peterson-Falzone and Figueroa (1989) and also reported by others (Garner, 1967a, 1967b; Roberts et al, 1975). Peterson-Falzone and Figueroa (1989) observed that there was a predominance of males among those patients showing significant change in cranial base angulation over time. Longitudinal data on normal subjects by Riolo et al (1974) indicated that the cranial base angle became about 0.5^0 more acute in normal males and 1.5^0 more obtuse in females between 6 and 16 years old by which time growth of the cranial base was essentially completed. However, the spheno-occipital synchondrosis does not fuse until 18 to 25 years of age (Moore and Lavelle, 1974) and continued growth of the posterior cranial base in males has been measured until 21 years (Laitman and Crelin, 1976; Roche and Lewis, 1976). This could have the effect of making the cranial base angle more acute and thus shorten the anteroposterior depth of the pharyngeal lumen. (Note that in VCF, the posterior cranial base was abnormally short, the cranial base angle obtuse, and the pharynx excessively deep.)

It is, therefore, interesting to note that among TC subjects in this study there appeared to be a relationship between age and resonance. Mild or moderate hypernasality was only present in TC subjects 6 years old or younger (Table 5.1). Subjects between 8 and 17 years old had normal resonance or intermittent hypernasality and all subjects with cleft palate only who were older than that had normal

resonance[30]. TC was the only group in which there seemed to be an age effect on resonance, and the only group in which subjects with the largest amount of adenoid tissue were the most hypernasal. Obviously this must be studied longitudinally because in such a small sample these data may have been sensitive to peculiarities of referral patterns. Subjects with hypernasality may have been treated at a younger age, the subjects referred later may have had normal resonance and presented as adults for treatment of craniofacial anomalies, or may have been diagnosed following examination of an affected relative. However, if longitudinal studies corroborate this trend of better resonance with age, there would be important implications for treatment of children with TC. That anesthesia is difficult in TC because of restricted mouth opening, small pharyngeal width, and difficulty visualizing the glottis (perhaps because of the retropositioned tongue and curved epiglottis) has already been discussed. It has been suggested that pharyngeal flap should be avoided in TC because of severe surgical and post-operative risks (Shprintzen, 1988b). If resonance in TC improves because of increasing flexure of the cranial base and associated morphological and physiological changes, there would be a more favorable prognosis for improvement of hypernasality without the treatment dilemma posed by the surgical risks. Ironically, the same pharyngeal changes may

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[30]The single subject over 20 years who was hypernasal had bilateral cleft lip and palate.

increase the risk of obstructive apnea (Arvystas and Shprintzen, 1991).

Airway height. The vertical distance from the Frankfort horizontal to the hyoid plane in TC was the longest of the four syndromes but within the normal range. However, all of the airway measures between the palatal plane and hyoid were abnormally long. Therefore, the abnormal elongation of the vocal tract occurs primarily between the palatal plane and the hyoid plane which lengthens the oropharynx and hypopharynx. This would suggest that the palatal plane is abnormally high, possibly compressing the nasal capsule and shrinking the nasopharyngeal space. An inferiorly placed hyoid bone with reduced posterior pharyngeal space has been reported in adults with obstructive sleep apnea who were otherwise normal (Guilleminault et al, 1984).

The TC vocal tract was oriented diagonally downward and backward with an obtuse nasopharyngeal angle. Even though the palatal plane was angulated, it intersected the posterior pharyngeal wall at the same angle as normal. This abnormal position may further compromise the nasopharyngeal space and, together with abnormal height of the nasal capsule, may contribute to the prevalence of nasal obstruction which has been reported in TC (Roberts et al, 1975).

Articulation in TC. The vocal tract morphology in Treacher Collins syndrome may suggest a predisposition for tongue backing errors and nasal turbulence or even nasal

snorting (posterior velar fricative) because of the movement of multiple soft tissue structures (velum, tongue) of normal size in a very small vocal tract. The tendency toward tongue backing errors which was noted in the prevalence study in this project was also mentioned in published reports of isolated nasal snorting as a finding in TC (Peterson-Falzone and Pruzansky, 1976).

Correspondence between nasopharyngoscopy and multi-view videofluoroscopy. The lack of complete correspondence between nasopharyngoscopy and videofluoroscopy is the basis for performing both examinations to accurately describe velopharyngeal function (Shprintzen and Golding-Kushner, 1989). As seen in Appendix E, nasopharyngoscopy showed VPI in 1 of 8 subjects with TC and base view fluoroscopy revealed VPI in 2 of 5, including one who appeared to achieve closure on endoscopy. However, lateral and frontal view fluoroscopy revealed small velopharyngeal gaps in another 4 subjects. Most of these subjects had lateral gaps (air escaping through the velopharyngeal port around the sides of the velum which was in contact with the posterior pharyngeal wall). This could have resulted from lateral pharyngeal wall motion occurring at a different vertical level than the velum with velar elevation mechanically obstructed by contact with the PPW.

One might expect the highest degree of agreement between nasopharyngoscopy and videofluoroscopy to occur in the narrow pharynx syndromes where the entire velopharyngeal port was

almost always visible in a single endoscopic view. However, the largest number of inter-view disagreements on the presence of VPI occurred in TC with disagreement between views in 4 of 8 cases, followed by S with disagreement on 2 of 8 cases who had both videofluoroscopic and nasopharyngoscopic examinations. In each case of disagreement, gaps were detected in lateral and/or frontal view fluoroscopy but not on base view or endoscopy. There was complete inter-view agreement in VDW, but the one subject who achieved velopharyngeal closure as seen endoscopically did not have fluoroscopic examination. There was one subject with VCF who appeared to achieve closure on lateral view fluoroscopy but not on any other fluoroscopic view or on endoscopy. This was the only case of endoscopy underestimating closure in comparison with other views. The abnormal shape of the TC vocal tract may make this group most vulnerable to viewing errors because of difficulty in obtaining an adequate "head on" examination of the velopharyngeal port in both nasopharyngoscopy and en face fluoroscopy. It has been demonstrated that the configuration of the pharynx and plane of closure, especially in young children, may make direct observation of the velopharyngeal port by endoscopy difficult (Pigott and Makepeace, 1982; Golding-Kushner et al, 1991).

All subjects with TC had active velar and lateral pharyngeal wall motion. Because of the very small lumen to be traversed during speech, even a small amount of displacement resulted high movement ratios, and gaps tended to be very small. The velum moved against the posterior pharyngeal wall,

but because of its slope, the body of the velum made contact with the PPW before forming a velar "knee." This phenomenon was similar to their lingual activity, in which contact was made with one structure against another prior to complete execution of the gestures which are normally produced, giving the impression of various structures bumping into each other, interfering with normal movement. This could result in nasal turbulence caused by nasal air escape through a very small constriction or could contribute to a perception of hypernasality. In fact, 60% of the subject subgroup with TC were perceived as hypernasal, but the mean severity rating was only 0.5 (very mild or intermittent).

The prevalence of VPI and hypernasality in these subgroups of subjects with Stickler and especially TC seemed discordant with the prevalence of VPI in previous studies which included many of the same subjects (Gereau and Shprintzen, 1988). Sample size may have been a factor. However, the study cited reported on VPI and not resonance, and, as seen in Appendix E, the degree of perceived hypernasality among the subjects in this study was often discordant with the size of the velopharyngeal gap seen on base view fluoroscopy and nasopharyngoscopy. It is a known phenomenon that the size of the velopharyngeal gap is not the sole determinant of nasality or of nasal emission (Warren, 1967). The unpredictable relationship between gap size and perceived nasality has specifically been reported in hearing

impaired subjects (Seaver et al, 1980; Lock and Seaver, 1984)[31]. Another factor potentially affecting the perception of hypernasality in TC is posterior tongue carriage which blocks the oral cavity and reduces the probability of oral resonance (McDonald and Koepp-Baker, 1951).

The source of discrepancy between VPI and hypernasality might also be related application of the perceptual term "hypernasal" to describe some other unusual resonance characteristic produced by abnormal vocal tract shape or volume other than VPI but which was perceived or simply labeled as "hypernasal" for lack of a better term. It has been suggested that the actual resonance characteristic of TC "defies" description (Peterson-Falzone, 1982).

The difference in apparent prevalence of VPI and prevalence of hypernasality might also have resulted from certain classification and statistical methods used in this study which violated basic tenets of clinical practice in several ways. First, in order to reduce variability in measurement of velopharyngeal gaps due to phonetic context, all measurements were made during production of a sustained

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[31]Seaver et al (1980) found that of 19 out of 26 hearing impaired adults who were rated as hypernasal, only 5 actually had nasal emission. Lock and Seaver (1984) examined 5 profoundly deaf adults using lateral cineradiography. All 5 were rated as hypernasal but only 2 of 5 had evidence of VPI on the cine, and there was no relationship between the degree of perceived nasality and the presence of velopharyngeal opening during sentence production. No other radiographic views were used. These two studies and the current project highlight the need to examine the velopharyngeal port using multiple imaging techniques and views, but also suggest that there are other factors in addition to velopharyngeal closure which contribute to the perception of hypernasality.

isolated /s/. While all of the videotapes were reviewed to be sure that the velopharyngeal movement in that phonetic context was representative of both maximum and habitual closure, other aspects of velopharyngeal closure such as the timing of movements were not taken into account. However, a listener's perception of hypernasality is based on the presence of excessive nasal resonance during connected speech and not during production of a single phoneme. Also, the perception is probably influenced by acoustic changes affecting the spectral characteristics of vocalic sounds, not consonants (Trost, 1981; Skolnick and Cohn, 1989). This is discussed in more detail at the end of this section.

A second methodological issue was that multiple measurements which were made of every component movement and surface area measurement were not in complete agreement (ie, velar displacement measured from endoscopy, base view fluoroscopy, and lateral view fluoroscopy; presence of VPI measured from endoscopy and three fluoroscopic views, etc). It was impossible within the limitations of this study with small numbers of subjects in each syndrome group, and also beyond the scope of this study, to test the correlation of measurements from each view. Previous research has shown that endoscopy often underestimates the amount of lateral pharyngeal wall motion because of the inability to see through moving tissue (Henningsson and Isberg, 1988; Shprintzen and Golding-Kushner, 1989). Also, movement seen in the en face fluoroscopic view may be misinterpreted if the lateral and frontal views are not examined to enable the observer to

distinguish movement at different vertical levels of the pharynx (Skolnick and Cohn, 1989). However, in this study, every tracing of the velopharyngeal port, including the endoscopic view, was measured independently of every other image.

VPI was often not detected in every view, especially in TC where velopharyngeal gaps were very small or inconsistent but, because of the emphasis in this study on quantification of gap size, the VPI prevalence statistic was based on the en face fluoroscopic and/or endoscopic views from which the surface area measurements were made. However, there were several cases in which VPI was detected in lateral or frontal view fluoroscopy but not revealed in en face or endoscopic view, perhaps related to a large adenoid area obscuring informative examination (Appendix E).

Differences among views may also have been related to ascertainment of subjects, subject selection for individual procedures, and procedural problems affecting the tracings from which measurements were made. For example, some subjects with perceived normal resonance did not have fluoroscopic examination to avoid unnecessary radiation exposure. If lateral and frontal view fluoroscopy showed absent movement, or if the patient was poorly cooperative, an en face view was not always done. Identification of the presence and shape of velopharyngeal gaps from endoscopy may have been influenced by photographic artifacts related to the interpretation of dark or light areas. When this resulted in interrater discrepancies, the videotape of the examination was jointly

reviewed until agreement was reached (and the agreed measure was included in the analysis of the experimental group data). However, both raters might have misinterpreted the photograph. Another problem related to photographic artifact was that of measuring and tracing a three dimensional image in a two dimensional plane. Large amounts of movement could often be seen on the videotape or even detected in the rest-phonation photograph pairs. However, if movement was upward toward the endoscope the overlaid tracings suggested small displacements. This problem did not arise in tracing the fluoroscopic images because movement images were already reduced to a single plane.

In order to reduce data for statistical analysis, two variables were created to combine data from endoscopy and videofluoroscopy, one to identify the presence of VPI (BASE-N-VPI) and one to quantify gap size (HABCLOS). However, this resulted in violation of one of the most fundamental concepts in the imaging of velopharyngeal closure, that diagnosis must be based on both nasopharyngoscopy and at least frontal and lateral view fluoroscopy (Skolnick et al., 1973; Skolnick and Cohn, 1989; Shprintzen and Golding-Kushner, 1989). Also, intermittent VPI was coded as "no VPI" because best closure was used as the standard. Even occasional VPI was apparently perceptually salient and resulted in a rating of +hypernasal. Conversely, there were five subjects with perceptually normal resonance in spite of VPI in all views (2 with S, 3 with VDW).

The degree of coupling between the nasal and oral cavities is one parameter affecting resonance. Coupling of the oral and nasal cavities causes changes in the acoustic spectrum of vowels in the region of the first formant (F1) with the insertion of a pole-zero pair[32] (House and Stevens, 1956). As velopharyngeal opening increases, the additional pole shows increased prominence because of increased spacing between the pole and zero and there may be an increase in the F1 bandwidth with a shift in vowel height toward neutral (Hawkins and Stevens, 1985). Curtis (1968) pointed out that the perception of hypernasality may depend on additional characteristics of the vocal tract and not only on the size of the velopharyngeal gap. Various characteristics of the vocal tract such as overall size of the resonator and characteristics of its lining (soft tissue characteristics) also play a role (Borden and Harris, 1980). Nasal resistance is another factor.

Velo-cardio-facial Syndrome

As reported in the literature, VCF was characterized by platybasia of the basicranium (Arvystas and Shprintzen, 1984). The posterior cranial base was short, and the mandibular body was small, consistent with Robin sequence. The velum in VCF was shortest and thinnest of all four syndromes at least in part because of a high prevalence of OSMCP and SMCP. The soft

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[32]A pole is a resonance or formant (energy band), in this case, the response of the coupled nasal cavity. An antiresonance is the decrease in formant intensity (diffusion of energy) because of increased size of the resonator.

tissue of the posterior pharyngeal wall at the level of the palatal plane and velar midpoint was also thinner than normal although the area of the adenoid as measured from lateral cephalograph was normal. However, the size of the functional adenoid, that is, the size of the adenoid at the plane of closure as seen endoscopically was deficient in half of the subjects, consistent with the thin PPW 1-2 measurement. Anteroposterior lengthening of the airway was present at all levels of the pharynx in VCF.

The highest hyoid placement occurred in VCF, resulting in the shortest vertical airway frame but the area of the airway was normal, suggesting that this shortening compensated for the increased width. The skeletal framework of the airway contained proportionately more lumen than the other three syndromes studied. The vertical level of the hyoid may have been related to age (the VCF group was the youngest). However, age peers with the other syndromes had longer palatal plane to hyoid distances. This may suggest a degree of laryngeal immaturity in VCF consistent with the relatively high prevalence of higher than normal vocal pitch which was present in 38% of the subjects in this subgroup (28% in the larger VCF group).

Velopharyngeal closure in VCF. VCF was the only syndrome with a bimodal distribution of velopharyngeal movement. Some subjects had excellent velar motion, and relatively small gaps. The relatively good motion which was present in 50% of the sample has not been reported to date but suggests that the

VCF population itself may be heterogeneous. However, even in the cases with relatively good closure, there tended to be very little LPW motion (most gaps were coronal or gross), and the little motion that occurred in some subjects resulted in a very small percentage of the pharynx traversed because of the increased distance in the large pharynx. Inter-LPW distance was not measured in this study, but both LPW's were rarely visible in a single endoscopic view (they were in TC), and inter-LPW distance in a prior study was increased (Shprintzen, 1982).

In half of the subjects with VCF, there was minimal or absent movement of the palate and lateral pharyngeal walls. Complete absence of velopharyngeal movement could not be attributed to increased pharyngeal width alone, although width explains low ratios when movement occurred.

Gereau and Shprintzen (1988) observed that all subjects with VCF who had good V-P closure also had large adenoids. As seen in Figure 5.3, it was more the case in the current sample that all subjects with VCF who had large adenoids (>40% of the closure plane) achieved (relatively) good velopharyngeal closure. The largest adenoid did not result in the smallest gap, and two of the six VCF subjects with good closure had small adenoids; both were under 7-1/2 years of age suggesting that their adenoid was small and not involuted. All four subjects with gross VPI had small adenoids (20% or less of the closure plane). In those subjects, velar and pharyngeal motion was nearly absent, suggesting that, as with pharyngeal width, adenoid hypoplasia alone was not the cause of VPI.

Pharyngeal hypotonia has been cited as one explanation for the severely deficient movement in VCF (Shprintzen, 1982; Arvystas and Shprintzen, 1984). The diagnosis of pharyngeal hypotonia was always based on the absence of movement during phonation. However, this appears to be a diagnosis by default or presumption. There may be some contribution of hypotonia to the VPI, but deglutition is unaffected and hypotonia might be expected express itself in some function other than speech. Perhaps hypotonia in the presence of reduced pharyngeal resistance (the combination of a large vocal tract and absent adenoid) affects the learning of volitional movements or those programmed for speech. The relationship between pharyngeal hypotonia and adenoid hypoplasia has not been studied. It is possible that they have a common etiology (VCF) and are separate abnormalities. It is also possible that there is some critical adenoid size needed to provide the nasopharyngeal impedance necessary to drive the speech system, below which muscle movement ceases. A phenomenon whereby velopharyngeal gestures appear to be abandoned has been referred to as "functional surrender" (Hagerty et al., 1968), "discouraged" motion (Morris, 1968), and "palatal surrender" (B. J. McWilliams, personal communication, September 3, 1991). This may help to explain the exacerbation of VPI which occurs during glottal stop speech and might also suggest a role for Passavant's ridge in both normal and cleft subjects. The ridge often occurs at a different vertical level than maximum velar movement and often seems not to contribute to velopharyngeal closure (Glaser et al, 1979). If there is a

critical resistance level needed to drive the vocal tract valves, then the ridge may serve an important function, even when not contributing directly to closure.

Support for the possibility that nasopharyngeal resistance plays a role not only in the modification of sounds, but actually in invoking pharyngeal motion may be inferred from observation of certain subjects using speech bulbs[33]. In many subjects with VPI, the pharyngeal portion of the appliance may be reduced in size over a period of several months, accompanied by an increase in pharyngeal wall motion thereby decreasing the severity or even the presence of VPI (Blakely, 1960, 1969; Golding-Kushner, 1988; Golding-Kushner and Cisneros, 1989; McGrath and Anderson, 1990). In almost every case, increases in pharyngeal motion obtained over successive reductions are maintained during phonation with the speech appliance removed (Golding-Kushner, 1988; Golding-Kushner and Cisneros, 1989). However, in two patients treated at CCFD[34], the presence of the bulb was necessary for any movement to occur. Excellent pharyngeal motion closing 95% of the velopharyngeal port was elicited with appliances in

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[33]The speech bulb is a type of prosthesis which sits in the velopharynx to provide velopharyngeal closure during phonation, serving a similar role as a pharyngeal flap. It consists of a palatal portion which provides retention, and a pharyngeal extension. The wire of the pharyngeal extension terminates in an acrylic bulb which is modified in size and position so as to provide obturation of a velopharyngeal gap during phonation.

[34]The patients were an 8 year old boy with generalized congenital hypotonia and normal palate and a 12 year old girl with OSMCP and ptosis but no other diagnosed neurological problems.

place which had been large at the beginning of treatment but had been significantly reduced until there remained only slightly more acrylic that necessary to cover the supporting wire. However, when the appliances were removed (during the same endoscopic examination), there was a relapse to gross VPI with no pharyngeal or velar motion. In both of these subjects, the presence of even the smallest bulb was enough to prompt excellent velopharyngeal closure but with the bulb removed there was no motion whatsoever. Excellent motion resumed as soon as the appliance was replaced.

The role of the adenoid in speech development has not been investigated. It is known that the adenoid serves an important mechanical function in velopharyngeal closure in children, serving as the focal point for normal velopharyngeal (velar-adenoidal) closure (Gereau and Shprintzen, 1988). The adenoid may be detected at birth but grows rapidly during the sixth to twelfth months of life (Kahane, 1988) and has its peak growth by four years of age (Subtelny and Koepp-Baker, 1956). This corresponds to critical periods of speech development and may suggest a role for the adenoid in the programming of planned movements, perhaps related to both structural and physiological functions.

Pharyngeal hypotonia has also been cited as a causative factor in the prevalence of glottal speech in VCF but has not been studied systematically (Gereau and Shprintzen, 1988; LeBlanc et al, 1990, 1991; LeBlanc and Golding-Kushner, 1991). However, it was clear that articulation development was not related to adenoid size or to so-called pharyngeal hypotonia

because 12 of the 13 subjects had glottal speech development and the one subject with normal articulation had a relatively small adenoid. The single subject with good articulation had good (89%) closure, but all other subjects with relatively good closure had glottal speech histories. All of the subjects had normal articulation placement at the time that their resonance was rated and at the time of velopharyngeal imaging studies. Thin posterior pharyngeal wall tissue measurements were a group characteristic, suggesting that individuals with VCF may have muscle thinning that could affect pharyngeal function for speech.

van der Woude Syndrome

Craniofacial morphology in VDW has not previously been described but, like VCF, was characterized by an obtuse cranial base angle and anteroposterior lengthening of the vocal tract at the velo- and oropharyngeal levels. The platybasia was not as severe as in VCF, but lumen depth at the level of the palatal plane was longer. In addition, the ramus was long and posteriorly positioned in relation to sella, but its length was within the normal range, with a slightly flattened mandibular plane, again with measurements within the normal range. The velum was short, with thinning of the soft tissue of the posterior pharyngeal wall at the level of velopharyngeal closure. The airway was slightly elongated, but not as long as in TC and, like the slightly increased lumen depth, may have reflected the slightly older age of the subjects in this group. However, area of the vocal tract was

WNL. The similarity in displacement ratios between VDW and S suggested that VDW subjects had better movement because they had pharyngeal depth size the same or larger than VCF but closed the port to the same degree as Stickler, in which structures had a smaller distance to traverse. In the presence of normal pharyngeal width, these subjects may well have achieved velopharyngeal closure.

Gereau and Shprintzen (1988) stated that all subjects with VDW who achieved good closure had large adenoids. However, in this sample, closure achieved was not related to adenoid size (Figure 5.4).

Based on these profiles which were derived from examination of the 45 subjects in the second part of this project, the third and fourth hypotheses are partially rejected as stated in the null form:

3. Craniofacial morphology within specific syndromes is not homogeneous (i.e., syndrome specific). [The range of scores within each syndrome showed more spread than the control group for many variables, but, for the most part, measurements within a syndrome group resembled each other more than across groups.]
4. Craniofacial morphology is not related to vocal tract (upper airway) size or configuration. [Rejected, but morphology is not the only factor in vocal tract size.]

Certain craniofacial features were distinctive to a particular syndrome, but similarities existed consistent with

classification of syndromes according to pharyngeal width. The presence of basicranial kyphosis in S and TC shortened the pharyngeal lumen anteroposteriorly. Shortening of the hard palate in Stickler syndrome may have partially compensated this effect, resulting in a closer to normal vocal tract depth. The abnormal configuration of the vocal tract in TC may have exacerbated the pharyngeal narrowing. In both VCF and VDW, platybasia of the cranial base increased pharyngeal depth. However, there was more homogeneity within diagnostic groups than within pharyngeal width groups and skeletal, morphological, and physiological differences between the pharyngeal width pairs were often obscured by the linking of syndromes which was necessary for statistical analysis. Pharyngeal depth was greater in VDW than in VCF, but platybasia and VPI were more severe in VCF.

The remaining hypotheses were related to velopharyngeal function:

5. There is no difference in the prevalence of velopharyngeal insufficiency (VPI) in association with a "narrow pharynx" versus a "wide pharynx".
6. Cranial base abnormalities are not associated with the frequency of VPI following palate repair.
7. Craniofacial morphology and airway size or configuration in specific syndromes are not related to differences in velopharyngeal closure patterns.

Hypothesis five as stated must be rejected. There was a significantly higher prevalence of VPI in the wide pharynx group than in the narrow pharynx group. However, there was again a syndrome effect indicating that pharyngeal width was not the only, perhaps not even the most important, factor in predicting VPI. The prevalence of VPI was lowest in TC, the syndrome associated with the narrowest pharynx. Based on pharyngeal width alone, it was surprising that VPI occurred at all in TC. The gaps in this group tended to be very small and inconsistent, a pattern which would probably be categorized as "borderline" closure by McWilliams et al (1990), or "sometimes-but-not-always" (SBNA) by Morris (1984, 1990). Furthermore, the VPI rate was higher in VCF than in VDW although both syndromes had significantly wider than normal pharyngeal depths.

Hypothesis six and seven are partially rejected as stated. There was a significantly higher prevalence of VPI after palate repair and in SMCP in the presence of an obtuse cranial base angle than in the presence of an acute basicranium, most likely because of the effect of the configuration of the cranial base in shortening or lengthening the pharyngeal depth. Pruzansky (1976) predicted a simple relationship whereby platybasia causes an increased antero-posterior pharyngeal diameter which will result in VPI even without cleft palate. However, as discussed already, configuration of the cranial base was clearly not the only factor in the presence or severity of VPI. There were five subjects with extremely kyphotic cranial base measurements

below 115°, three with TC and two with S. The three TC subjects exhibited 100% closure while the two subjects with S had 90% and 45% closure during phonation, perhaps because of a larger airway in S than in TC. On the other hand, the single Stickler subject with platybasia (N-S-B of 142°) had complete velopharyngeal closure.

ADDITIONAL CAUTIONS FOR INTERPRETING THE DATA

A number of issues which must be considered in interpreting the results of this project have already been discussed, among them sample size, possible sources of ascertainment bias, subject selection, and certain other methodological issues. Clearly, individuals who are most mildly affected with craniofacial syndromes may never be diagnosed because of relatively normal appearance and speech. It may also be that the most severely affected individuals do not survive infancy. Infant mortality in S and TC has been attributed to Robin related upper airway obstruction such as glossoptosis, and infants with VCF may succumb to this or severe cardiac defects. Therefore, it may be impossible to examine the craniofacial and vocal tract morphology, velopharyngeal closure, and speech in the most and least severe cases. A more purely ascertained sample would have to be drawn from other sources in addition to craniofacial/cleft centers. Subjects could then be examined for SMCP and their airways and speech could be studied. While presenting enormous logistical challenges, this would provide a greater appreciation of the spectrum of morphology and physiology of

these syndromes. This would provide information on the degree to which the groups in both parts of this study are representative samples.

Although other cephalometric data were collected, statistical analysis and discussion were limited to morphologic measurements which were in proximity to the vocal tract or thought to be associated with configuration of the pharyngeal lumen. Other craniofacial features pertaining to facial height and contour must be included in a complete description of syndrome morphology.

Table 5.1. Age, hypernasality, cranial base angle (N-S-B), and lumen depth at mid-velar level (Lum 2) of subjects with Treacher Collins syndrome. Note trend toward better resonance in older subjects.

CP #	Sex	Age (yr-mos)	Hypernasality[1]	N-S-B angle	Lum 2 depth (mm)
1903[2]	M	3-0	1.5	NA	NA
1656	M	5	1	138	16
2663[3]	M	6	2.0	126	4
3653[3]	M	8	0	124	8
1592	M	9	0	113	11
1156	F	12	0.5	125	5
2307	F	14	0.5	118	5
2129	F	17	0.5	125	7
1068	M	22	0	126	11
1132[3]	F	40	0	110	11
1110[3]	M	42	1.5	112	4
0005[2]	F	52	0	NA	NA

NA= not available

[1] severity rated on continuous scale from 0 (absent) to 3 (severe)

[2] speech reported in prevalence study; morphological and physiological data not available

[3] cleft lip and palate

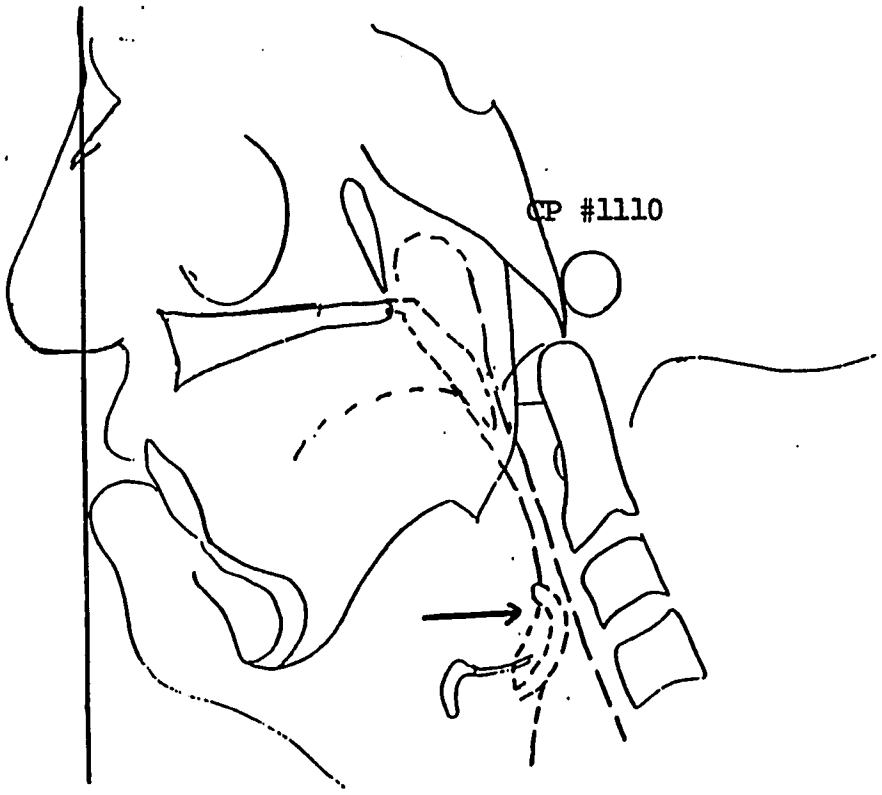

Figure 5.1. Lateral cephalometric tracing of subject with Treacher Collins syndrome showing forward curling of epiglottis.

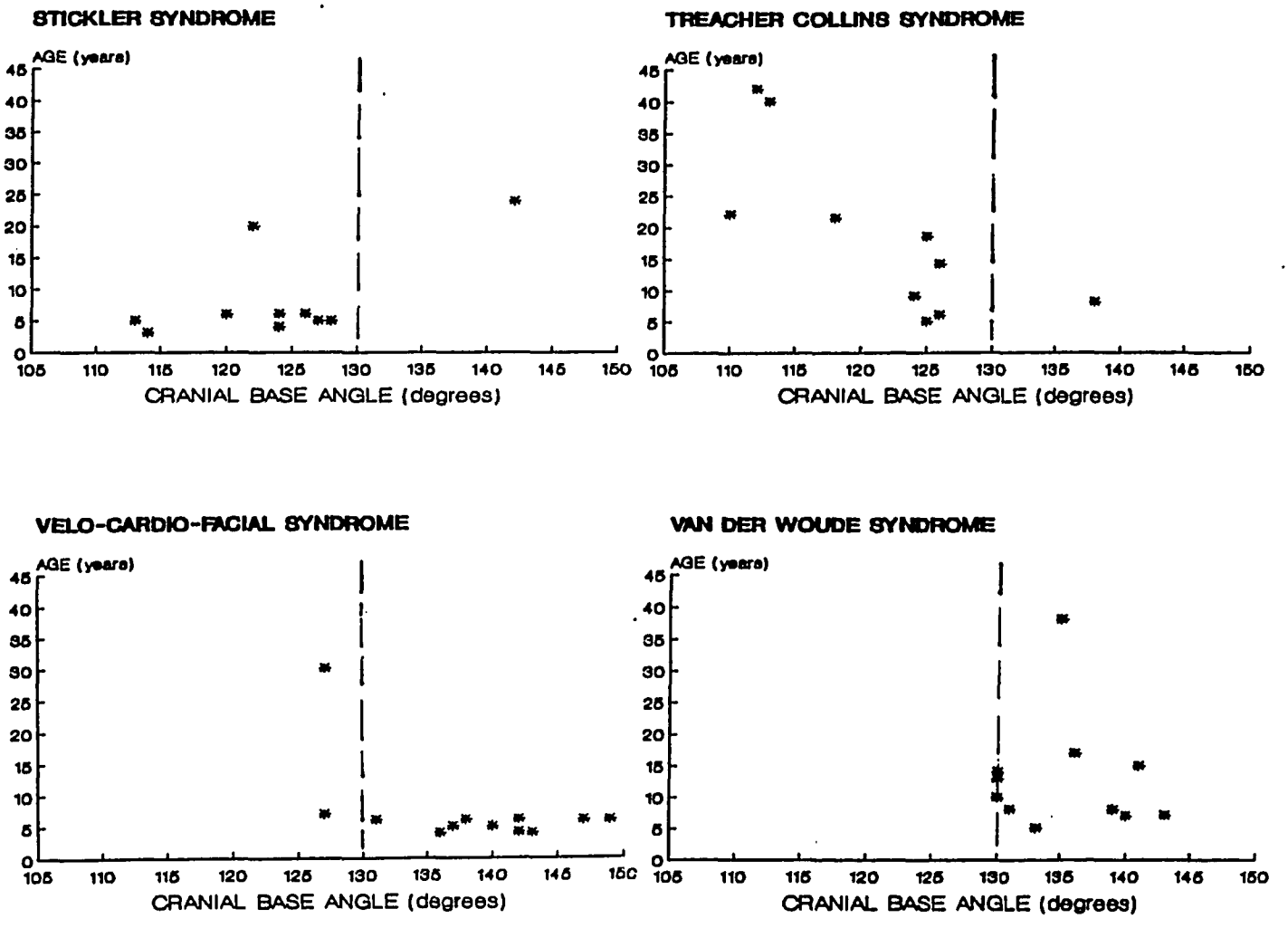

Figure 5.2. Scatterplot of cranial base angle (N-S-B) and age. In Treacher Collins syndrome, the cranial base was more kyphotic in older subjects than in younger subjects. (Mean cranial base angle for normals is 130^0.)

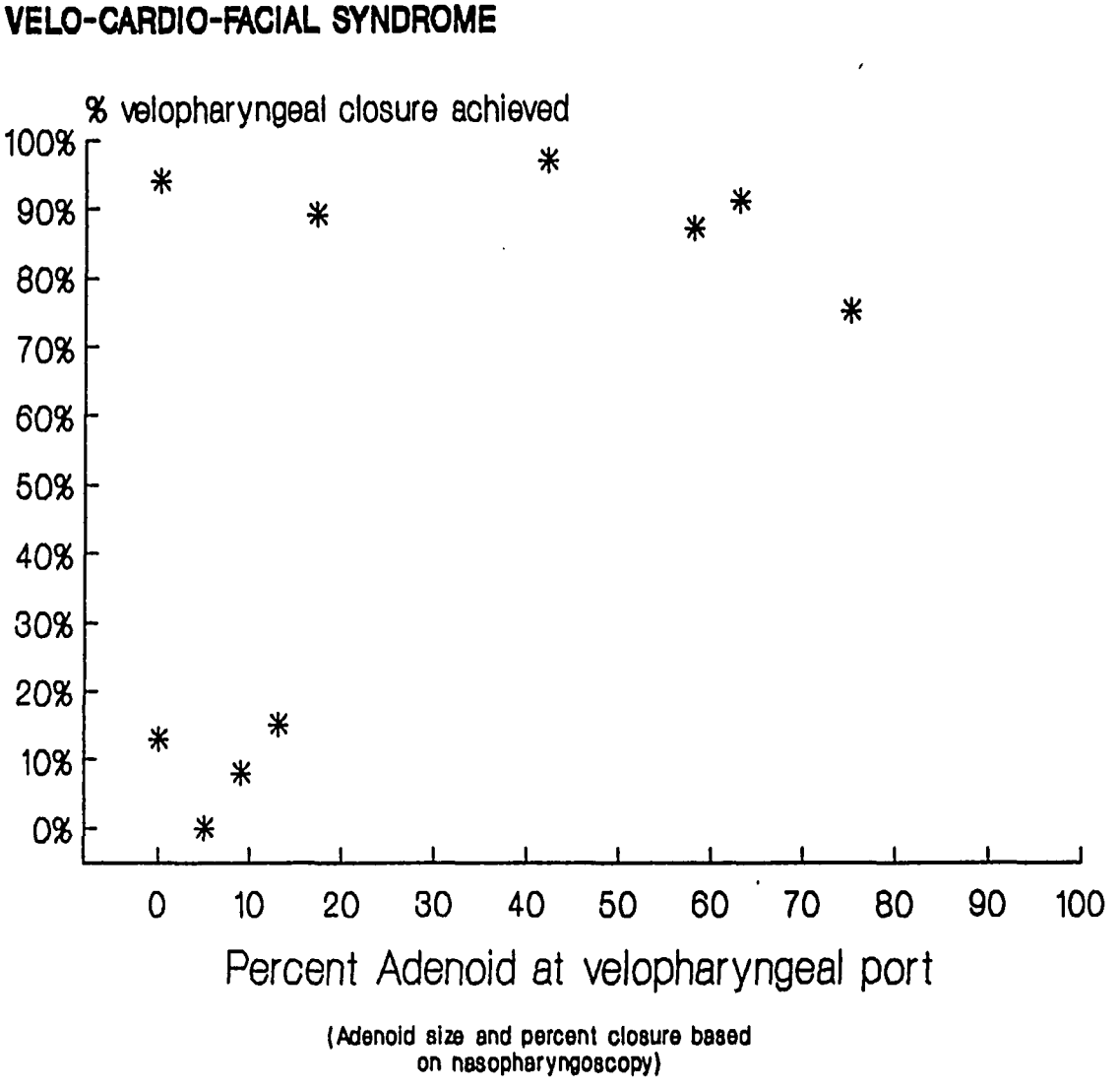

Figure 5.3. Relative adenoid size at the level of velopharyngeal closure and percent velopharyngeal closure achieved during sustained /s/ in velo-cardio-facial syndrome.

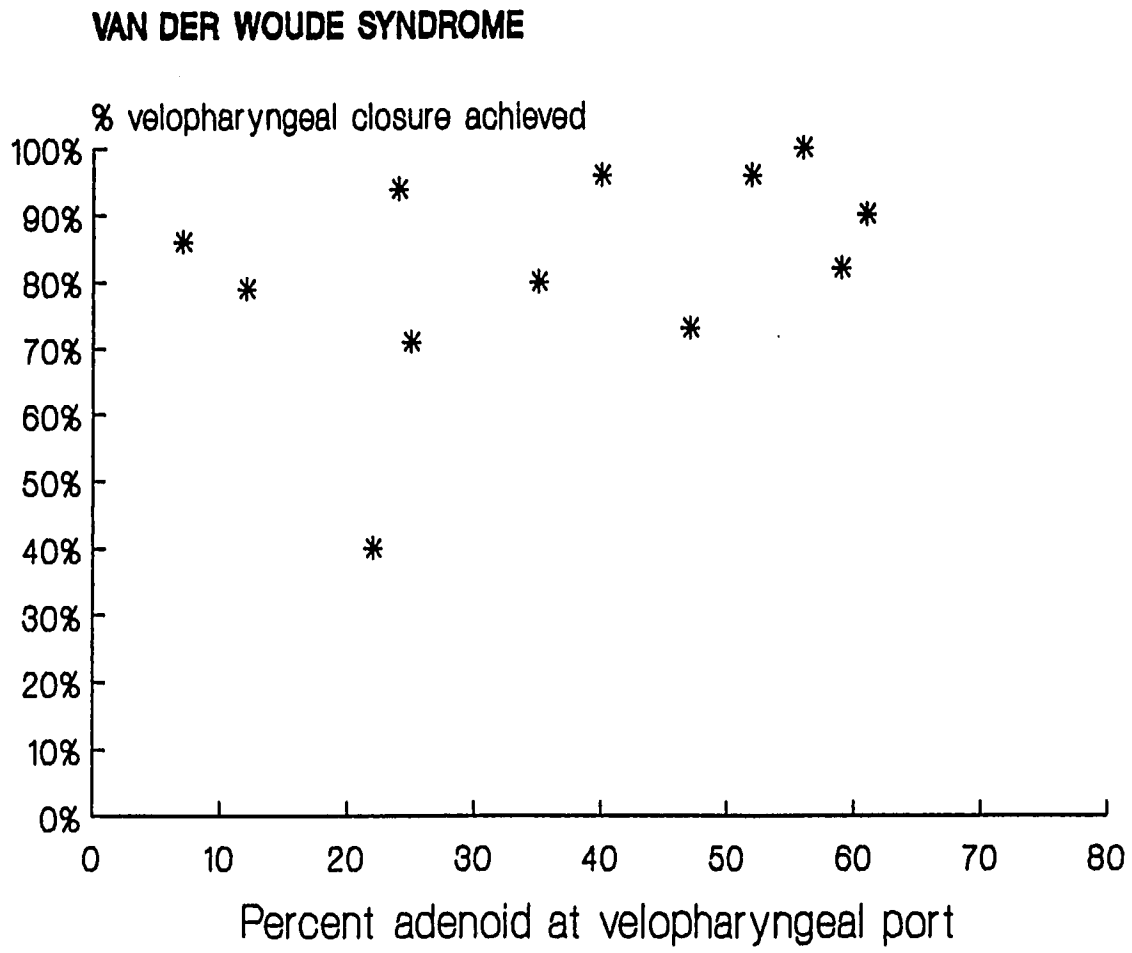

Figure 5.4. Relative adenoid size at the level of velopharyngeal closure and percent velopharyngeal closure achieved during sustained /s/ in van der Woude syndrome.

CHAPTER 6

SUMMARY

Sources of heterogeneity within the population of individuals with cleft palate might predispose certain patients to a particular speech outcome regardless of surgical technique or age at the time of primary palatoplasty. One possible source of variability in the speech production of subjects with cleft palate is skeletal morphology. Subjects with four syndromes associated with cleft palate, Stickler syndrome (S), Treacher Collins syndrome (TC), velo-cardio-facial syndrome (VCF), and van der Woude syndrome (VDW), were included in this study to examine the possibility that velopharyngeal function in subjects with clefts is influenced by differences in underlying cranial morphology and resultant vocal tract shape. Syndromic subsets of individuals with cleft palate were examined because morphology within a syndrome is presumed to vary less than in unselected clefts.

The preliminary part of this project was a study to identify the prevalence of resonance and articulation abnormalities in 129 individuals with cleft palate and these four syndromes. Information on the speech and resonance characteristics associated with specific syndromes provides guidance for the nature and timing of treatment and in expectations regarding palate repair. The second part of the project was a study of the morphologic characteristics and

velopharyngeal function in a portion of the same sample. Skeletal measurements and measurements of vocal tract depth and height were made from lateral cephalometric tracings. Measurements of velopharyngeal gestures and gap size were made from videotapes of nasopharyngoscopic and multi-view videofluoroscopic examinations. To increase the power of statistical analysis, syndromes were considered in pairs according to pharyngeal width.

CONCLUSIONS

Caution must be exercised in interpretation and generalization of the data. As in all clinical studies, biases exist at every level of investigation which may affect measurement outcome, beginning with the referral pattern to the institution(s) from which subjects are ascertained to the examinations to which they are subjected in the course of clinical management. However, several conclusions may be drawn.

1. Cranial base and vocal tract morphology and velopharyngeal closure is more homogeneous within craniofacial syndrome groups than within pharyngeal width groups. Craniofacial morphology and vocal tract configuration were most abnormal in Treacher Collins syndrome.

2. Craniofacial morphology was largely syndrome specific and was correlated with vocal tract size and configuration. Length of the anterior and posterior cranial base varied with the cranial base angle and lumen depth. Basicranial kyphosis shortened the pharyngeal lumen anteroposteriorly. Shortening of the hard palate in Stickler syndrome may have partially compensated this effect, resulting in a closer to normal vocal tract depth. The anterior cranial base in S was shorter than in TC, but the anticipated effect of this on the airway would be to decrease rather than increase pharyngeal depth. The abnormal configuration of the vocal tract in TC may have exacerbated the pharyngeal narrowing. Platybasia of the cranial base increased pharyngeal depth.

3. Craniofacial morphology, airway size, and airway shape in specific syndromes were related to differences in velopharyngeal closure patterns, but were not the sole determinants of VPI.

    a. There was a significantly higher prevalence of VPI in the wide pharynx group than in the narrow pharynx group. However, the VPI rate was higher in VCF than in VDW although both syndromes had significantly wider than normal pharyngeal depth.

b. There was a significantly higher prevalence of VPI after palate repair and in SMCP in the presence of an obtuse cranial base angle than in the presence of an acute basicranium, most likely because of the effect of the configuration of the cranial base in shortening or lengthening the pharyngeal depth.

c. Although subjects with TC had the lowest prevalence and severity of VPI, their patterns of velopharyngeal and lingual movements were most abnormal.

4. There was a difference in the prevalence and severity of VPI, resonance disorders, and compensatory speech disorders in different syndromes. Differences seemed to be related to cranial base angulation and vocal tract volume as well as to other factors, some of which remain unspecified.

a. The rank ordering of syndromes according to the prevalence and severity of VPI and VPI related speech disorders from lowest to highest was: Treacher Collins, Stickler with airway obstruction in infancy, Stickler without history of obstruction and van der Woude (no difference), and velo-cardio-facial syndrome. Hyponasality, muffled oral

resonance and tongue backing errors were most common in TC.

1) There seemed to be an age effect in TC which was interesting in light of increasing basicranial kyphosis with increasing age observed in longitudinal studies of TC. Speech symptoms were more apparent in younger subjects than in subjects in whom growth of the cranial base was complete. It must be kept in mind that this study was cross sectional and not longitudinal.

2) There seemed to be an airway-size effect in Stickler syndrome. Subjects with history of airway obstruction in infancy had better velopharyngeal closure and fewer speech symptoms than subjects who did not have early airway obstruction.

3) VCF was the only syndrome with a bimodal distribution of velopharyngeal movement, and the only syndrome of the four considered in which complete absence of movement occurred. Subjects with VCF had thin soft tissue of the posterior pharyngeal wall and thin, short soft palates suggesting muscle deficiency. Resonance in VCF was almost always moderately

to severely hypernasal, regardless of articulation and velopharyngeal gap size.

4) There was a very high prevalence of glottal stop speech in VCF which cannot be attributed to pharyngeal "hypotonia."

5. The presence and type of cleft palate should be considered in studies of craniofacial morphology and velopharyngeal physiology.

6. Hypernasality and glottal speech were significantly more prevalent in SMCP than in repaired overt clefts. This, along with the higher prevalence of diagnosed submucous clefts in the wide pharynx syndromes may reflect an ascertainment bias related to speech production. Subjects with VCF who have submucous cleft palate seem to be at highest risk for speech and resonance abnormalities because of the combination of structural and, possibly, neurologic abnormalities.

7. The measurement of adenoid size from nasopharyngoscopy and lateral cephalographs often did not agree with each other. The measurement of functional adenoid size was more valid from nasopharyngoscopy because it reflected the amount of tissue at the level of velopharyngeal closure which cannot be determined from still lateral radiographs.

8. Velopharyngeal movements must be examined using a minimum of three views including lateral and frontal videofluoroscopy and nasopharyngoscopy or en face MVF, and each view must be used to properly interpret every other view. Furthermore, no single measurement adequately represents velopharyngeal closure in a given subject. Multiple measurements should be provided.

   a. The Towne view had better agreement with other fluoroscopic views and endoscopy than the base view, although there were too few studies to determine if this was a consistent finding. Stringer and Witzel (1989) reported good agreement between nasopharyngoscopy and the Towne view.

   b. Multiple views were particularly important in subjects with a very narrow pharynx or an abnormally shaped pharynx, such as in TC, and in subjects who had a large percentage of adenoid tissue at in the field of view. In those cases, nasopharyngoscopy provided a view of tissue morphology and movement. However, the Towne and base views provided a more complete en face view because of the lack of interference by the palate or secretions with the view. Frontal view fluoroscopy provided the only view of lateral pharyngeal wall motion along the vertical extent of the pharynx and a more clear appreciation of

relative pharyngeal width. Lateral view provided the only unobstructed view of lingual motion which was essential for correct interpretation of velar motion, and a view of velar motion.

c. Multiple views were less important in subjects with gross VPI where nasopharyngoscopy clearly showed complete absence of motion and there was neither static nor moving tissue to obscure the view. However, even in those cases the frontal and lateral projections were often informative and some motion was at times detected.

d. Base view fluoroscopy was inadequate in Stickler and Treacher Collins syndromes.

9. Although velopharyngeal gap size cannot be meaningfully measured from lateral or frontal view videofluoroscopy, the presence of VPI can be reliably detected from these views. In TC, these views detected gaps which were missed in en face fluoroscopy and endoscopic studies.

10. Group ratings of videofluoroscopic examinations were much more reliable than individual ratings. This conclusion was also reached for ratings of nasopharyngoscopic examinations by D'Antonio et al, 1989.

DIRECTIONS FOR FUTURE RESEARCH

Many issues remain unresolved and deserve further investigation.

1. A three dimensional model of the vocal tract should be constructed to develop a more accurate model for the relationship between vocal tract abnormalities and perceived disorders of oral and nasal resonance. This may also help to explain the fact that some subjects with barely detected and intermittent velopharyngeal gaps present with abnormal hypernasality while some subjects with obvious VPI have perceptually normal speech.

2. Acoustic studies of subjects with craniofacial syndromes are needed to more accurately define oral and nasal resonance characteristics including those perceived as "muffled" or "hypernasal." Results should be correlated with vocal tract morphology (preferably 3-D reconstructions) and with velopharyngeal function.

3. It should be determined if there is a critical adenoid size and/or critical level of pharyngeal/nasopharyngeal resistance which is required to drive the vocal tract valves and to produce pharyngeal motion.

4. If a critical level of airway resistance exists, it should be determined if this requirement changes after speech production skills are established.

5. The morphologic characteristics and velopharyngeal movement patterns should be compared for cleft and noncleft subjects with the same syndromes. This issue arises because the V-P gaps in TC were often not central, i.e., not due to the palatal defect. The gaps seemed to be related to the other morphological abnormalities. Large enough samples should be examined to make possible separate consideration of subjects according to type of cleft (overt and submucous cleft palate, cleft lip and palate). In this study, 8 of the 10 Stickler clefts were overt and all of the VCF clefts were submucous. Comparison of the VDW data from this study with published reports suggest that VPI may be more prevalent and severe in cleft lip and palate than in cleft palate only. This may also be true in TC.

6. Craniofacial morphology and vocal tract size measurements were fairly homogeneous in VCF but there was a bimodal distribution of measurements of velopharyngeal closure. It is not known whether this is related to the vocal tract resistance issue raised above, or to the possibility that there are two distinct VCF populations. Studies of velo-cardio-facial syndrome at the genetic level are in progress, and the diagnosis has been confirmed at the molecular level in one of the subjects in this study with a large adenoid and good velopharyngeal closure (R. Goldberg, May 15, 1991,

personal communication). Genetic data when correlated with phenotype will provide some insight.

7. The prevalence of high pitched voice, hoarseness, and the suggestion of morphological immaturity of the larynx in VCF indicates a need for closer investigation of laryngeal function in VCF. Consideration should be given to the possible relationship between pharyngeal hypotonia, thin soft tissue within the vocal tract, and the vocal tract filter function. Acoustic and physiologic studies are needed.

8. The nature of the pharyngeal hypotonia presumed in VCF should be investigated.

9. Given the morphological differences between Stickler and van der Woude syndromes, large differences in their velopharyngeal gap size were predicted. It is possible that the subjects in this study represented the most sever Stickler cases in terms of clefting resulting in the largest Stickler vocal tracts, but the least severe (in terms of clefting) VDW subjects. Further research is needed to determine why large differences were not present.

10. Published longitudinal data indicates that the cranial base angle in TC becomes more acute with increasing age. The implications of this in vocal tract size and

articulation should be studied. On the other hand, cross sectional and limited longitudinal data suggest that the cranial base angle in S may become more obtuse with increasing age. Longitudinal data on skeletal and vocal tract growth is needed in all four syndromes.

11. Individuals with nonsyndromic cleft palate should be studied to determine if their velopharyngeal function varies with cranial base angle and vocal tract depth.

12. Larger numbers of subjects with craniofacial syndromes should be examined to gain an appreciation of the spectrum of craniofacial morphology, clefting, and velopharyngeal physiology. Multicenter studies are needed to obtain sufficient numbers of subjects, and should include subjects ascertained via Craniofacial and cleft palate centers as well as from other specialty clinics such as ophthalmology and cardiology.

Appendix A-1. Data collection form for prevalence study.

DEMOGRAPHIC AND SPEECH INFO

NA= info not available

COL#	LABEL
1	CP#_____
2	AGE AT REFERRAL TO CCFD _____
3	GENDER 1= male 2= female
4	ESTAB DX 1= S (1 & 2 "NARROW") 2= TC 3= VCF (3 & 4 "WIDE") 4= VDW
5	REFER DX 1= S 2= TC 3= VCF 4= VDW 5= Robin sequence 6= apnea/airway 7= cleft palate 8= failure to thrive (FTT) 9= speech/VPI 10= multiple congenital anomalies (MCA) 11= developmental delay 12= "abnormal" palate 13= suspected neurologic prob 14= malocclusion 15= psychological/psychiatric prob 16= micrognathia 17= no dx given
6	REF REASON 1= airway/apnea 2= cleft palate 3= feeding prob 4= FTT 5= to determine dx 6= speech/hypernasality 7= ears 8= devel delay 9= came w/family member 10= orthognathic/maxillofacial surg 11= pharyngeal flap/implant failure 12= no reason or dx stated as reason
7	CLEFT 1= overt cleft palate (CP) 2= submucous (SMCP) 3= occult SMCP (OSMCP)
8	REPAIR AGE _____ ("-"or 99.99 =no surgery)
9	GLOSSOPEXY/TRACHEOTOMY YES NO
10A	AUDIO-R 0= WNL TYPE: CHL 1= MILD LOSS S-N 2= MOD LOSS MIXED 3= SEVERE LOSS
10B	AUDIO-L 0= WNL TYPE: CHL 1= MILD LOSS S-N 2= MOD LOSS MIXED 3= SEVERE LOSS
11	ARTICULATION DEVELOPMENT 0= WNL 1= developmental errors 2= dental errors 3= intermit nasal turb/occas snort 4= glottal/compensatory 5= hearing related 6= tongue backing 7= nasal snort only 8= fistula related
12	ARTICULATION AT TIME OF TESTING 0= WNL 1= developmental errors 2= dental errors 4= glottal/compensatory 5= hearing related 6= tongue backing 7= nasal snort only 8= fistula related
13	HYPERNASALITY 0= NONE 1= MILD 2= MODERATE 3= SEVERE
14	HYPONASALITY 0= NONE 1= MILD 2= MODERATE 3= SEVERE
15	ORAL RESONANCE 0= WNL 2= CUL-DE-SAC 1= MUFF 3= POT-IN-MOUTH
16	VOCAL QUALITY 0= WNL 1= HOARSE
17	PITCH 0= WNL 1= HIGH 2= LOW
18a	RECEPTIVE LANGUAGE N= WNL L= LOW
18b	EXPRESSIVE LANGUAGE N= WNL L= LOW

Appendix A-2. Age at time of referral to CCFD and gender of subjects in prevalence study.

GROUP	MEDIAN AGE AT ASCERTAINMENT yr-mos Range (yrs)	MALE N Row % Column %	FEMALE N Row % Column %	TOTAL N Percent
STICKLER (S)	1-9 birth to 33	14 48.28 28.00	15 51.72 18.99	29 22.48
TREACHER COLLINS (TC)	12-0 birth to 52	5 45.45 10.00	6 54.55 7.59	11 8.53
VELO-CARDIO-FACIAL (VCF)	5-5 birth to 57	28 37.84 56.00	46 62.16 58.23	74 57.36
VAN DER WOUDE (VDW)	8-0 birth to 39	3 20.00 6.00	12 80.00 15.19	15 11.63
NARROW PHARYNX (S, TC)	3-9	19 47.50 38.00	21 52.50 26.58	40 31.01
WIDE PHARYNX (VCF, VDW)	6-0	31 34.83 62.00	58 65.17 73.42	89 68.99
TOTAL Percent	5-1	50 38.76	79 61.24	129 100.00

Referral age x Pharyngeal width: Kruskal-Wallis Test, $p<.02$
Referral age x Diagnosis: Kruskal-Wallis Test, $p<.002$

Gender x Pharyngeal width: Chi-square, $p=$ ns
Gender x Diagnosis: Chi-square, $p=$ ns

ns = not significant

Appendix A-3. Cleft type among subjects in prevalence study.

N Row % Column % GROUP	OVERT CLEFT PALATE	SUBMUCOUS CLEFT PALATE (SMCP)	OCCULT SMCP (OSMCP)	TOTAL Percent
STICKLER (S)	23 79.31 43.40	6 20.69 11.76	0	29 22.48
TREACHER COLLINS (TC)	4 36.36 7.55	7 63.64 13.73	0	11 8.53
VELO-CARDIO-FACIAL (VCF)	15 20.27 28.30	34 45.95 66.67	25 33.78 100.00	74 57.36
VAN DER WOUDE (VDW)	11 73.33 20.75	4 26.67 7.84	0	15 11.63
NARROW PHARYNX (S, TC)	27 67.50 50.94	13 32.50 25.49	0	40 31.01
WIDE PHARYNX (VCF, VDW)	26 29.21 49.06	38 42.70 74.51	25 28.09 100.00	89 68.99
TOTAL Percent	53 41.09	51 39.53	25 19.38	129 100.00

Cleft type x Pharyngeal width: Chi Square, $p<.0001$
Cleft type x Diagnosis: insufficient cell size for valid statistical analysis

Appendix A-4. Age of subjects in prevalence study at time of palate repair according to pharyngeal width and syndrome (Stickler= S, Treacher Collins= TC; velo-cardio-facial= VCF; van der Woude= VDW).

GROUP Syndrome	N	MEDIAN AGE at PALATE REPAIR	RANGE
NARROW PHARYNX	26	1 y 4 m	
S	22	1 y 4 m	6 m to 4 y 1 m
TC	4	1 y 4 m	1 y 2 m to 2 y
WIDE PHARYNX	26	1 y 3 m	
VCF	15	2 y	9 m to 4 y (12 y[35])
VDW	11	1 y	8 m to 1 y 4 m
TOTAL	52	1 y 4 m	6 m to 4 y

Age x Pharyngeal width: Kruskal-Wallis Test, ns
Age x Diagnosis: Kruskal-Wallis Test, $p<.04$
Age x Diagnosis (excluding single late-repair subject): ns

ns = not significant

[35]One subject with VCF had not undergone palate repair due to lack of services in her country of origin. She was referred to CCFD upon arrival in the U.S. at age 12 years and underwent surgery at that time. Her speech and resonance data were excluded from analysis.

Appendix A-5. Referring diagnosis (dx) of subjects in prevalence study.

N Column % Row % REFERRING DX	ESTABLISHED Dx: STICKLER (S) N=29	ESTABLISHED Dx: TREACHER COLLINS (TC) N=11	ESTABLISHED Dx: VELO-CARDIO-FACIAL (VCF) N=74	ESTABLISHED Dx: VAN DER WOUDE (VDW) N=15	NARROW PHARYNX (S, TC) N=40	WIDE PHARYNX (VCF, VDW) N=89	TOTAL Percent N= 129
CORRECT DX (col % only)	3 10.34	5 45.45	7 9.46	2 13.33	8	9	17 13.00
ROBIN SEQUENCE	15 51.72 78.95	2 18.18 10.53	2 2.70 10.53	0	17 42.50 89.47	2 2.25 10.53	19 14.73
AIRWAY OBSTR. (col % only)	0	0	1 1.35	0	0	1 1.12	1 .78
CLEFT PALATE	10 34.48 26.32	0	17 22.97 44.74	11 22.97 44.74	10 25.00 26.32	28 31.46 73.68	38 29.46
FAILURE TO THRIVE (col %)	0	0	2 2.70	0	0	2 2.25	2 1.55
SPEECH DISORDER or VPI	0	0	29 39.19 96.67	1 6.67 3.33	0	30 33.71 100.00	30 23.26
MULTIPLE CONGENITAL ANOMALIES	0	1 9.09 25.00	3 4.05 75.00	0	1 2.50 25.00	3 3.37 75.00	4 3.10
DEVEL DELAY (col %)	0	0	2 2.70	0	0	2 2.25	2 1.55
"ABNORMAL" PALATE	0	1 9.09 20.00	4 5.41 80.00	0	1 2.50 20.00	4 4.49 80.00	5 3.88
POSS NEURO DIS (Col %)	0	0	3 4.05	0	0	3 3.37	3 2.33
DENTOFACIAL DISORDER	0	0	1 1.35 50.00	1 6.67 50.00	0	2 2.25 100.00	2 1.55
PSYCHIATRIC DIS (col %)	0	0	1 1.35	0	0	1 1.12	1 .78
MICROGNATHIA	0	1 9.09 50.00	1 1.35 50.00	0	1 2.50 50.00	1 1.12 50.00	2 1.55
NO DX GIVEN	1	1	1	0	2	1	3 2.33

Chi-square: insufficient cell size for valid statistical analysis

Appendix A-6. Reason for referral to CCFD of subjects in prevalence study.

N Column % Row % REFERRAL REASON	ESTABLISHED Dx: STICKLER (S) N=29	ESTABLISHED Dx: TREACHER COLLINS (TC) N=11	ESTABLISHED Dx: VELO-CARDIO-FACIAL (VCF) N=74	ESTABLISHED Dx: VAN DER WOUDE (VDW) N=15	NARROW PHARYNX (S, TC) N=40	WIDE PHARYNX (VCF, VDW) N=89	TOTAL N Percent Total N=129
AIRWAY/APNEA	5 17.24 50.00	3 27.27 30.00	2 2.70 20.00	0	8 20.00 80.00	2 2.25 20.00	10 7.75
CLEFT PALATE	9 31.03 52.94	0	3 4.05 17.65	5 33.33 29.41	9 22.50 52.94	8 8.99 47.06	17 13.18
FEEDING PROBLEM (Column % only)	1 3.45	0	0	0	1 2.50	0	1 .78
FAILURE TO THRIVE (Column % only)	0	0	1 1.35	0	0	1 1.12	1 .78
POR DIAGNOSIS	1 3.45 33.33	0	2 2.70 66.67	0	1 2.50 33.33	2 2.25 66.67	3 2.33
SPEECH OR RESONANCE DISORDER	10 34.48 13.89	1 9.09 1.39	53 71.62 73.61	8 53.33 11.11	11 27.50 15.28	61 68.54 84.72	72 55.81
EAR PROBLEM (Column % only)	0	0	1 1.35	0	0	1 1.12	1 .78
DEVEL DELAY (Column % only)	0	0	1 1.35	0	0	1 1.12	1 .78
RELATIVE WAS A PATIENT	3 10.34 33.33	2 18.18 22.22	4 5.41 44.44	0	5 12.50 55.56	4 4.49 44.44	9 6.98
FOR TREATMENT OF DENTOFACIAL PROB	0	3 27.27 60.00	1 1.35 20.00	1 6.67 20.00	3 7.50 60.00	2 2.25 40.00	5 3.88
PHAR FLAP FAILURE (Column % only)	0	0	5 6.76	0	0	5 5.62	5 3.88
REASON NOT GIVEN OR DIAGNOSIS STATED AS REASON	0	2 18.18 50.00	1 1.35 25.00	1 6.67 25.00	2 5.00 50.00	2 2.25 50.00	4 3.10

Chi-square: insufficient cell size for valid statistical analysis

Appendix A-7. Surgical management of airway obstruction by glossopexy or tracheotomy among subjects in prevalence study.

N Row % Column % GROUP	SURGERY NEEDED	NO SURGERY	TOTAL
STICKLER (S)	10 34.38 66.67	19 65.52 16.67	29 22.48
TREACHER COLLINS (TC)	3 27.27 20.00	8 72.73 7.02	11 8.53
VELO-CARDIO-FACIAL (VCF)	2 2.70 13.33	72 97.30 63.16	74 57.36
VAN DER WOUDE (VDW)	0	15 100.00 13.16	15 11.63
NARROW PHARYNX (S, TC)	13 32.50 86.67	27 67.50 23.68	40 31.01
WIDE PHARYNX (VCF, VDW)	2 2.25 13.33	87 97.75 76.32	89 68.99
TOTAL Percent	15 11.63	114 88.37	129 100.00

Surgical airway management x Pharyngeal width:
Fisher's Exact Test, $p<.00001$

Surgical airway management x Syndrome:
insufficient cell size for valid statistical analysis

Appendix A-8. Audiometric data for worse ear of subjects in prevalence study based on the 3-frequency average of 500 Hz, 1000 Hz, and 2000 Hz[36].

N Row % Column % GROUP	NORMAL HEARING 0-25 db	MILD HEARING LOSS 26-45 dB	MODERATE HEARING LOSS 46-60 dB	SEVERE HEARING LOSS 61+ dB	TOTAL N %
STICKLER (S)	14 51.85 15.56	9 33.33 45.00	4 (incl. 2 mixed) 14.81 28.57	0	2 21.60
TREACHER COLLINS (TC)	0	2 20.00 10.00	7 70.00 50.00	1 mixed 10.00 100.00	10 8.00
VELO-CARDIO FACIAL (VCF)	62 84.93 68.89	8 10.96 40.00	3 4.11 21.43	0	73 58.40
VAN DER WOUDE (VDW)	14 93.33 15.56	1 6.67 5.00	0	0	15 12.00
NARROW PHARYNX (S, TC)	14 37.84 15.56	11 29.73 55.00	11 29.73 78.57	1 2.70 100.00	37 29.60
WIDE PHARYNX (VCF, VDW)	76 86.36 84.44	9 10.23 45.00	3 3.41 21.43	0	88 70.40
TOTAL Percent	90 72.00	20 16.00	14 11.20	1 .80	125 100.0 0

Chi-square: insufficient cell size for valid statistical analysis

[36]All losses conductive except as noted. Most subjects had normal hearing in at least one ear.

Appendix A-9. Receptive and expressive language skills of subjects in prevalence study.

N Row % Column % GROUP	RECEPTIVE LANGUAGE LOW	RECEPTIVE LANGUAGE NORMAL	EXPRESSIVE LANGUAGE LOW	EXPRESSIVE LANGUAGE NORMAL	TOTAL N Percent
STICKLER (S)	9 33.33 11.54	18 66.67 37.50	10 37.04 12.66	17 62.96 36.17	27 21.43
TREACHER COLLINS (TC)	5 50.00 6.41	5 50.00 10.42	6 60.00 7.59	4 40.00 8.51	10 7.94
VELO-CARDIO- FACIAL (VCF)	63 85.14 80.77	11 14.86 22.92	63 85.14 79.75	11 14.86 23.40	74 58.73
VAN DER WOUDE (VDW)	1 6.67 1.28	14 93.33 29.17	0	15 100.00 31.91	15 11.90
NARROW PHARYNX (S, TC)	14 37.84 17.95	23 62.16 47.92	16 43.24 20.25	21 56.76 44.68	37 29.37
WIDE PHARYNX (VCF, VDW)	64 71.91 82.05	25 28.09 52.08	63 70.79 79.75	26 29.21 55.32	89 70.63
TOTAL Percent	78 61.90	48 38.10	79 62.70	47 37.30	126 100.00

Receptive language x Diagnosis: Chi-square, $p<.0001$
Expressive language x Diagnosis: Chi-square, $p<.0001$

Receptive language x Pharyngeal width: Chi-square, $p<.0001$
Expressive language x Pharyngeal width: Chi-square, $p<.01$

Appendix A-10. Language according to audiometric status of subjects in prevalence study.

N Row % Column % HEARING[37]	NORMAL LANGUAGE	DELAYED LANGUAGE	TOTAL Percent
NORMAL 0-25 dB	28 43.08 68.29	37 56.92 71.15	65 69.89
MILD HL 26-45 dB	6 46.15 14.63	7 53.85 13.46	13 13.98
MODERATE HL 46-65 dB	7 50.00 17.07	7 50.00 13.46	14 15.05
SEVERE HL 66+ dB	0	1 100.00 1.92	1 1.08
TOTAL Percent	41 44.09	52 55.91	93 100.00

[37]Audiometric data for worse ear based on the 3-frequency average of 500 Hz, 1000 Hz, and 2000 Hz

Appendix A-11. Pattern of articulation development of subjects in prevalence study.

N Column % Row % ERROR TYPE	ESTABLISHED DIAGNOSIS: STICKLER (S)	ESTABLISHED DIAGNOSIS: TREACHER COLLINS (TC)	ESTABLISHED DIAGNOSIS: VELO-CARDIO-FACIAL (VCF)	ESTABLISHED DIAGNOSIS: VAN DER WOUDE (VDW)	NARROW PHARYNX (S, TC)	WIDE PHARYNX (VCF, VDW)	TOTAL N Percent
NORMAL	12 44.44 60.00	2 20.00 10.00	1 1.35 5.00	5 33.33 25.00	14 37.84 70.00	6 6.74 30.00	20 15.87
DEVELOPMENTAL ERRORS	2 7.41 16.67	1 10.00 8.33	8 10.81 66.67	1 6.67 8.33	3 8.11 25.00	9 10.11 75.00	12 9.52
ERRORS 2° MALOCCLUSION	1 3.70 25.00	2 20.00 50.00	0	1 6.67 25.00	3 8.11 75.00	1 1.12 25.00	4 3.17
NASAL ESCAPE or TURB ONLY (column %)	0	0	0	1 6.67	0	1 1.12	1 .79
GLOTTAL and VPI RELATED COMPENSATORY ERRORS	10 37.04 12.20	1 10.00 1.22	65 87.84 79.27	6 40.00 7.32	11 29.73 13.41	71 79.78 86.59	82 65.08
ERRORS 2° HEARING LOSS (column %)	1 3.70	0	0	0	1 2.70	0	1 .79
TONGUE BACKING (column %)	0	3 30.00	0	0	3 8.11	0	3 2.38
ISOLATED NASAL SNORTING	1 3.70 50.00	1 10.00 50.00	0	0	2 5.41 100.00	0	2 1.59
ERRORS 2° ORONASAL FISTULA (Column %)		0	0	1[38] 6.67	0	1 1.12	1 .79
TOTAL Percent	27 21.43	10 7.94	74 58.73	15 11.90	37 29.37	89 70.63	126 100.00

Chi-square: insufficient cell size for valid statistical analysis

Categories were combined for examination of trends as follows (see Results and Discussion):

Larger Category	Original categories included
Normal	Normal, Developmental, Obligatory errors (dental, hearing, nasal escape and reduced intraoral pressure due to VPI or oronasal fistula)
Glottal	Glottal and VPI-related compensatory (nasal snorting, pharyngeal fricatives)
Tongue backing	Tongue backing, isolated nasal snorting

[38]The fistula-related errors produced by this subject were nasal turbulence and a sibilant distortion which were "obligatory" based on the size and position of the fistula. They did not involve tongue placement errors which would have been considered compensatory and not obligatory.

Appendix A-12. Prevalence of articulation disorders according to syndrome and age at time of referral to Center for Craniofacial Disorders. Early subjects (E) were referred before age 2 years and late referrals (L) were over age 2 years.

Group	SS	SS	TCS	TCS	VCF	VCF	VDW	VDW
Early or Late	E	L	E	L	E	L	L	E
Number of Subjects	14	13	1	9	6	68	5	10
ARTIC DEVEL[39]	Percent of subjects in each group							
NORMAL	79	38	0	56	17	12	60	60
GLOTTAL	21	54	0	11	83	88	40	40
TONGUE BACKING	0	8	100	33	0	0	0	0

[39]Categories were combined for examination of trends as follows:

Category	Original categories included
Normal	Normal, Developmental, Obligatory errors (dental, hearing, nasal escape and reduced intraoral pressure due to VPI or oronasal fistula)
Glottal	Glottal and VPI-related compensatory (nasal snorting, pharyngeal fricatives)
Tong. bck	Tongue backing, isolated nasal snorting

Appendix A-13. Predominant articulation development patterns according to audiometric status (3-frequency average in worse ear) of subjects in prevalence study.

N Row % Column % HEARING	NORMAL ARTICULATION	GLOTTAL SPEECH	TONGUE BACKING	TOTAL Percent
NORMAL 0-25 dB	23 35.38 60.53	41 63.08 82.00	1 1.54 20.00	65 69.89
MILD HL 26-45 dB	6 46.15 15.79	6 46.15 12.00	1 7.69 20.00	13 13.98
MODERATE HL 46-60 dB	8 57.14 21.05	3 21.43 6.00	3 21.43 60.00	14 15.05
SEVERE HL 61+ dB	1 100.00 2.63	0	0	1 1.08
TOTAL Percent	38 40.86	50 53.76	5 5.38	93 100.00

Audio x Articulation: (Kruskal-Wallis Test, p=.0019)

Appendix A-14. Articulation according to language skills of subjects in prevalence study.

N Row % Column % ARTICULATION[40]	NORMAL LANGUAGE	DELAYED LANGUAGE	TOTAL Percent
NORMAL ARTICULATION[41]	24 63.16 58.54	14 36.84 26.92	38 40.86
GLOTTAL ARTICULATION	14 28.00 34.15	36 72.00 69.23	50 53.76
TONGUE BACKING	3 60.00 7.32	2 40.00 3.85	5 5.38
TOTAL Percent	41 44.09	52 55.91	93 100.00

Insufficient cell size for valid statistical analysis.

[40]Articulation prior to any therapeutic intervention.

[41]Includes normal, obligatory, and developmental errors.

Appendix A-15. Oral resonance of subjects in prevalence study.

N Row % Column % GROUP	NORMAL ORAL RESONANCE	MUFFLED ORAL RESONANCE	"POTATO-IN-THE-MOUTH" RESONANCE	TOTAL N Percent
STICKLER (S)	23 85.19 20.00	1 3.70 14.29	3 11.11 75.00	27 21.43
TREACHER COLLINS (TC)	5 50.00 4.35	5 50.00 71.43	0	10 7.94
VELO-CARDIO-FACIAL (VCF)	72 97.30 62.61	1 1.35 14.29	1 1.35 25.00	74 58.73
VAN DER WOUDE (VDW)	15 100.00 13.04	0	0	15 11.90
NARROW PHARYNX S, TC	28 75.68 24.35	6 16.22 85.71	3 8.11 75.00	37 29.37
WIDE PHARYNX VCF, VDW	87 97.75 75.65	1 1.12 14.29	1 1.12 25.00	89 70.63
TOTAL Percent	115 91.27	7 5.56	4 3.17	126 100.00

Abnormal oral resonance x Pharyngeal width:
Fisher's Exact Test, $p<.0002$
Oral resonance x Diagnosis: insufficient cell size for valid statistical analysis

Appendix A-16. Frequency and severity of hypernasality of subjects in prevalence study.

N Column % Row % GROUP	NORMAL RESONANCE	HYPERNASAL RESONANCE	SEVERITY OF HYPERNASALITY Number and Percent of the hypernasal subjects INTERMIT	MILD	MILD/MOD	MODERATE	MOD/SEV	SEVERE	MEAN SEVERITY
STICKLER (S) N=24	11 57.89 45.83	13 17.57 54.17	2 15%	6 46%	0	4 31%	0	1 8%	1.4
TREACHER COLLINS (TC) N=10	4 21.05 40.00	6 8.11 60.00	3 50%	1 17%	1 17%	1 17%	0	0	1.0
VELO-CARDIO- FACIAL (VCF) N=46	0	46 62.16 100.00	0	8 17%	0	14 30%	0	24 52%	2.3
VAN DER WOUDE (VDW) N=13	4 21.05 30.77	9 12.16 69.23	2 22%	2 22%	0	2 22%	1 11%	2 22%	1.7
NARROW PHARYNX (S, TC) N=34	15 78.95 44.12	19 25.68 55.88	5 26%	7 37%	1 5%	5 26%	0	1 5%	1.3
WIDE PHARYNX (VCF, VDW) N=59	4 21.05 6.78	55 74.32 93.22	2 4%	10 18%	0	16 29%	1 2%	26 47%	2.2
TOTAL N= 93 Percent	19 20.43	74 79.57	7 9%	17 23%	1 2%	21 28%	1 2%	27 36%	

Presence of hypernasality x pharyngeal width:
Fisher's Exact Test, $p<.00003$

Severity of hypernasality x syndrome:
Kruskal-Wallis Test, $p<.0001$

Severity of hypernasality- Post-hoc analysis:
VCF versus S/TC: Wilcoxon Rank Sum Test, $p<.0001$
VDW versus S/TC: Wilcoxon Rank Sum Test, not signif.

Appendix A-17. Nasal resonance according to type of cleft palate for subjects in prevalence study.

N Row % Column % RESONANCE	SUBMUCOUS AND OCCULT SUBMUCOUS CLEFT PALATE	REPAIRED OVERT CLEFT PALATE	TOTAL Percent
NORMAL NASAL RESONANCE	7 36.84 12.96	12 63.16 30.77	19 20.43
HYPERNASAL	47 63.51 87.04	27 36.49 69.23	74 79.57
TOTAL Percent	54 58.06	39 41.94	93 100.00

Hypernasality x Cleft type: Fisher's Exact Test, $p<.05$

Appendix A-18. Vocal quality of subjects in prevalence study according to hypernasality.

N Row % Column % RESONANCE	NORMAL VOCAL QUALITY	HOARSE VOCAL QUALITY	TOTAL Percent
NORMAL RESONANCE	17 94.44 21.79	1 5.56 7.14	18 19.57
HYPERNASAL	61 82.43 78.21	13 17.57 92.86	74 80.43
TOTAL Percent	78 84.78	14 15.22	92 100.00

Quality x Hypernasality: Fisher's Exact Test, p=ns

Appendix A-19. Frequency and severity of hyponasality of subjects in prevalence study. Mean severity rating is for hyponasal subjects only.

N Row % Column % GROUP	NORMAL	HYPONASAL RESONANCE	SEVERITY (N) INTERMIT	 MILD	MEAN SEVERITY RATING
STICKLER (S) N=24	22 92.7 25.3	2 8.3 33.33	0	2	1.0
TREACHER COLLINS (TC) N=10	8 80.0 9.2	2 20.0 33.33	1	1	.75
VELO-CARDIO-FACIAL (VCF) N=46	44 95.7 50.6	2 4.3 33.33	1	1	.75
VAN DER WOUDE (VDW) N=13	13 100.00 14.9	0	0	0	0.0
NARROW PHARYNX S, TC; N=34	30 88.2 34.5	4 11.8 66.66	1	3	
WIDE PHARYNX VCF, VDW; N=59	57 96.6 65.5	2 3.4 33.33	1	1	
TOTAL N=93 Percent	87 93.5	6 6.5	2	4	

Frequency of hyponasality x Pharyngeal width:
Fisher's Exact Test: ns

Severity of hyponasality x Pharyngeal width:
Wilcoxon Rank Sum Test: ns

Severity of hyponasality x Syndrome:
Kruskal-Wallis Test: ns

ns= not significant

Appendix A-20. Vocal quality of subjects in prevalence study.

N Row % Column % GROUP	NORMAL VOCAL QUALITY	HOARSE VOCAL QUALITY	TOTAL N Percent
STICKLER (S)	21 80.77 20.00	5 19.23 25.00	26 20.80
TREACHER COLLINS (TC)	10 100.00 9.52	0	10 8.00
VELO-CARDIO-FACIAL (VCF)	60 81.08 57.14	14 18.92 70.00	74 59.20
VAN DER WOUDE (VDW)	14 93.33 13.33	1 6.67 5.00	15 12.00
NARROW PHARYNX (S, TC)	31 86.11 29.52	5 13.89 25.00	36 28.80
WIDE PHARYNX (VCF, VDW)	74 83.15 70.48	15 16.85 75.00	89 71.20
TOTAL Percent	105 84.00	20 16.00	125 100.00
NO GLOSSOPEXY OR TRACHEOTOMY	94 83.19 89.52	19 16.81 95.00	113 90.40
GLOSSOPEXY OR TRACHEOTOMY	11 91.67 10.48	1 8.33 5.00	12 9.60
TOTAL Percent	105 84.00	20 16.00	125 100.00

Quality x Pharyngeal width: Fisher's Exact Test, ns

Quality x airway surgery: Fisher's Exact Test, ns

Quality x syndrome: insufficient cell size for valid statistical analysis

ns= not significant

Appendix A-21. Vocal pitch of subjects in prevalence study.

N Row % Column % GROUP	NORMAL VOCAL PITCH	HIGH PITCH	LOW PITCH	TOTAL N Percent
STICKLER (S)	23 88.46 23.47	1 3.85 4.17	2 7.69 66.67	26 20.80
TREACHER COLLINS (TC)	7 70.00 7.14	2 20.00 8.33	1 10.00 33.33	10 8.00
VELO-CARDIO-FACIAL (VCF)	53 71.62 54.08	21 28.38 87.50	0	74 59.20
VAN DER WOUDE (VDW)	15 100.00 15.31	0	0	15 12.00
NARROW PHARYNX S, TC	30 83.33 30.61	3 8.33 12.50	3 8.33 100.00	36 28.80
WIDE PHARYNX VCF, VDW	68 76.40 69.39	21 23.60 87.50	0	89 71.20
TOTAL Percent	98 78.40	24 19.20	3 2.40	125 100.00
NO GLOSSOPEXY OR TRACH	89 78.76 90.82	22 19.47 91.67	2 1.77 66.67	113 90.40
GLOSSOPEXY OR TRACH	9 75.00 9.18	2 16.67 8.33	1 8.33 33.33	12 9.60
TOTAL Percent	98 78.40	24 19.20	3 2.40	125 100.00

Insufficient cell size for valid statistical analysis

Appendix A-22. Demographic, speech, language, and audiometric data of subjects in prevalence study. Listed by cleft type within syndrome group. (Codes defined in Appendix A-1).

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
CP#	REF AGE	SEX	EST DX	REF DX	REF REAS	CP	REP AGE	GLO TRA	AUD	ART DEV	ART TST	HY-PER	HY-PO	ORAL RES	VOC QUA	P	LAN R,E
1774	0.02	2	1	5	2	1	1.10	N	0	0	0	0	0	0	0	0	N,N
3734	0.03	1	1	1	2	1	0.10	Y	0	1	1	0	0	0	0	0	N,N
3476	19.00	2	1	1	6	1	1.00	N	1	2	1	2	0	1	1	2	L,L
3642	0.01	1	1	7	2	1	1.02	Y	0	0	0	0	0	0	0	0	N,N
3122	0.00	1	1	5	1	1	0.10	Y	1	0	0	1	0	0	0	0	N,N
2708	0.01	1	1	5	3	1	-	N	NA	NA	NA	NA	NA	NA	NA	NA	NA
2643	0.05	1	1	5	2	1	1.03	N	0	1	1	1	0	0	0	0	N,L
1829	2.09	1	1	5	6	1	1.03	N	0	4	4	3	0	0	0	0	N,N
2267	5.01	1	1	7	9	1	1.06	Y	0	0	0	0	0	3	0	0	L,L
1330	12.02	2	1	7	6	1	1.08	N	1	4	0	2	0	0	0	0	N,N
722	0.00	1	1	7	2	1	1.08	N	0	4	0	3	0	0	0	1	L,L
1505	4.00	2	1	5	6	1	3.06	Y	1	4	0	1	0	0	0	0	L,L
3098	0.00	2	1	5	1	1	0.09	Y	0	0	0	0	0	0	0	0	N,N
1075	13.00	2	1	5	6	1	1.08	N	0	4	0	1	0	0	1	0	N,N
175	0.07	2	1	5	2	1	2.02	Y	0	4	7	1	0	0	0	0	L,L
3786	4.05	2	1	7	6	1	1.11	N	1	4	0	0.5	0	3	0	0	N,N
802	1.00	2	1	5	2	1	1.00	N	0	0	0	0.5	0	0	0	0	L,L
2100	2.01	2	1	5	1	1	0.11	Y	NA	NA	NA	NA	NA	NA	NA	NA	NA
1991	1.10	1	1	1	5	1	3.00	N	2	4	1	2	0	0	0	0	N,N
2649	0.01	1	1	5	1	1	1.03	Y	2	0	0	0	1	0	TR	TR	L,L
2268	0.03	1	1	5	1	1	0.08	Y	2	0	0	0	1	0	1	2	L,L
932	3.09	1	1	5	6	1	4.01	N	1	4	NA	3	0	0	1	0	N,N
1177	1.11	2	1	7	2	1	2.03	N	1	0	0	0	0	0	0	0	N,N
4	32.00	2	1	7	9	2	-	N	2	5	5	1	0	0	0	0	N,N
1931	0.02	1	1	5	2	2	-	N	0	0	0	0	0	0	0	0	N,N
3	30.00	2	1	17	9	2	-	N	0	0	0	0	0	0	0	0	N,N
2228	5.00	2	1	7	6	2	-	N	1	4	4	1	0	0	0	0	L,L

Appendix A-22 (continued). Demographic, speech, language, and audiometric data of subjects in prevalence study.

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
CP#	REF AGE	SEX	EST DX	REF DX	REF REAS	CP	REP AGE	GLO TRA	AUD	ART DEV	ART TST	HY-PER	HY-PO	ORAL RES	VOC QUA	P	LAN R,E
3453	5.03	1	1	7	6	2	-	N	0	7	0	0	0	3	0	0	N,N
3236	5.04	2	1	7	6	2	-	N	1	0	0	2	0	0	1	0	N,N
2663	6.02	2	2	5	10	1	2.00	Y	1	7	0	2	0	0	0	0	L,L
1903	0.01	1	2	5	1	1	1.06	Y	2	6	6	1.5	0	0	0	0	L,L
2307	14.00	2	2	2	1	1	1.02	N	2	1	1	0.5	0.5	0	0	0	N,N
3575	0.00	1	2	2	1	1	1.04	Y	NA	NA	NA	NA	NA	NA	NA	NA	NA
1132	40.00	2	2	2	9	2	-	N	2	2	2	0	0	1	0	1	N,N
1656	5.00	1	2	12	6	2	-	N	2	6	1	1	0	1	0	0	N,L
1156	12.00	2	2	2	12	2	-	N	2	4	1	0	1	1	0	0	L,L
2129	17.00	2	2	16	10	2	-	N	2	6	2	0.5	0	0	0	0	N,N
1592	9.00	1	2	2	12	2	-	N	3	0	0	0.5	0	1	0	1	L,L
1068	22.00	1	2	10	10	2	-	N	2	2	2	0	0	1	0	2	N,N
5	52.00	2	2	17	9	2	-	N	1	0	0	0	0	0	0	0	L,L
2998	3.08	1	3	7	6	1	2.01	N	0	4	0	2	0	0	1	1	N,N
2501	0.01	2	3	7	2	1	1.01	N	0	4	4	3	0	0	0	1	L,L
3678	5.00	1	3	3	6	1	1.06	N	0	4	4	3	0	0	0	1	L,L
2747	22.00	2	3	9	11	1	1.30	N	0	4	0	2	0	0	0	0	L,L
1606	6.03	2	3	7	6	1	2.11	N	1	4	1	3	0	0	0	0	L,L
942	4.00	2	3	10	6	1	2.00	N	2	1	0	3	0	0	1	0	L,L
1426	16.06	2	3	7	6	1	1.03	N	0	4	0	3	0	0	0	0	L,L
610	0.02	2	3	3	2	1	1.02	N	1	4	4	3	0	0	0	0	L,L
3369	0.00	1	3	6	1	1	0.11	Y	NA	4	NA	3	0	0	0	1	L,L
3494	13.00	2	3	7	6	1	12.0	N	0	4	4	3	0	0	0	0	L,L
2727	9.05	2	3	3	6	1	1.00	N	0	4	0	3	0	0	0	0	L,L
1526	0.03	1	3	5	2	1	1.05	N	1	4	4	3	0	0	0	0	N,N
2	26.00	2	3	7	9	1	2.06	N	0	4	1	2	1	0	1	0	N,N
917	15.00	1	3	7	6	1	4.05	N	0	4	0	2	0	0	1	0	L,L
772	11.00	2	3	7	6	1	2.00	N	0	4	0	1	0	0	0	1	L,L

Appendix A-22 (continued). Demographic, speech, language, and audiometric data of subjects in prevalence study.

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
CP#	REP AGE	SEX	EST. DX	REF DX	REF REAS	CP	REP AGE	GLO TRA	AUD	ART DEV	ART TST	HY-PER	HY-PO	ORAL RES	VOC QUA	P	LAN R,E
2739	2.03	1	3	7	6	2	-	N	0	4	0	1	0	0	0	1	L,L
2115	30.00	2	3	9	6	2	-	N	1	4	0	2	0	0	0	1	L,L
725	5.09	2	3	9	6	2	-	N	0	4	1	3	0	0	0	0	L,L
2109	0.03	1	3	5	1	2	-	Y	1	4	4	3	0	0	0	1	L,L
2585	57.00	2	3	12	6	2	-	N	0	4	0	3	0	0	0	0	L,L
1282	9.11	1	3	12	6	2	-	N	0	4	0	3	0	0	0	0	L,L
2516	4.00	1	3	3	6	2	-	N	0	4	4	3	0	0	0	0	L,L
864	5.00	2	3	9	6	2	-	N	2	4	1	3	0	0	0	0	L,L
1273	13.04	1	3	3	12	2	-	N	0	1	1	3	0	0	0	0	L,L
984	6.05	1	3	10	6	2	-	N	0	1	0	2	0	0	0	0	L,L
2485	5.00	1	3	11	11	2	-	N	0	1	0	2	0	0	0	0	L,L
2234	6.00	2	3	11	6	2	-	N	0	4	4	3	0	0	0	0	L,L
3300	4.01	2	3	9	6	2	-	N	0	4	4	3	0	0	0	1	L,L
3770	6.02	1	3	7	6	2	-	N	0	0	0	1	0	0	0	1	N,N
1267	7.00	2	3	7	11	2	-	N	1	4	1	1	0	0	0	0	L,L
579	4.09	2	3	9	6	2	-	N	0	4	0	3	0	0	0	1	L,L
1578	17.60	2	3	16	10	2	-	N	0	4	2	1	0	1	1	0	L,L
2402	19.00	2	3	14	6	2	-	N	0	4	0	1	0	0	0	0	L,L
1	24.50	2	3	17	9	2	-	N	0	4	0	3	0	0	0	0	L,L
3020	4.09	2	3	9	6	2	-	N	0	4	4	3	0	0	1	0	N,N
2059	25.00	2	3	13	6	2	-	N	0	4	0	2	0	0	0	0	N,N
1230	5.00	1	3	9	6	2	-	N	0	4	4	3	0	0	0	0	L,L
1439	11.08	2	3	13	6	2	-	N	0	4	0	3	0	0	0	0	L,L
2543	5.00	1	3	7	6	2	-	N	0	4	4	1	0	0	0	0	L,L
595	0.06	2	3	8	4	2	-	N	0	1	0	1	0	0	0	0	L,L
1335	17.00	2	3	15	6	2	-	N	0	4	0	3	0	0	1	0	L,L
2549	35.00	1	3	7	9	2	-	N	0	4	0	2	0	0	0	0	L,L
2982	3.00	2	3	7	6	2	-	N	0	4	0	3	0	3	0	0	L,L

Appendix A-22 (continued). Demographic, speech, language, and audiometric data of subjects in prevalence study.

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
CP#	REF AGE	SEX	EST DX	REF DX	REF REAS	CP	REP AGE	GLO TRA	AUD	ART DEV	ART TST	HY-PER	HY-PO	ORAL RES	VOC QUA	P	LAN R,E
2158	9.00	2	3	9	6	2	-	N	0	4	0	2	0	0	0	0	L,L
2056	11.00	2	3	12	6	2	-	N	0	4	1	2	0	0	0	0	L,L
2442	3.06	1	3	9	6	2	-	N	0	4	4	3	0	0	1	0	L,L
3137	37.00	1	3	7	6	2	-	N	1	4	4	3	0	0	0	0	L,L
1648	3.05	1	3	7	8	2	-	N	0	4	0	3	0	0	0	1	L,L
2755	5.05	2	3	7	6	2	-	N	0	4	0	3	0	0	0	1	N,N
2150	13.00	1	3	12	6	3	-	N	0	4	1	3	0.5	0	0	0	L,L
941	5.00	1	3	9	6	3	-	N	0	4	4	3	0	0	1	0	L,N
2644	6.06	2	3	9	9	3	-	N	0	4	0	3	0	0	0	0	N,N
2421	10.00	2	3	9	6	3	-	N	0	4	0	2	0	0	0	0	L,L
711	4.00	2	3	9	6	3	-	N	0	4	0	2	0	0	0	1	L,L
1239	7.00	2	3	9	6	3	-	N	1	4	0	3	0	0	0	0	L,L
2524	3.00	2	3	9	6	3	-	N	0	4	0	2	0	0	1	1	L,L
638	3.02	2	3	10	6	3	-	N	0	1	1	3	0	0	1	1	L,L
2368	3.04	2	3	3	7	3	-	N	0	1	0	1	0	0	0	0	L,L
3423	6.01	1	3	8	5	3	-	N	0	4	4	3	0	0	0	1	L,L
3002	19.00	2	3	3	5	3	-	N	0	4	0	1	0	0	0	0	L,L
2828	4.00	1	3	9	6	3	-	N	0	4	4	3	0	0	0	0	N,L
1875	5.00	1	3	9	6	3	-	N	2	1	1	2	0	0	0	0	L,L
2318	4.00	2	3	9	6	3	-	N	0	4	4	3	0	0	1	0	L,L
2895	5.06	2	3	13	11	3	-	N	0	4	0	3	0	0	0	1	L,L
1227	4.09	2	3	9	6	3	-	N	0	4	NA	3	0	0	0	0	N,N
1778	5.00	1	3	9	6	3	-	N	0	4	0	3	0	0	0	0	L,L
741	4.01	2	3	9	6	3	-	N	0	4	0	3	0	0	0	0	L,L
1452	4.08	2	3	9	6	3	-	N	0	4	1	3	0	0	0	0	L,L
2963	7.08	1	3	9	11	3	-	N	0	4	0	2	0	0	0	0	L,L
2006	6.00	2	3	9	6	3	-	N	0	4	0	3	0	0	0	1	L,L
978	12.00	1	3	9	6	3	-	N	0	4	0	2	0	0	1	1	N,N

Appendix A-22 (continued). Demographic, speech, language, and audiometric data of subjects in prevalence study.

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
CP#	REF AGE	SEX	EST DX	REF DX	REF REAS	CP	REP AGE	GLO TRA	AUD	ART DEV	ART TST	HY-PER	HY-PO	ORAL RES	VOC QUA	P	LAN R,E
2877	5.03	1	3	9	6	3	-	N	0	4	4	2	0	0	0	1	L,L
3235	4.01	2	3	9	6	3	-	N	0	4	4	2	0	0	0	0	L,L
1953	5.00	2	3	9	6	3	-	N	0	4	4	3	0	0	1	0	L,L
3175	0.06	1	4	7	2	1	0.10	N	0	8	0	0	0	0	0	0	N,N
2244	22.00	2	4	7	6	1	1.00	N	0	0	0	2	0	0	0	0	N,N
1070	0.00	2	4	4	2	1	1.05	N	0	4	0	0	0	0	0	0	N,N
2980	8.00	2	4	7	6	1	1.00	N	0	4	4	3	0	0	0	0	N,N
3617	0.01	2	4	7	2	1	0.11	N	1	NA	1	0.5	0	0	0	0	N,N
794	0.05	1	4	7	2	1	0.11	N	0	0	0	0.5	0	0	0	0	N,N
1651	0.00	2	4	4	2	1	1.04	N	0	4	0	0	0	0	0	0	N,N
2883	9.00	2	4	7	12	1	1.00	N	0	0	0	3	0	0	0	0	N,N
2274	6.03	1	4	7	6	1	1.05	N	0	4	4	2	0	0	0	0	L,N
2596	16.00	2	4	7	6	1	1.03	N	0	4	0	3	0	0	0	0	N,N
3525	15.00	2	4	14	10	1	1.00	N	0	2	2	0	0	0	0	0	N,N
1369	14.08	2	4	7	6	2	-	N	0	4	0	2	0	0	1	0	N,N
1831	8.03	2	4	7	6	2	-	N	0	0	0	2.5	0	0	0	0	N,N
3161	7.09	2	4	9	6	2	-	N	0	1	0	1	0	0	0	0	N,N
2459	39.00	2	4	7	6	2	-	N	0	0	0	1	0	0	0	0	N,N

Appendix B-1. Pearson Correlation Coefficients (*r*) and levels of significance (*p*) for interrater reliability of cephalometric measurements. Values are listed for entire sample (ALL), narrow pharynx group (NAR), and wide pharynx group (WIDE).

VARIABLE	*r* ALL	*p* ALL	*r* NAR[1]	*p* NAR	*r* WIDE[2]	*p* WIDE
H-N-S	.99	.0001	.99	.0001	.99	.0001
N-S	.98	.0001	.98	.0001	.97	.0001
LUM 2	.96	.0001	.93	.0003	.96	.0001
LUM 3	.91	.0001	.95	.0001	.90	.0001
LUM 5	.95	.0001	.93	.0003	.97	.0001
PPW 2	.93	.0001	.90	.0009	.96	.0001
PPW 4	.87	.0001	.91	.0006	.84	.0002
PPW 5	.81	.0001	.89	.0011	.78	.0010
A-PPW	.76	.0001	.53	ns	.84	.0002
PP1-PPW	.77	.0001	.93	.0003	.68	.0077

ns = not significant

[1] narrow pharynx = Stickler, Treacher Collins syndromes

[2] wide pharynx = velo-cardio-facial, van der Woude syndromes

Appendix B-2. Comparison of selected cephalometric measurements on normal control subjects to published population data.

	CONTROLS (THIS STUDY)		NORMAL (PUBLISHED)		
VARIABLE	**MEAN**	**S.D.**	**MEAN**	**S.D.**	**REFERENCE**
AGE	8.9	1.3	9.0		Riolo et al, 1974
LINEAR (mm)					
S-B	44.3	2.7	43.0	2.7	Riolo et al, 1974
S-Ar	30.5	2.9	32.0	2.6	Riolo et al, 1974
N-S	70.7	3.7	69.0	3	Bjork, 1955
Go-Me	69.7	5.0	67.1	3.1	Riolo et al, 1974
Ar-Go	39.7	4.1	42.0	3.5	Bjork, 1955
PNS-ANS	50.7	3.7	52.3	2.9	Riolo et al, 1974
ANGULAR (°)					
PPl-MPl	29.4	3.8	27.9	4.3	Riolo et al, 1974
FH-MPl	28.9	5.0	29.0	4.9	Riolo et al, 1974
N-S-B	130.9	4.2	129.7	4.6	Riolo et al, 1974
N-S-Ar	125.0	3.8	123.0	5.0	Bjork, 1955

Appendix B-3. Median values, ranges and significance levels for cephalometric measurements (in alphabetical order) according to pharyngeal width and syndrome[42].

Median Range VARIABLE	CONTROL (CTL) N=15	NARROW (NAR) (S, TC) N=20	WIDE (VCF, VDW) N=25	STICKLER (S) N=10	TREACHER COLLINS (TC) N=10	VELO-CARDIO-FACIAL (VCF) N=13	VAN DER WOUDE (VDW) N=12	P NAR x CTL	P WIDE x CTL	P NAR x WIDE
A-PPW°	126 114, 162	148.5[43] 125, 180	130 105, 154	144 125, 165	157 131, 180	127 105, 145	133.5 111, 154	.0007	ns	.001
AD[44] mm	80.8 0, 332.2	n=17; 29.5 0, 270.5	n=24; 54.3 0, 527.8	49.5 0, 270.5	0 0, 102.1	40.8 0, 527.8	66.2 0, 213	.04	ns	ns
ANS-PNS°	50 47, 59	45 31, 53	47 36, 56	42 31, 53	48 35, 51	47 36, 56	47.5 41, 54	.002	.009	ns
ANS-PNS-V°	139 121, 144	136 115, 149	140 128, 153	138 130, 149	128 115, 139	141 128, 153	139 132, 146	ns	ns	.04
Ar-Go mm	41 30, 44.5	38.5 18, 51	40 31, 55	38.5 31, 51	37.5 18, 48	38 31, 48	43.5 37, 55	ns	ns	ns
AW[45] mm	849 558, 1250	n=17; 490 189, 1175	n=24; 986 546, 1593	695.2 386, 1175	337.3 189, 784	856 546, 1593	1013.5 732, 1340	.019	ns	.0005
BL WDTH mm	44 38, 50	40 29, 58	45 37, 59	42 32, 58	37 29, 48	45 37, 51	45.5 39.5, 59	.01	ns	.004
BL mm area	3408 2281, 4025	2547 1688, 5636	3108 1941, 5180	2963 1688, 5636	2527 1930, 4593	2725 1941, 5180	3664 2715, 4870	ns	ns	ns
BL HGHT mm	65 42, 81	71.5 47.5, 88	61 50, 89	66.8 47.5, 88	74 61, 88	57 50, 88	72.8 55, 89	ns	ns	ns
PH-MPI°	30 22, 35.5	38 26, 62	29 20, 38	32.3 26, 41	41.5 28, 62	31 23, 38	28.5 20, 38	.001	ns	.0003
Go-Me mm	71 60, 77	63 48, 72	65 51, 82	60.5 50, 71	65.5 48, 72	61 51, 76	68.5 65, 82	.004	ns	ns
H-N-S°	7 3, 19	10.5 0, 20	8 3, 24	10.5 0, 19	10.5 1, 20	9 6, 24	7 3, 12.5	ns	ns	ns
H-PH°	3 0, 9	6.5 1, 18	3 0, 31	2 1, 10	11 1, 18	4 0, 31	3 1, 14	.05	ns	ns

[42]probability values from Wilcoxon Rank Sum Test

[43]A-PPW measurement had poor interrater reliability for narrow pharynx subjects.

[44]Subjects who had undergone adenoidectomy were excluded from this measure.

[45]Subjects who had undergone adenoidectomy were excluded from this measurement.

Median Range VARIABLE	CONTROL (CTL) N=15	NARROW (NAR) (S, TC) N=20	WIDE (VCF, VDW) N=25	STICKLER (S) N=10	TREACHER COLLINS (TC) N=10	VELO-CARDIO-FACIAL (VCF) N=13	VAN DER WOUDE (VDW) N=12	P NAR x CTL	P WIDE x CTL	P NAR x WIDE
LAH mm	25 17, 33	34.5 19, 56	27 17, 50	31 20, 43	38 19, 56	22 17, 33	32.5 18, 50	.001	ns	.01
LUM 1 mm	16 11, 21	14 8, 25	22 14, 31	14.5 11, 25	12 8, 18	20 14, 31	23 17, 31	.008	.0008	.0001
LUM 2 mm	12 8, 20	10 4, 17	16 9, 29	10 5, 17	7.5 4, 16	16 9, 23	16 13, 29	.004	.0003	.0001
LUM 3 mm	10 7, 15	8.8 3, 16	14 6, 22	9.5 5, 16	6 3, 12	14 6, 22	14 7, 17	.05	.004	.0002
LUM 4 mm	11 7, 20	8 3, 17	15 3, 22	11.5 8, 17	7 3, 10	15 11, 22	14.5 3, 22	.04	.01	.0001
LUM 5 mm	13 8, 17	8 2, 17	12 4, 22	9.5 6.5, 17	5.5 2, 10	14 7, 22	12 4, 17	.0001	ns	.0001
LUM 6 mm	10 5, 15	5.5 2, 19	10 3, 19	6 3, 19	5.5 2, 12	12 3, 19	8 5, 16	.02	ns	.005
MPI-PPI°	30 23, 39	34.5 22, 53	32 11, 40	31 22, 42	37 25, 53	33 27, 40	29.5 11, 35	ns	ns	ns
MPL-Hy°	13 8, 26	20 9, 36	14 6, 28	15 9, 22	27 12, 36	11 6, 28	17.5 10, 23	.02	ns	.01
N-S mm	70 65, 76	64.5 60, 78	70 62, 77	62 60, 77	67 62, 78	70 62, 74	70 68, 77	.01	ns	.01
N-S-Ar°	125 119, 130	114.5 102, 129	128 114, 136.5	114.5 102, 129	114.5 102, 127	125 114, 136.5	128 116, 134	.0002	ns	.0001
N-S-B°	130 123, 138	124 124, 142	138 127, 149	124 113, 142	124.5 110, 138	140 127, 149	135.5 130, 143	.0006	.003	.0001
PCTSKAW [46]	24 19.3, 34	n=17; 18.8 8.8, 28.4	n=24; 28.1 22.1, 37.6	22.7 16.4, 28.4	13.2 8.8, 24	30.1 22.1, 34.2	27.5 19.6, 37.6	.004	.01	.0001
PCTVTAD [47]	10.2 0, 31.8	n=17; 5 0, 36.9	n=24; 6.1 0, 32.9	9.1 0, 36.9	0 0, 11.1	3.9 0, 32.9	6.8 0, 14.4	ns	ns	ns
PNS-V mm	33 27, 37	28 16, 39	25 16, 46	26 16, 38	29.5 19, 39	24 16, 30	26 20, 46	ns	.0008	ns

[46]PCTSKAW is the percent of the skeletal frame ("Block") which is occupied airway. Subjects who had undergone adenoidectomy were excluded from this measurement.

[47]PCTVTAD is the percent of the vocal tract which is occupied by adenoid tissue. Subjects who had undergone adenoidectomy were excluded from this measure.

Median Range VARIABLE	CONTROL (CTL) N=15	NARROW (NAR) (S, TC) N=20	WIDE (VCF, VDW) N=25	STICKLER (S) N=10	TREACHER COLLINS (TC) N=10	VELO-CARDIO-FACIAL (VCF) N=13	VAN DER WOUDE (VDW) N=12	P NAR x CTL	P WIDE x CTL	P NAR x WIDE
PFI-V mm	20 14, 28	19 9, 35	16 8, 32	18.5 9, 28	23 12, 35	14 8, 25	18.5 10, 32	ns	.01	ns
PFI-Hy mm	44 38, 58	55 37, 80	43 31, 69	50.5 37, 65	62 42, 80	35 31, 56	48 36, 69	.006	ns	.003
PFI-PPW°	98 84, 117	104 83, 130	100 86, 120	99.5 83, 122	108 95, 130	97 86, 114	101 88, 120	ns	ns	ns
PPW 1 mm	19 17.5, 27	18.5 4, 29	12 4, 25	21.5 13, 29	16 4, 24	12 5, 19	13 4, 25	ns	.0001	.005
PPW 2 mm	14 5, 18	13.5 3, 22	9 4, 15	15 6, 20	10 3, 22	10 4, 14	8 4, 15	ns	.0003	.006
PPW 3 mm	7 3, 10	6 2, 19	6 1.5, 10	6 2, 10	7 4, 19	5 3, 8	6.5 1.5, 10	ns	.02	ns
PPW 4 mm	6 3, 10	6 3, 11	5 2, 8	5 3, 8	7.5 3, 11	5 2, 8	4.5 3, 8	ns	ns	.03
PPW 5 mm	4 3, 6	4 2, 9	4 2, 7	5 2, 9	4 3, 6	4 2, 6	4 2, 7	ns	ns	ns
PPW 6 mm	4 3, 5	4 2, 6	4 1, 14	4 3, 6	4 2, 6	4 1, 7	3.5 2, 14	ns	ns	ns
S-Ar mm	30 24, 35	30 21, 38	29 21, 41	27.5 21, 36	33.5 28, 38	26 21, 30	35 28, 41	ns	ns	ns
S-Ba mm	44 40, 49	43 33, 58	39 33, 53	41.8 35, 52	45 33, 58	37 33, 41	43 39, 53	ns	.002	.04
V WDTH mm	7 7, 10	7 4, 9	6 4, 10	7 4, 9	7 5, 9	6 4, 8	7.3 4, 10	ns	.02	ns

Appendix B-4. Median values and ranges for physical dimensions of the hard and soft palate according to type of cleft palate.

median range VARIABLE	OVERT CLEFT PALATE[48] (N=21)	SUBMUCOUS CLEFT PALATE (N=19)	OCCULT SUBMUCOUS CLEFT PALATE (N=5)
length of hard palate ANS-PNS mm	43 31, 53	48 40, 56	46 36, 52
length of soft palate PNS-V mm	28 18, 46	27 16, 38	24 18, 27
velar thickness V-WDTH mm	7.5 5, 10	6 4, 8	6 4, 8

Kruskal-Wallis Test for differences among cleft types:
ANS-PNS: p=.04
PNS-V: not significant
V-WDTH: p=.003

[48]Includes subjects with repaired incomplete cleft palate and repaired cleft lip and palate.

Appendix B-5. Cephalometric measurements of normal subjects.

ID	GENDER	C.A.	H-N-S	N-S-B	H-FH	FH-MPL
N1	2	9	5	133	4	32
N2	1	9	5	130	3	35.5
N3	2	8.08	7	123	0	30
N4	2	9	8	131	3	35
N5	2	10	5	130	4	23
N6	1	10	8	125	0	30
N7	2	8	19	132	7	22
N8	1	11	9	130	2	24
N9	2	9	6	127	1	35
N10	1	7	7	130	0	23.5
N11	2	8	15	137	1	32
N12	2	11	9	129	5	33
N13	1	10	7	133	4	29
N14	2	8	4	136	6	27
N15	1	7	3	138	9	22

Appendix B-5 (continued). Cephalometric measurements of normal subjects.

ID	N-S	S-Ar	Ar-Go	Go-Me	ANS-PNS	N-S-Ar
N1	65	24	44	67	48	119
N2	68	28	41	60	47	130
N3	66	30	32	62	47	120
N4	69	32	44.5	66	49	129
N5	71	32	40	75	57	129
N6	76	35	39	67	54	123
N7	69	32	43	65	50	125
N8	76	33	41	71	59	124.5
N9	67	28	41	71	51	119
N10	73	30	36	74	50	124
N11	72	30	30	74	49	130
N12	70	34	40	75	48	125
N13	75	30	43	71	54	123
N14	75	27	41	70	50	128
N15	68	33	40	77	48	127

Appendix B-5 (continued). Cephalometric measurements of normal subjects.

ID	A-PPW	PPl-PPW	ANS-PNS-V	PNS-V	V WDTH	MPl-Hy
N1	117	110	121	33	7	20
N2	140	98	134	27	7	12
N3	126	117	134	28	7	15
N4	134	103	135	34	7	11
N5	118	95	144	33	7	15
N6	162	115	140	37	10	26
N7	135	116	139	29	7	18
N8	121	88	132	27	8	12
N9	137	102	132	33	10	14
N10	125	87	122	29	7	8
N11	125	93	144	33	8	15
N12	128	98	139	32	7	13
N13	115	92	142	27	9	12
N14	136	104	144	33	7	9
N15	114	84	143	36	8	11

Appendix B-5 (continued). Cephalometric measurements of normal subjects.

ID	PP1-V	PP1-Hy	LAH	S-Ba	MP1-PP1	LUM1
N1	28	53	25	43	30	16
N2	19	49	30	40	31	17
N3	20	42	22	47	32	16
N4	14	44	30	47	30	18
N5	19	40	21	41	29	12
N6	25	58	33	49	27	16
N7	19	47	28	44	26	18
N8	20	48	28	47	23	17
N9	25	42	17	40	32	19
N10	20	40	20	43	29	14
N11	20	39	19	44	39	15
N12	20	43	23	47	30	11
N13	17	46	29	44	30	15
N14	19	38	19	44	29.5	21
N15	21	48	27	44	24	20

Appendix B-5 (continued). Cephalometric measurements of normal subjects.

ID	LUM2	LUM3	LUM4	LUM5	LUM6	PPW1
N1	12	9	10	13	8	26
N2	14	9	10	11	11	19
N3	12	10	10	11	11	20
N4	10	9	12	12	12	19
N5	11	10	10.5	13	5	19
N6	9	7	7	13	15	23
N7	14	13	17	15	8	19
N8	13	11	11	10	13	20
N9	12	11	10	14	8	18
N10	12	13	18	13	12	22
N11	14	10	7	13	5	19
N12	8	9	12	11.5	6	23
N13	12	10	11	8	5	17.5
N14	20	15	20	17	15	18
N15	13	9	13	12	10	27

Appendix B-5 (continued). Cephalometric measurements of normal subjects.

ID	PPW2	PPW3	PPW4	PPW5	PPW6	IMS Po
N1	11	3	3	3	3	322
N2	11	8	4	4	4	537
N3	10.5	7	7	4	5	552
N4	15	7	6	4	4	348
N5	14	6	4	3	4	332
N6	18	10	10	4	3	371
N7	13	7	6	4	4	335
N8	14	8.5	6	6	5	331
N9	5	7	5	5	4	147
N10	11	6	5	4	3.5	525
N11	18	5	7.5	4	4	296
N12	14	10	9	4	5	278
N13	15	7	4	4	5	476
N14	12	7	6	5	5	220
N15	18	6.5	5	4	4.5	619

Appendix B-5 (continued). Cephalometric measurements of normal subjects.

ID	Po DIAM	PO AREA	AD mm	PCTVTAD	BL WDTH	BL HGHT
N1	10	78.50	23.65	2.71	46	73
N2	14	153.86	62.46	5.53	42	71
N3	12	113.04	81.91	12.11	38	64
N4	10	78.50	79.18	8.12	43.5	60
N5	10	78.50	332.21	31.84	44	42
N6	11	94.99	0.00	0.00	42	81
N7	10	78.50	110.84	10.61	43	65
N8	10	78.50	77.79	7.88	45.5	68
N9	7.5	44.16	80.80	8.37	41	66
N10	12	113.04	67.61	10.81	41	60
N11	10	78.50	188.29	21.77	44	65
N12	9.5	70.85	46.38	7.06	44	51
N13	12	113.04	88.34	10.17	46.5	70
N14	9	63.59	147.11	10.20	50	63
N15	14	153.86	164.30	18.79	44	71

Appendix B-5 (continued). Cephalometric measurements of normal subjects.

ID	BLCK area	AW mm	PCTSKAW
N1	3537.86	848.63	23.99
N2	3725.30	1067.28	28.65
N3	2281.07	594.69	26.07
N4	2560.05	871.17	34.03
N5	3153.24	656.37	20.82
N6	3737.70	965.72	25.84
N7	2970.81	902.16	30.37
N8	3407.52	909.98	26.71
N9	3633.43	853.69	23.50
N10	2367.17	557.88	23.57
N11	3516.85	677.59	19.27
N12	2825.19	587.67	20.80
N13	3485.48	753.52	21.62
N14	4024.64	1250.31	31.07
N15	3295.93	695.48	21.10

Appendix B-6. Cephalometric data of experimental subjects.

ID CP#	GENDER 1=M,2=F	CLEFT 1=REP CP 2=SMCP 3=OSMCP 4,5=CLP	C.A.	DX 1=SS 2=TCS 3=VCF 4=VDW	H-N-S angle
1075	2	1	23.11	1	19.0
1505	2	1	5.00	1	17.0
1829	1	1	3.07	1	0.0
2267	1	1	6.06	1	15.0
2643	1	1	6.07	1	12.0
3122	1	1	4.04	1	10.0
3236	2	2	5.02	1	11.0
3453	1	2	5.05	1	4.0
3476	2	1	20.0	1	7.0
3786	2	1	6.03	1	6.0
1068	1	2	22.00	2	14.0
1110	1	5	42.0	2	1.0
1132	2	2	40.0	2	7.0
1156	2	2	21.4	2	20.0
1592	1	2	9.00	2	5.0
1656	1	1	5.05	2	6.0
2129	2	2	18.4	2	13.0
2307	2	1	14.11	2	12.0
2663	2	1	6.03	2	20.0
3653	1	4	8.10	2	9.0
1239	2	3	7.02	3	16.0
2115	2	2	30.09	3	8.0
2234	2	2	6.07	3	12.0
2516	1	2	4.01	3	7.0
2543	1	2	5.00	3	6.0
2644	2	3	6.09	3	11.0
2739	1	2	5.06	3	7.0
2877	1	3	5.04	3	24.0
2982	2	2	6.07	3	7.0
3020	2	2	4.10	3	9.0
3235	2	3	4.04	3	9.0
3423	1	3	6.01	3	24.0
3770	1	2	6.04	3	7.0
1070	2	1	13.00	4	7.0
1369	2	2	14.09	4	7.0
1651	2	1	10.04	4	10.0
1831	2	2	8.07	4	9.0
2274	1	1	5.06	4	9.0
2459	2	2	38.11	4	4.0
2596	2	1	17.00	4	12.0
2883	2	1	8.05	4	3.0
2980	2	1	8.02	4	12.5
3161	2	2	7.04	4	6.0
3525	2	1	15.02	4	3.0
794	1	1	7.08	4	6.0

Appendix B-6 (continued). Cephalometric data of experimental subjects.

ID CP#	N-S-B angle	H-FH angle	FH-MPl (Go-Gn) angle	N-S mm	S-Ar mm
1075	142.0	7.0	26.0	77.0	32.0
1505	128.0	2.0	30.0	62.0	21.0
1829	114.0	6.0	41.0	74.0	36.0
2267	124.0	10.0	40.0	66.0	25.0
2643	126.0	1.5	30.0	64.0	29.0
3122	124.0	2.0	31.0	62.0	27.0
3236	113.0	2.0	30.0	60.0	25.0
3453	127.0	2.0	37.0	62.0	26.0
3476	122.0	2.0	41.0	61.0	30.0
3786	120.0	1.0	33.5	60.0	28.0
1068	126.0	18.0	62.0	72.0	33.0
1110	112.0	7.0	32.0	78.0	38.0
1132	110.0	3.5	28.0	76.0	38.0
1156	125.0	10.0	46.0	62.0	30.0
1592	113.0	10.0	39.0	63.0	34.0
1656	138.0	1.0	36.0	65.0	34.0
2129	125.0	15.0	39.0	68.0	28.0
2307	118.0	14.0	52.0	68.0	28.0
2663	126.0	13.0	47.0	63.0	30.0
3653	124.0	12.0	44.0	66.0	34.0
1239	127.0	9.0	35.0	73.0	30.0
2115	147.0	0.0	30.0	72.0	27.0
2234	137.0	2.0	23.0	70.0	25.0
2516	143.0	2.0	27.0	67.0	24.0
2543	138.0	2.0	38.0	74.0	27.0
2644	142.0	3.0	35.0	74.0	25.0
2739	131.0	9.0	32.0	70.0	30.0
2877	140.0	9.0	27.0	70.0	26.0
2982	127.0	4.0	27.0	70.0	26.0
3020	149.0	1.5	29.0	62.0	24.0
3235	140.0	5.0	36.0	65.0	21.0
3423	142.0	31.0	33.0	64.0	26.0
3770	136.0	4.0	31.0	65.0	23.0
1070	139.0	1.0	22.0	69.0	37.0
1369	143.0	3.0	30.0	77.0	39.0
1651	135.0	1.0	21.0	71.0	40.0
1831	140.0	4.0	21.0	68.0	29.0
2274	130.0	3.0	32.0	76.0	30.0
2459	130.0	7.0	28.0	68.0	41.0
2596	130.0	5.0	29.0	74.0	36.0
2883	133.0	1.0	29.0	72.0	36.0
2980	141.0	1.0	27.0	69.0	34.0
3161	131.0	3.0	29.0	69.0	29.0
3525	136.0	14.0	20.0	74.0	28.0
794	139.0	6.0	38.0	69.0	33.0

Appendix B-6 (continued). Cephalometric data of experimental subjects.

ID CP#	Ar-Go mm	Go-Me mm	ANS-PNS mm	N-S-Ar angle	A-PPW angle
1075	48.0	71.0	44.0	129.0	125.0
1505	32.0	53.0	31.0	114.0	165.0
1829	51.0	71.0	53.0	102.0	145.0
2267	39.0	59.0	42.0	112.0	143.0
2643	38.0	50.0	42.5	119.0	161.0
3122	40.0	57.0	42.0	124.0	126.0
3236	35.0	62.0	40.0	104.0	125.0
3453	36.0	65.0	46.0	119.0	127.0
3476	40.0	69.0	35.0	115.0	157.0
3786	31.0	58.0	39.0	113.0	149.0
1068	47.0	67.0	51.0	111.0	162.0
1110	42.5	71.0	51.0	102.0	180.0
1132	41.5	67.0	49.0	106.0	152.0
1156	31.0	64.0	47.0	120.0	148.0
1592	29.0	56.0	46.0	111.0	163.0
1656	40.0	72.0	46.0	127.0	131.0
2129	35.0	48.0	51.0	118.0	170.0
2307	48.0	58.0	50.0	108.0	165.0
2663	21.0	55.0	42.0	121.0	142.0
3653	18.0	68.0	35.0	120.0	143.0
1239	31.0	73.0	52.0	114.0	105.0
2115	48.0	76.0	56.0	132.0	136.0
2234	38.0	61.0	48.0	129.0	145.0
2516	37.0	55.0	44.0	123.0	108.0
2543	38.0	64.0	49.0	128.0	127.0
2644	39.0	65.0	46.0	124.0	105.0
2739	37.0	62.0	50.0	125.0	138.0
2877	41.0	58.0	46.0	128.0	115.0
2982	43.0	65.0	52.0	124.0	109.0
3020	40.0	58.0	46.0	136.5	121.0
3235	37.0	51.0	36.0	123.0	133.0
3423	36.0	53.0	47.0	134.0	132.0
3770	34.0	57.0	43.0	119.0	130.0
1070	52.0	73.0	42.0	134.0	154.0
1369	42.0	82.0	54.0	128.0	135.0
1651	45.0	73.0	41.0	128.0	149.0
1831	39.0	68.0	48.0	128.0	132.0
2274	40.0	65.0	48.0	116.0	129.0
2459	55.0	75.0	45.0	122.0	111.0
2596	49.0	75.0	47.0	122.0	129.0
2883	45.0	72.0	43.0	126.0	123.0
2980	37.0	65.0	49.0	134.0	136.0
3161	40.0	74.0	50.0	133.0	150.0
3525	45.0	79.0	49.0	128.0	150.0
794	41.0	69.0	46.0	131.0	126.0

Appendix B-6 (continued). Cephalometric data of experimental subjects.

ID CP#	PPl-PPW angle	ANS-PNS-V angle	PNS-V mm	V WDTH mm	MPl-Hy mm
1075	110.0	141.0	33.0	8.0	19.0
1505	122.0	146.0	33.0	5.0	11.0
1829	90.0	132.0	38.0	9.0	16.0
2267	92.0	130.0	20.0	8.5	22.0
2643	102.0	138.0	29.0	7.0	21.0
3122	93.0	137.0	28.0	7.0	14.0
3236	83.0	138.0	20.0	6.0	9.0
3453	106.0	148.0	16.0	4.0	12.0
3476	101.0	137.0	24.0	9.0	21.0
3786	98.0	149.0	18.0	6.0	9.0
1068	103.0	127.0	38.0	8.0	32.0
1110	105.0	130.0	35.0	7.0	36.0
1132	95.0	123.0	34.0	6.0	20.0
1156	117.0	123.0	31.0	8.0	27.0
1592	130.0	139.0	24.0	7.0	20.0
1656	117.0	139.0	28.0	9.0	12.0
2129	111.0	135.0	25.0	6.0	34.0
2307	116.0	124.0	24.0	7.0	27.0
2663	95.0	129.0	19.0	5.0	32.0
3653	105.0	115.0	39.0	9.0	19.0
1239	97.0	137.0	27.0	8.0	17.0
2115	104.0	128.0	30.0	6.0	28.0
2234	114.0	150.0	23.0	4.0	17.0
2516	90.0	143.0	29.0	8.0	9.0
2543	97.0	153.0	29.0	5.0	11.0
2644	90.0	150.0	22.0	6.0	10.0
2739	106.0	142.0	27.0	5.0	10.0
2877	97.0	144.0	24.0	7.0	7.0
2982	86.0	138.0	21.0	6.0	6.0
3020	93.0	131.0	27.0	6.0	14.0
3235	97.0	133.0	18.0	4.0	12.0
3423	104.0	141.0	24.0	4.0	10.0
3770	101.0	129.0	16.0	5.0	15.0
1070	100.0	134.0	42.0	8.0	20.0
1369	100.0	132.0	27.0	5.0	23.0
1651	102.0	140.0	46.0	7.0	20.0
1831	91.0	144.0	21.0	4.0	10.0
2274	108.0	146.0	22.0	7.0	13.0
2459	88.0	133.0	25.0	8.0	19.0
2596	120.0	146.0	20.0	7.0	19.0
2883	88.0	142.0	30.0	8.0	16.0
2980	110.0	133.0	28.0	7.5	10.0
3161	108.0	138.0	31.0	6.0	14.0
3525	104.0	142.0	25.0	10.0	12.5
794	96.0	136.0	23.5	8.0	20.0

Appendix B-6 (continued). Cephalometric data of experimental subjects.

ID CP#	PPl-V mm	PPl-Hy mm	LAH mm	S-Ba mm	MPl-PPl angle
1075	20.0	56.0	36.0	50.0	25.0
1505	19.0	39.0	20.0	35.0	33.0
1829	28.0	65.0	37.0	52.0	42.0
2267	15.0	52.0	37.0	42.0	31.0
2643	19.0	49.0	30.0	44.0	25.0
3122	18.0	48.0	30.0	41.5	31.0
3236	14.0	37.0	23.0	40.0	22.0
3453	26.0	54.0	28.0	42.0	37.0
3476	16.0	59.0	43.0	39.0	42.0
3786	9.0	41.0	32.0	38.0	29.0
1068	30.0	75.0	45.0	53.0	42.0
1110	27.0	80.0	53.0	58.0	40.0
1132	29.0	65.0	36.0	47.0	28.0
1156	26.0	59.0	33.0	33.0	37.0
1592	16.0	42.0	26.0	44.0	53.0
1656	12.0	45.0	33.0	46.0	37.0
2129	17.0	64.0	47.0	41.0	25.0
2307	20.0	60.0	40.0	47.0	41.0
2663	14.0	70.0	56.0	44.0	36.0
3653	35.0	54.0	19.0	40.0	27.0
1239	19.0	52.0	33.0	40.0	30.0
2115	25.0	56.0	31.0	39.0	32.0
2234	11.0	41.0	30.0	36.0	29.0
2516	17.0	35.0	18.0	33.0	35.0
2543	12.0	32.0	20.0	37.0	40.0
2644	11.0	33.0	22.0	36.0	39.0
2739	16.0	34.0	18.0	36.0	34.0
2877	14.0	34.0	20.0	37.0	33.0
2982	8.0	35.0	27.0	41.0	30.0
3020	21.0	43.0	22.0	36.0	27.0
3235	11.0	31.0	20.0	37.0	34.0
3423	15.0	32.0	17.0	38.0	36.0
3770	13.0	43.0	30.0	37.0	31.0
1070	32.0	69.0	37.0	43.0	11.0
1369	20.0	58.0	38.0	53.0	27.0
1651	30.0	62.0	32.0	47.0	22.0
1831	12.0	36.0	24.0	39.0	32.0
2274	13.0	37.0	24.0	43.0	32.0
2459	18.0	68.0	50.0	49.0	22.0
2596	11.0	46.0	35.0	42.0	35.0
2883	19.0	50.0	31.0	46.0	31.0
2980	20.0	38.0	18.0	42.0	27.0
3161	21.0	44.0	23.0	43.0	28.0
3525	10.0	43.0	33.0	39.0	34.0
794	16.0	53.0	37.0	41.5	32.0

Appendix B-6 (continued). Cephalometric data of experimental subjects.

ID CP#	LUM1 mm	LUM2 mm	LUM3 mm	LUM4 mm	LUM5 mm
1075	25.0	17.0	14.0	12.0	10.0
1505	15.0	10.0	9.0	16.0	17.0
1829	16.0	10.0	5.0	13.0	9.0
2267	11.0	7.0	10.0	17.0	10.0
2643	14.0	9.0	8.5	11.0	10.0
3122	15.0	5.0	10.0	8.0	8.0
3236	15.0	11.0	9.0	8.0	9.0
3453	14.0	13.0	14.0	14.0	11.0
3476	12.0	10.0	16.0	11.0	6.5
3786	13.0	10.0	7.0	8.0	8.0
1068	12.0	11.0	6.0	7.0	5.0
1110	11.0	4.0	3.0	3.0	4.0
1132	12.0	11.0	6.0	7.0	6.0
1156	14.0	5.0	3.5	5.0	4.0
1592	15.0	11.0	10.0	7.0	6.0
1656	18.0	16.0	12.0	10.0	10.0
2129	16.0	7.0	6.0	6.0	5.0
2307	9.0	5.0	6.0	7.0	9.0
2663	8.0	4.0	9.0	3.0	2.0
3653	10.0	8.0	8.0	7.0	6.0
1239	14.0	11.0	14.0	19.0	18.0
2115	23.0	15.0	12.0	11.0	9.0
2234	16.0	12.0	15.0	20.0	19.0
2516	15.0	9.0	6.0	11.0	11.0
2543	23.0	20.0	14.0	14.0	14.0
2644	30.0	23.0	17.0	17.0	20.0
2739	18.0	16.0	13.0	13.0	12.0
2877	31.0	23.0	21.0	21.0	21.0
2982	16.0	13.0	14.0	13.0	10.0
3020	22.0	16.0	15.0	15.0	18.0
3235	23.0	18.0	22.0	22.0	22.0
3423	20.0	15.0	12.0	12.0	12.0
3770	19.0	16.0	14.0	16.0	7.0
1070	20.0	15.0	7.0	13.0	12.0
1369	20.0	16.0	14.0	16.0	14.5
1651	27.0	16.0	7.0	9.0	11.0
1831	28.0	29.0	17.0	15.0	12.0
2274	17.0	16.0	14.0	14.0	12.0
2459	24.0	13.0	8.0	3.0	4.0
2596	27.0	21.0	17.0	15.0	14.0
2883	26.0	18.0	12.0	12.0	10.0
2980	17.0	15.0	14.0	22.0	10.0
3161	31.0	19.0	17.0	19.0	17.0
3525	18.0	15.0	10.0	12.0	10.0
794	22.0	17.0	15.0	15.0	12.0

Appendix B-6 (continued). Cephalometric data of experimental subjects.

ID CP#	LUM6 mm	PPW1 mm	PPW2 mm	PPW3 mm	PPW4 mm
1075	3.0	13.0	6.0	6.0	5.0
1505	19.0	29.0	16.0	5.0	6.0
1829	8.0	29.0	10.0	8.0	8.0
2267	7.5	27.0	18.0	10.0	6.0
2643	11.0	20.0	20.0	2.5	5.0
3122	3.0	25.0	14.0	6.0	5.0
3236	5.0	19.0	13.0	2.0	5.0
3453	5.0	13.0	10.0	6.0	3.0
3476	5.0	23.0	16.0	6.0	8.0
3786	7.0	15.0	16.0	3.0	5.0
1068	5.0	24.0	20.0	11.0	8.0
1110	2.0	16.0	10.0	9.0	9.0
1132	5.0	16.0	5.0	6.0	8.0
1156	6.0	11.0	18.0	4.0	6.0
1592	9.0	16.0	10.0	4.0	10.0
1656	9.0	4.0	8.0	5.0	3.0
2129	2.0	18.0	9.0	5.0	5.0
2307	12.0	19.0	3.0	8.0	7.0
2663	5.0	21.0	22.0	19.0	4.0
3653	9.0	11.0	15.0	11.0	11.0
1239	18.0	12.0	11.0	5.0	5.0
2115	6.0	8.0	4.0	3.0	2.0
2234	18.0	19.0	11.0	6.0	5.0
2516	6.0	11.0	10.0	8.0	8.0
2543	12.0	17.0	12.0	6.0	6.0
2644	17.0	5.0	4.0	3.0	3.0
2739	9.0	14.0	8.0	4.0	4.0
2877	19.0	7.0	4.0	4.0	3.0
2982	3.0	19.0	12.0	6.0	5.0
3020	11.0	18.0	9.0	5.0	5.0
3235	15.0	12.0	10.0	3.0	3.0
3423	9.0	10.0	7.0	6.0	6.0
3770	12.0	11.0	14.0	4.0	7.0
1070	8.0	18.0	12.0	8.0	8.0
1369	11.0	15.0	9.0	6.0	4.0
1651	7.0	24.0	4.0	6.0	5.0
1831	5.0	7.0	7.0	4.0	4.0
2274	6.0	9.0	8.0	10.0	8.0
2459	7.0	4.0	9.0	7.0	3.0
2596	11.0	9.0	7.0	5.0	4.0
2883	8.0	12.0	11.0	8.0	4.0
2980	11.0	25.0	15.0	7.0	6.0
3161	16.0	16.0	5.0	6.0	5.0
3525	10.0	8.0	6.0	1.5	3.0
794	6.0	14.0	8.0	8.0	6.0

Appendix B-6 (continued). Cephalometric data of experimental subjects.

ID CP#	PPW5 mm	PPW6 mm	s/p(T&)A? 1=N 2=Y 3=?	IMS PO	PO DIAM mm
1075	5.0	4.0	1	160.0	9.0
1505	5.0	6.0	2	206.0	10.0
1829	9.0	4.0	1	412.0	15.0
2267	4.0	5.0	1	260.0	10.0
2643	5.0	4.0	1	350.0	13.0
3122	5.0	4.5	1	399.0	12.5
3236	4.0	3.0	1	360.0	12.0
3453	2.0	3.0	1	369.0	13.0
3476	4.0	4.0	1	511.0	12.0
3786	5.0	5.0	1	136.0	9.0
1068	4.0	3.0	3	165.0	10.0
1110	4.0	4.0	1	385.0	12.0
1132	4.0	4.0	1	580.0	12.0
1156	4.0	6.0	2	450.0	12.0
1592	4.0	6.0	1	159.0	9.0
1656	3.0	2.0	1	216.0	10.0
2129	3.0	3.0	1	421.0	12.0
2307	5.0	4.0	1	271.0	10.0
2663	6.0	2.0	1	402.0	12.0
3653	5.0	5.0	1	350.0	11.0
1239	6.0	4.0	1	142.0	10.0
2115	2.0	3.0	1	171.0	9.0
2234	5.0	6.0	1	172.0	9.0
2516	4.0	6.0	1	208.0	10.0
2543	6.0	4.0	1	152.0	10.0
2644	3.0	3.0	1	175.0	9.0
2739	4.0	4.0	1	370.0	11.0
2877	3.0	1.0	1	211.0	10.0
2982	5.0	5.0	1	284.0	12.0
3020	6.0	7.0	1	441.0	12.0
3235	3.0	3.0	1	323.0	12.0
3423	6.0	5.0	1	330.0	12.0
3770	3.0	4.0	1	198.0	10.0
1070	7.0	14.0	1	288.0	12.0
1369	4.0	3.0	1	359.0	11.0
1651	3.0	3.0	1	110.0	7.0
1831	3.0	5.0	1	335.0	10.5
2274	5.0	5.0	1	131.0	9.0
2459	4.0	5.0	2	221.0	9.0
2596	3.0	3.0	1	369.0	14.0
2883	4.0	4.0	1	290.0	12.0
2980	4.0	5.0	1	379.0	11.0
3161	4.0	3.0	1	311.0	12.0
3525	2.0	2.0	1	271.0	11.0
794	3.0	2.0	1	314.0	10.0

Appendix B-6 (continued). Cephalometric data of experimental subjects.

ID CP#	PO AREA	AD mm SQ	BL WDTH trace mm PTM-Ba	BL HGHT trace mm FH-HyPl	BLOCK mm convert
1075	63.6	0.0	58.0	80.0	5236.2
1505	78.5	0.0	37.0	54.0	2113.4
1829	176.6	149.6	52.0	88.0	5635.7
2267	78.5	125.0	40.0	67.0	3654.2
2643	132.7	117.5	42.0	67.0	3379.5
3122	122.7	270.5	41.5	66.5	2541.4
3236	113.0	49.6	42.0	47.5	1688.1
3453	132.7	49.3	45.5	54.0	2510.9
3476	113.0	33.0	43.0	81.0	3518.4
3786	63.6	29.5	32.0	52.0	2545.7
1068	78.5	0.0	41.0	80.0	4592.5
1110	113.0	0.0	37.0	88.0	2897.3
1132	113.0	0.0	37.0	80.0	2505.6
1156	113.0	0.0	30.0	73.0	2203.3
1592	63.6	0.0	29.0	76.0	2463.0
1656	78.5	102.1	48.0	68.0	3270.8
2129	113.0	0.0	38.0	70.0	2971.5
2307	78.5	0.0	32.0	74.0	1929.5
2663	113.0	14.9	37.0	74.0	2256.0
3653	95.0	0.0	40.0	61.0	2547.5
1239	78.5	0.0	46.0	70.0	5180.4
2115	63.6	0.0	48.0	88.0	4322.7
2234	63.6	102.8	40.0	66.0	2704.6
2516	78.5	40.8	45.0	56.0	2575.8
2543	78.5	527.8	45.0	54.0	3630.6
2644	63.6	123.5	45.0	58.0	2779.2
2739	95.0	25.9	45.0	50.0	2457.8
2877	78.5	99.7	51.0	57.0	3055.2
2982	113.0	198.6	41.0	56.0	2685.5
3020	113.0	44.6	45.0	60.0	3107.7
3235	113.0	0.0	42.0	50.0	2039.6
3423	113.0	0.0	37.0	55.0	1940.5
3770	78.5	0.0	42.5	57.0	2724.5
1070	113.0	0.0	46.0	74.0	3730.3
1369	95.0	213.0	59.0	85.0	4869.6
1651	38.5	0.0	45.0	77.0	3596.8
1831	86.5	99.5	42.0	55.0	2714.5
2274	63.6	85.9	45.0	61.0	3850.0
2459	63.6	0.0	50.0	89.0	3742.6
2596	153.9	157.6	39.5	80.0	3956.6
2883	113.0	170.3	48.0	73.0	3829.7
2980	95.0	63.9	47.0	57.0	2977.6
3161	113.0	43.6	41.0	71.0	2957.2
3525	95.0	0.0	42.5	72.5	3400.9
794	78.5	68.5	46.0	70.0	3514.5

Appendix B-6 (continued). Cephalometric data of experimental subjects.

ID CP#	AW mm convert	PCTSKAW relative lumn size	PCTVTAD relative ad size
1075	1175.1	22.4	0.0
1505	536.5	25.4	0.0
1829	1078.6	19.1	12.2
2267	883.4	24.2	12.4
2643	700.5	20.7	14.4
3122	415.9	16.4	36.9
3236	386.2	22.9	11.4
3453	689.9	27.5	6.7
3476	630.2	17.9	5.0
3786	721.9	28.4	3.8
1068	561.9	12.2	0.0
1110	306.8	10.6	0.0
1132	489.6	19.5	0.0
1156	310.2	14.1	0.0
1592	364.3	14.8	0.0
1656	783.9	24.0	11.1
2129	261.0	8.8	0.0
2307	189.2	9.8	0.0
2663	208.1	9.2	6.3
3653	471.1	18.5	0.0
1239	1593.2	30.8	0.0
2115	1020.0	23.6	0.0
2234	812.9	30.1	11.2
2516	569.1	22.1	6.4
2543	993.1	27.4	32.9
2644	856.0	30.8	12.6
2739	657.2	26.7	3.7
2877	1014.2	33.2	9.0
2982	657.9	24.5	23.2
3020	1063.0	34.2	3.9
3235	660.4	32.4	0.0
3423	546.4	28.2	0.0
3770	908.3	33.3	0.0
1070	1044.8	28.0	0.0
1369	1340.4	27.5	13.3
1651	884.7	24.6	0.0
1831	1016.3	37.4	8.6
2274	979.5	25.4	8.1
2459	731.9	19.6	0.0
2596	1119.1	28.3	12.0
2883	1010.7	26.4	14.4
2980	733.1	24.6	7.8
3161	1112.2	37.6	3.8
3525	930.6	27.4	0.0
794	1101.8	31.3	5.7

Appendix C-1. Pearson correlation coefficients for intrarater and interrater reliability of nasopharyngoscopic measurements.

VARIABLE	Intrarater r. KGK-KGK	Interrater r. KGK-RJS
VELAR DISPLACEMENT	.99	.99
PPW DISPLACEMENT	.91	.98
LEFT LPW DISPLACEMENT	.93	.91
RIGHT LPW DISPLACEMENT	.93	.93
PERCENT OF VELOPHARYNGEAL CLOSURE ACHIEVED[49]	.98	.97
PRESENCE OF VPI		26/30 (87%)
SHAPE OF V-P GAP		25/30 (83%)

$p < 0.0001$ for every comparison.

[49]Interrater reliability of the rating of percent closure of the velopharyngeal port was based on a comparison of computer measurement by KGK and visualized estimate by RJS.

Appendix C-2. Nasopharyngoscopic data: experimental subjects[50].

CP#	DX	PHON	MAX? 1=Y, 2=N	HAB?	V
1829	1	S	1	1	0.63
2267	1	S	1	1	0.45
2643	1	S	1	1	1
3122	1	S	1	1	1
3236	1	S	1	1	0.83
3453	1	S	1	1	1
3476	1	S	1	1	0.85
3786	1	S	1	1	0.6
1110	2	S	1	1	1
1132	2	S	1	1	1
1156	2	S	1	1	1
1592	2	S	1	1	1
1656	2	S	1	1	1
2307	2	S	1	1	1
2663	2	S	1	1	0.55
3653	2	S	1	1	1
1239	3	S	1	1	0.76
2115	3	S	1	1	0.9
2516	3	S	1	1	0
2644	3	T	1	1	0.17
2739	3	S	1	1	0.9
2877	3	S	1	1	0.9
2982	3	S	1	1	0.9
3020	3	S	1	1	0.14
3423	3	S	1	1	0.04
3770	3	S	1	1	0.95
1070	4	S	1	1	1
1369	4	S	1	1	0.95
1651	4	S	1	1	1
1831	4	P	2	1	0.38
2274	4	P	1	1	0.27
2459	4	S	1	1	0.63
2596	4	S	1	1	0.05
2883	4	P	1	2	0.1
2980	4	S	1	1	0.5
3161	4	S	1	1	0.89
3525	4	S	1	1	1
794	4	S	1	1	0.9

[50]Diagnosis 1: Stickler; 2: Treacher Collins; 3: velo-cardio-facial; 4: van der Woude. V= velar displacement.

Appendix C-2 (continued). Nasopharyngoscopic data: experimental subjects.

CP#	PPW	L-LPW	R-LPW	%AD	%CLOS
1829	0	0.12	0.1	0.23	0.43
2267	0	0	0	0.52	0.57
2643	0	CNV	CNV	0.47	0.87
3122	0	0.27	0.16	0.62	0.99
3236	0.3	0.36	0.46	0.35	0.97
3453	0	CNV	CNV	0.43	0.95
3476	0	0.28	0.26	0.43	0.99
3786	0	CNV	0.2	0.75	0.75
1110	0	0.43	0.37	0	0.99
1132	0	0.3	0.3	0	1
1156	0	0.5	0.5	0	1
1592	0	CNV	CNV	0.66	1
1656	0	CNV	CNV	0.8	1
2307	0	CNV	CNV	0.62	1
2663	0.08	0.18	0.35	0.51	0.89
3653	0	0.43	0.4	0.37	1
1239	0	0.31	0.21	0	0.94
2115	0.3	0.1	0.1	0.58	0.85
2516	0	0	0	0.05	0
2644	0	0	0	0.13	0.15
2739	0	0.2	0.2	0.63	0.91
2877	0	0.38	0.46	0.42	0.97
2982	0	0.1	0.07	0.75	0.88
3020	0	0	0	0.09	0.08
3423	0	0.03	0.03	0	0.1
3770	0	0	CNV	0.17	0.91
1070	0	0.06	CNV	0.61	0.85
1369	0	CNV	CNV	0.24	0.94
1651	0	0	0	0.56	1
1831	0.3	0.28	0.3	0.35	0.78
2274	0	0.18	0.18	0.47	0.51
2459	0.33	0.36	0.28	0.59	0.99
2596	0.06	0.15	CNV	0.22	0.4
2883	0.2	0.38	0.33	0.12	0.79
2980	0	0.2	0.25	0.25	0.71
3161	0	0.38	0.44	0.4	0.98
3525	0	0.33	0.3	0.07	0.86
794	0	0.35	0.25	0.52	0.96

(CNV= could not visualize)

Appendix C-2 (continued). Nasopharyngoscopic data: experimental subjects.

CP#	SHAPE
1829	CO
2267	CO
2643	B
3122	I
3236	CI
3453	I
3476	L
3786	CO
1110	I
1132	N
1156	N
1592	N
1656	N
2307	N
2663	CO
3653	N
1239	CI
2115	CO
2516	G
2644	G
2739	CO
2877	CI
2982	CO
3020	G
3423	G
3770	B
1070	L
1369	CO
1651	N
1831	CI
2274	CO
2459	L
2596	CO
2883	S
2980	CI
3161	CI
3525	B
794	CO

Appendix D-1. Pearson correlation coefficients and levels of significance for interrater reliability of measurements from multi-view videofluoroscopy.

VARIABLE: Pearson *r* *p* value	N	KGK-SR	KGK-GROUP[51]	SR-GROUP
EN FACE VIEW VELAR DISPLACEMENT	14	.55 .04	.93 .0001	.80 .0006
EN FACE VIEW PPW DISPLACEMENT	13	.46 ns	.89 .0001	.43 ns
EN FACE VIEW L-LPW DISPLACEMENT	14	.76 .002	.73 .003	.90 .0001
EN FACE VIEW R-LPW DISPLACEMENT	14	.92 .0001	.94 .0001	.94 .0001
EN FACE VIEW % VP CLOSURE ACHIEVED[52]	14	.89 .0001	NOT DONE	NOT DONE
FRONTAL VIEW L-LPW DISPLACEMENT	31	.78 .0001	.97 .0001	.88 .0001
FRONTAL VIEW R-LPW DISPLACEMENT	31	.85 .0001	.94 .0001	.96 .0001
LATERAL VIEW VELAR DISPLACEMENT	30	.75 .0001	.93 .0001	.83 .0001
LATERAL VIEW PPW DISPLACEMENT	30	.49 .006	.68 .0001	.84 .0001
AGREEMENT BY PHARYNGEAL WIDTH		KGK-SR ALL CASES:	KGK-SR NARROW PHARYNX:	KGK-SR WIDE PHARYNX:
FRONTAL VIEW PRESENCE OF VPI	31	30/31 97%	9/10 90%	21/21 100%
LATERAL VIEW PRESENCE OF VPI	30	29/30 97%	10/10 100%	19/20 95%

[51]Group measurement was done by the same two raters making measurements together one month after the initial independent measurements.

[52]Interrater reliability of the rating of percent closure of the velopharyngeal port was based on a comparison of computer measurement by KGK and visualized estimate by SR.

Appendix D-2. Direction of velar motion as seen on lateral view videofluoroscopy.

N Row % Column % GROUP	NONE	POSTERIOR	POSTERO-SUPERIOR	SUPERIOR	TIP-HINGE	TOTAL N Percent
STICKLER (S)	0	0	1 11.11 7.14	8 88.89 47.06	0	9 24.32
TREACHER COLLINS (TC)	0	2 25.00 66.67	3 37.50 21.43	3 37.50 17.65	0	8 21.62
VELO-CARDIO-FACIAL (VCF)	2 16.67 100.00	0	6 50.00 42.86	3 25.00 17.65	1 8.33 100.00	12 32.43
VAN DER WOUDE (VDW)	0	1 12.50 33.33	4 50.00 28.57	3 37.50 17.65	0	8 21.62
NARROW PHARYNX (S, TC)	0	2 11.76 66.67	4 23.53 28.57	11 64.71 64.71	0	17 45.95
WIDE PHARYNX (VCF, VDW)	2 10.0 100.00	1 5.00 33.33	10 50.00 71.43	6 30.00 35.29	1 5.00 100.00	20 54.05
TOTAL Percent	2 5.41	3 8.11	14 37.84	17 45.95	1 2.70	37 100.00

Inadequate cell size for valid statistical analysis.

Appendix D-3. Direction of posterior pharyngeal wall motion as seen on lateral view videofluoroscopy.

N Row % Column % GROUP	NONE	ANTERIOR	ANTERO-INFERIOR	ANTERO-SUPERIOR	OUTWARD	TOTAL
STICKLER (S)	4 44.44 26.67	5 55.56 26.32	0	0	0	9 24.32
TREACHER COLLINS (TC)	1 12.50 6.67	6 75.00 31.58	1 12.50 100.00	0	0	8 21.62
VELO-CARDIO-FACIAL (VCF)	8 66.67 53.33	3 25.00 15.79	0	0	1 8.33 100.00	12 32.43
VAN DER WOUDE (VDW)	2 25.00 13.33	5 62.50 26.32	0	1 12.50 100.00	0	8 21.62
NARROW PHARYNX (S, TC)	5 29.41 33.33	11 64.71 57.89	1 5.88 100.00	0	0	17 45.95
WIDE PHARYNX (VCF, VDW)	10 50.00 66.67 100.00	8 40.00 42.11	0	1 5.00 100.00	1 5.00 100.00	20 54.05
TOTAL Percent	15 40.54	19 51.35	1 2.70	1 2.70	1 2.70	37 100.00

Inadequate cell size for valid statistical analysis.

Appendix D-4. Contour of lateral pharyngeal wall motion as seen on frontal view videofluoroscopy[53].

N Row % Column % GROUP	NONE N	BALLOON B	SHELF Sh	VERTICAL V	TOTAL Percent
STICKLER (S)	0	6 66.67 31.58	2 22.22 28.57	1 11.11 10.00	9 24.32
TREACHER COLLINS (TC)	0	5 62.50 26.32	0	3 37.50 30.00	8 21.62
VELO-CARDIO- FACIAL (VCF)	1 8.33 100.0	3 25.00 15.79	3 25.00 42.86	5 41.67 50.00	12 32.43
VAN DER WOUDE (VDW)	0	5 62.50 26.32	2 25.00 28.57	1 12.50 10.00	8 21.62
NARROW PHARYNX (S, TC)	0	11 64.71 57.89	2 11.76 28.57	4 23.53 40.00	17 45.95
WIDE PHARYNX (VCF, VDW)	1 5.00 100.0	8 40.00 42.11	5 25.00 71.43	6 30.00 60.00	20 54.05
TOTAL Percent	1 2.70	19 51.35	7 18.92	10 27.03	37 100.00

B/Sh or V/N x pharyngeal width:
Fisher's Exact Test, not significant

[53]Data are reported for contour of left lateral pharyngeal wall (LPW) motion. The right LPW could not be visualized in one subject with VCF because of an inadequate barium coat, and one subject with Stickler syndrome had a balloon contour on the left and shelf-like movement on the right. There were no other differences in contour between the right and left lateral pharyngeal walls.

Appendix D-5. Videofluoroscopic data of experimental subjects[54].

CP#		DX	PHON	HAB?	BASE V	BASE PPW
1075		1	S	Y	0.5	0.2
1505		1	S	Y	NA	NA
1829		1	S	Y	NA	NA
2267		1	S	Y	NA	NA
2643		1	S	Y	0.39	0.18
3122		1	S	Y	NA	NA
3236		1	S	Y	0.25	0.4
3453		1	S	Y	CNV	CNV
3476	TWN	1	S	Y	0.7	0.27
1068		2	S	Y	0.21	0.21
1110		2	S	Y	1	0
1156	TWN	2	S	Y	1	0
1656		2	S	Y	NA	NA
2129		2	T	Y	NA	NA
2307		2	S	Y	NA	NA
2663	TWN	2	P	N	0.63	0
3653		2	S	Y	NA	NA
2115		3	S	Y	0.6	0.06
2234		3	S	N	NA	NA
2516		3	S	Y	0	0
2543		3	S	Y	NA	NA
2644		3	S	Y	0.21	0.11
2739		3	T	Y	NA	NA
2877		3	S	Y	NA	NA
2982		3	S	Y	0.24	0.3
3020		3	S	Y	NA	NA
3235		3	S	Y	NA	NA
3423	TWN	3	S	N	0.05	0
3770		3	S	Y	0.48	0.13
1070	TWN	4	S	Y	0.67	0.24
1831		4	S	Y	0.23	0.05
2274		4	S	Y	0.48	0
2459		4	S	Y	0.26	0.1
2883		4	P	Y	0.24	0.12
2980		4	S	Y	NA	NA
3161		4	S	Y	0.35	CNV
3525		4	S	Y	0.63	0.03

[54]Dx 1: Stickler, 2: Treacher Collins; 3: velo-cardio-facial; 4: van der Woude; NA= not available; CNV= could not visualize; TWN= Towne view en face in place of base view

Appendix D-5 (continued). Videofluoroscopic data of experimental subjects[55].

CP#		BASE LLPW	BASE RLPW	BASE %CLOS	EST %CLOS-R	BASE SHAPE
1075		0.36	0.38	0.9	0.9	CI
1505		NA	NA	NA	0.5	NA
1829		NA	NA	NA	NA	NA
2267		NA	NA	NA	0.9	NA
2643		0.35	0.45	0.94	0.85	S
3122		NA	NA	NA	NA	NA
3236		0.34	0.42	0.85	0.7	CO
3453		0.1	0.05	CNV	0.6	N
3476	TWN	0.42	0.33	0.95	NA	S
1068		0.5	0.5	1	NA	N
1110		0.5	0.5	1	NA	N
1156	TWN	0.44	0.44	1	NA	N
1656		NA	NA	NA	0.5	NA
2129		NA	NA	NA	NA	NA
2307		NA	NA	NA	0.85	NA
2663	TWN	0.1	0.12	0.7	NA	CO
3653		NA	NA	0.99	NA	NA
2115		0.33	0.33	0.89	0.8	CO
2234		NA	NA	NA	NA	NA
2516		0	0	0	0	G
2543		NA	NA	NA	0.9	NA
2644		0.26	0.36	0.84	0.6	CI
2739		NA	NA	NA	0.9	NA
2877		NA	NA	NA	NA	NA
2982		0.27	0.27	0.75	0.7	CO
3020		NA	NA	NA	0	NA
3235		NA	NA	NA	0.3	NA
3423	TWN	0.05	0.05	0.15	0.2	G
3770		0.29	0.29	0.86	0.6	CI
1070	TWN	0.5	0.32	0.98	NA	C
1831		0.34	0.39	0.82	0.8	S
2274		0.5	0.41	0.95	0.85	CI
2459		0.3	0.35	0.82	0.85	CI
2883		0.32	0.34	0.79	NA	S
2980		NA	NA	NA	0.25	NA
3161		0.42	0.37	0.93	0.85	CI
3525		0.31	0.22	0.86	0.9	CO

[55]NA= not available; BASE %CLOS= computerized measure of gap size; EST %CLOS-R= estimate of gap size by rater two; SHAPE: CI= circular, S= sagittal, CO= coronal, N= none, G= gross

Appendix D-5 (continued). Videofluoroscopic data of experimental subjects[56].

CP#		FRONTAL LLPW	FRONTAL RLPW	FRONTAL CNTR/L	FRONTAL CNTR/R	FRONTAL DIR/L
1075		0.49	0.49	B	B	M
1505		0.34	0.32	B	S	M
1829		0.21	0.17	B	B	SM
2267		0.36	0.32	S	S	M
2643		0.42	0.39	B	B	M
3122		0.33	0.4	B	B	M
3236		0.34	0.34	B	B	M
3453		0.05	0.05	V	V	N
3476	TWN	0.48	0.45	S	S	M
1068		0.5	0.5	B	B	M
1110		0.33	0.7	V	B	M
1156	TWN	0.5	0.5	B	B	M
1656		0.14	0.05	V	V	M
2129		0.22	0.33	B	S	M
2307		0.5	0.45	B	B	M
2663	TWN	0.11	0.11	V	V	M
3653		0.63	0.35	B	B	M
2115		0.23	0.37	S	S	M
2234		0.22	0.21	B	B	M
2516		-0.1	-0.1	B	B	O
2543		0.46	0.51	S	B	M
2644		0.27	0.28	V	S	M
2739		0.19	0.2	V	V	M
2877		0.25	0.29	V	V	M
2982		0.31	CNV	S	CNV	M
3020		0	0	N	N	N
3235		0.05	0.4	V	S	M
3423	TWN	0.1	0.09	V	V	M
3770		0.3	0.47	B	B	M
1070	TWN	0.53	0.28	S	S	M
1831		0.4	0.44	B	B	M
2274		0.53	0.5	B	B	M
2459		0.38	0.5	S	S	M
2883		0.25	0.18	B	V	M
2980		0.24	0.26	V	V	M
3161		0.46	0.44	B	B	M
3525		0.1	0.4	B	S	M

[56]CNV= could not visualize; L=left, R= right; CNTR (contour): B= balloon, S= shelf, V= vertical, N= none; Frontal DIR (direction of LPW): M= medial, SM= superomedial, O= outward.

Appendix D-5 (continued). Videofluoroscopic data of experimental subjects[57].

CP#		FRONTAL DIR/R	FRONTAL LEAK?	LATERAL V	LATERAL DIR/V	LATERAL PPW
1075		M	Y	0.56	S	0.2
1505		SM	Y	0.74	S	0
1829		SM	Y	0.4	S	0
2267		M	Y	0.95	S	0
2643		M	Y	0.6	S	0.1
3122		M	O	1	PS	0.23
3236		M	Y	0.6	S	0.42
3453		N	N	1	S	0
3476	TWN	M	Y	0.63	S	0.27
1068		M	N	0.58	PS	0.5
1110		M	N	0.76	P	0.29
1156	TWN	M	N	1	PS	0.3
1656		M	Y	0.8	S	0
2129		M	Y	0.62	S	0.09
2307		M	Y	0.66	PS	0.1
2663	TWN	M	Y	0.23	P	0.17
3653		M	Y	0.86	S	0.33
2115		M	Y	0.83	PS	0.1
2234		M	Y	0.8	PS	0
2516		O	Y	0	N	0
2543		M	Y	0.89	PS	0
2644		M	Y	0.88	S	0
2739		M	Y	0.9	S	-0.1
2877		M	Y	0.84	PS	0
2982		CNV	Y	0.86	PS	0.2
3020		N	Y	0	N	0
3235		M	Y	0	PS	0
3423	TWN	M	Y	0.28	T-H	0
3770		M	Y	0.82	S	0.1
1070	TWN	M	Y	1	S	0.25
1831		M	Y	0.43	S	0.33
2274		M	Y	0.67	PS	0.24
2459		M	Y	0.28	PS	0.29
2883		M	Y	0.15	P	0
2980		M	Y	0.31	PS	0
3161		M	Y	0.47	PS	0.38
3525		M	Y	0.92	S	0.1

[57]Leak (presence of VPI): Y= yes, N= no, O= occasional; Lateral DIR (Direction of velar motion): S= superior, PS= posterosuperior, N= none, T-H= tip hinge.

Appendix D-5 (continued). Videofluoroscopic data of experimental subjects[58].

CP#		LATERAL DIR/PW	LATERAL LEAK?
1075		A	Y
1505		N	Y
1829		N	Y
2267		N	Y
2643		A	Y
3122		A	O
3236		A	Y
3453		N	O
3476	TWN	A	Y
1068		AI	N
1110		A	O
1156	TWN	A	N
1656		N	Y
2129		A	Y
2307		A	Y
2663	TWN	A	Y
3653		A	Y
2115		A	N
2234		N	Y
2516		N	Y
2543		N	Y
2644		N	Y
2739		O	Y
2877		N	Y
2982		A	Y
3020		N	Y
3235		N	Y
3423	TWN	N	Y
3770		A	Y
1070	TWN	A	Y
1831		A	Y
2274		AS	Y
2459		A	Y
2883		N	Y
2980		N	Y
3161		A	Y
3525		A	Y

[58]Lateral DIR (Direction of posterior pharyngeal wall motion): A= anterior, N= none, AI= anteroinferior, O= outward, AS= anterosuperior; LEAK (presence of VPI): Y= yes, N= no, O= occasional

Appendix E. Prevalence data and selected cephalometric, nasopharyngoscopic, and fluoroscopic measurements of experimental subjects. (See Appendix A-1 for codes; "."=not available)

CP#	REFER AGE	GENDER	ESTAB DX	REF DX	REASON
1075	13.00	F	1	5	6
1505	4.00	F	1	5	6
1829	2.09	M	1	5	6
2267	5.01	M	1	7	9
2643	0.05	M	1	5	2
3122	0.00	M	1	5	1
3236	5.04	F	1	7	6
3453	5.03	M	1	7	6
3476	19.00	F	1	1	6
3786	4.05	F	1	7	6
1068	22.00	M	2	10	10
1110	28	M	2	2	10
1132	40.00	F	2	2	9
1156	12.00	F	2	2	12
1592	9.00	M	2	2	12
1656	5.00	M	2	12	6
2129	17.00	F	2	16	10
2307	14.00	F	2	2	1
2663	6.02	F	2	5	10
3653	8.9	M	2	2	10
1239	7.00	F	3	9	6
2115	30.00	F	3	9	6
2234	6.00	F	3	11	6
2516	4.00	M	3	3	6
2543	5.00	M	3	7	6
2644	6.06	F	3	9	9
2739	2.03	M	3	7	6
2877	5.03	M	3	9	6
2982	3.00	F	3	7	6
3020	4.09	F	3	9	6
3235	4.01	F	3	9	6
3423	6.01	M	3	8	5
3770	6.02	M	3	7	6
794	0.05	M	4	7	2
1070	0.00	F	4	4	2
1369	14.08	F	4	7	6
1651	0.00	F	4	4	2
1831	8.03	F	4	7	6
2274	6.03	M	4	7	6
2459	39.00	F	4	7	6
2596	16.00	F	4	7	6
2883	9.00	F	4	7	12
2980	8.00	F	4	7	6
3161	7.09	F	4	9	6
3525	15.00	F	4	14	10

Appendix E (continued). Experimental subjects: prevalence data and selected measurements.

CP#	CLEFT	REPAIR AGE	GLOSS/TRA	AUDIO (worse)	ARTIC DEVEL
1075	1	1.08	N	0	4
1505	1	3.06	Y	1	4
1829	1	1.03	N	0	4
2267	1	1.06	Y	0	0
2643	1	1.03	N	0	1
3122	1	0.10	Y	1	0
3236	2	99.99	N	1	0
3453	2	99.99	N	0	7
3476	1	1.00	N	1	2
3786	1	1.11	N	1	4
1068	2	99.99	N	2	2
1110	4	1.0	N	3	.
1132	2	99.99	N	2	2
1156	2	99.99	N	2	4
1592	2	99.99	N	3	0
1656	2	99.99	N	2	6
2129	2	99.99	N	2	6
2307	1	1.02	N	2	1
2663	1	2.00	Y	1	7
3653	4	5.0	N	1.5	.
1239	3	99.99	N	1	4
2115	2	99.99	N	1	4
2234	2	99.99	N	0	4
2516	2	99.99	N	0	4
2543	2	99.99	N	0	4
2644	3	99.99	N	0	4
2739	2	99.99	N	0	4
2877	3	99.99	N	0	4
2982	2	99.99	N	0	4
3020	2	99.99	N	0	4
3235	3	99.99	N	0	4
3423	3	99.99	N	0	4
3770	2	99.99	N	0	0
794	1	0.11	N	0	0
1070	1	1.05	N	0	4
1369	2	99.99	N	0	4
1651	1	1.04	N	0	4
1831	2	99.99	N	0	0
2274	1	1.05	N	0	4
2459	2	99.99	N	0	0
2596	1	1.03	N	0	4
2883	1	1.00	N	0	0
2980	1	1.00	N	0	4
3161	2	99.99	N	0	1
3525	1	1.00	N	0	2

Note: Cleft type 4 (cleft lip and palate) was coded as overt cleft (type 1) for statistical analyses

Appendix E (continued). Experimental subjects: prevalence data and selected measurements.

CP#	HYPER	HYPO	ORAL	QUALITY	PITCH
1075	1	0	0	1	0
1505	1	0	0	0	0
1829	3	0	0	0	0
2267	0	0	3	0	0
2643	1	0	0	0	0
3122	1	0	0	0	0
3236	2	0	0	1	0
3453	0	0	3	0	0
3476	2	0	1	1	2
3786	0.5	0	3	0	0
1068	0	0	1	0	2
1110	1.5	0	0	0	0
1132	0	0	1	0	1
1156	0	1	1	0	0
1592	0.5	0	1	0	1
1656	1	0	1	0	0
2129	0.5	0	0	0	0
2307	0.5	0.5	0	0	0
2663	2	0	0	0	0
3653	0	0	0	0	1
1239	3	0	0	0	0
2115	2	0	0	0	1
2234	3	0	0	0	0
2516	3	0	0	0	0
2543	1	0	0	0	0
2644	3	0	0	0	0
2739	1	0	0	0	1
2877	2	0	0	0	1
2982	3	0	3	0	0
3020	3	0	0	1	0
3235	2	0	0	0	0
3423	3	0	0	0	1
3770	1	0	0	0	1
794	0.5	0	0	0	0
1070	0	0	0	0	0
1369	2	0	0	1	0
1651	0	0	0	0	0
1831	2.5	0	0	0	0
2274	2	0	0	0	0
2459	1	0	0	0	0
2596	3	0	0	0	0
2883	3	0	0	0	0
2980	3	0	0	0	0
3161	1	0	0	0	0
3525	0	0	0	0	0

Appendix E (continued). Experimental subjects: prevalence data and selected measurements.

CP#	RECEP LANG	EXPRES LANG	NASO %CLOS	BASE %CLOS T=Towne	HABCLOS
1075	N	N	0.99	0.90	0.95
1505	L	L	.	0.80	0.80
1829	N	N	0.43	.	0.43
2267	L	L	0.57	.	0.57
2643	N	L	0.87	0.94	0.90
3122	N	N	0.99	.	0.99
3236	N	N	0.97	0.85	0.90
3453	N	N	0.95	.	0.95
3476	L	L	0.99	T-0.95	0.97
3786	N	N	0.75	.	0.75
1068	N	N	.	1.00	1.00
1110	N	N	1.00	1.00	1.00
1132	N	N	1.00	.	1.00
1156	L	L	1.00	T-1.00	1.00
1592	L	L	1.00	.	1.00
1656	N	L	1.00	.	1.00
2129	N	N	.	0.70	0.70
2307	N	N	1.00	.	1.00
2663	L	L	0.89	T-0.70	0.89
3653	N	N	1.00	0.99	1.00
1239	L	L	0.94	.	0.94
2115	L	L	0.85	0.89	0.87
2234	L	L	.	0.60	0.60
2516	L	L	0.00	0.00	0.00
2543	L	L	.	0.90	0.90
2644	N	N	0.15	0.84	0.15
2739	L	L	0.91	.	0.91
2877	L	L	0.97	.	0.97
2982	L	L	0.88	0.75	0.75
3020	N	N	0.08	.	0.08
3235	L	L	.	0.10	0.10
3423	L	L	0.10	T-0.15	0.13
3770	N	N	0.91	0.86	0.89
794	N	N	0.96	.	0.96
1070	N	N	0.85	T-0.98	0.90
1369	N	N	0.94	.	0.94
1651	N	N	1.00	.	1.00
1831	N	N	0.78	0.82	0.80
2274	L	N	0.51	0.95	0.73
2459	N	N	0.99	0.82	0.82
2596	N	N	0.40	.	0.40
2883	N	N	0.79	0.79	0.79
2980	N	N	0.71	.	0.71
3161	N	N	0.98	0.93	0.96
3525	N	N	0.86	0.86	0.86

Appendix E (continued). Experimental subjects: prevalence data and selected measurements.

CP#	%AD NASO	NV	FRLLPW	BASE & NASO SHAPE	BASE & NASO VPI/None
1075	0.00	0.90	0.49	CI	VPI
1505	.	.	0.34	CI	VPI
1829	0.23	0.63	0.21	CO	VPI
2267	0.52	0.45	0.36	CO	VPI
2643	0.47	1.00	0.42	CO	VPI
3122	0.62	1.00	0.33	I	N
3236	0.35	0.83	0.34	CI	VPI
3453	0.43	1.00	0.05	N	N
3476	0.43	0.85	0.48	L	VPI
3786	0.75	0.60	.	CO	VPI
1068	.	.	0.50	N	N
1110	0.00	1.00	0.33	I	N
1132	0.00	1.00	.	N	N
1156	0.00	1.00	0.50	N	N
1592	0.66	1.00	.	N	N
1656	0.80	1.00	0.14	N	N
2129	.	.	-0.10	CO	VPI
2307	0.62	1.00	0.50	N	N
2663	0.51	0.55	0.11	CO	VPI
3653	0.37	1.00	0.63	N	N
1239	0.00	0.76	.	CI	VPI
2115	0.58	0.90	0.23	CO	VPI
2234	.	.	0.22	CO	VPI
2516	0.05	0.00	-0.10	G	VPI
2543	.	.	0.46	CI	VPI
2644	0.13	0.17	0.27	G	VPI
2739	0.63	0.90	0.19	CO	VPI
2877	0.42	0.90	0.25	CI	VPI
2982	0.75	0.90	0.31	CO	VPI
3020	0.09	0.14	0.00	G	VPI
3235	.	.	0.05	G	VPI
3423	0.00	0.04	0.10	G	VPI
3770	0.17	0.95	0.30	CI	VPI
794	0.52	0.90	.	CO	VPI
1070	0.61	1.00	0.53	CI	VPI
1369	0.24	0.95	.	CO	VPI
1651	0.56	1.00	.	N	N
1831	0.35	0.38	0.40	CI	VPI
2274	0.47	0.27	0.53	CI	VPI
2459	0.59	0.63	0.38	CI	VPI
2596	0.22	0.05	.	CO	VPI
2883	0.12	0.10	-0.10	S	VPI
2980	0.25	0.50	0.24	CI	VPI
3161	0.40	0.89	0.46	CI	VPI
3525	0.07	1.00	0.10	CO	VPI

Appendix E (continued). Experimental subjects: prevalence data and selected measurements.

CP#	LATERAL LEAK? 0=occas	FRONTAL LEAK? 0=occas	N-S-B	N-S	S-Ba
1075	Y	Y	142	77	50
1505	Y	Y	128	62	35
1829	Y	Y	114	74	52
2267	Y	Y	124	66	42
2643	Y	Y	126	64	44
3122	O	O	124	62	41.5
3236	Y	Y	113	60	40
3453	O	N	127	62	42
3476	Y	Y	122	61	39
3786	.	.	120	60	38
1068	N	N	126	72	53
1110	O	N	112	78	58
1132	.	.	110	76	47
1156	N	N	125	62	33
1592	.	.	113	63	44
1656	Y	Y	138	65	46
2129	Y	Y	125	68	41
2307	Y	Y	118	68	47
2663	Y	Y	126	63	44
3653	Y	Y	124	66	40
1239	.	.	127	73	40
2115	N	Y	147	72	39
2234	Y	Y	137	70	36
2516	Y	Y	143	67	33
2543	Y	Y	138	74	37
2644	Y	Y	142	74	36
2739	Y	Y	131	70	36
2877	Y	Y	140	70	37
2982	Y	Y	127	70	41
3020	Y	Y	149	62	36
3235	Y	Y	140	65	37
3423	Y	Y	142	64	38
3770	Y	Y	136	65	37
794	.	.	139	69	41.5
1070	Y	Y	139	69	43
1369	.	.	143	77	53
1651	.	.	135	71	47
1831	Y	Y	140	68	39
2274	Y	Y	130	76	43
2459	Y	Y	130	68	49
2596	.	.	130	74	42
2883	Y	Y	133	72	46
2980	Y	Y	141	69	42
3161	Y	Y	131	69	43
3525	Y	Y	136	74	39

Appendix E (continued). Experimental subjects: prevalence data and selected measurements.

CP#	LUM2	LUM4	PPW2	PPW4	PPL-HY
1075	17	12	6	5	56
1505	10	16	16	6	39
1829	10	13	10	8	65
2267	7	17	18	6	52
2643	9	11	20	5	49
3122	5	8	14	5	48
3236	11	8	13	5	37
3453	13	14	10	3	54
3476	10	11	16	8	59
3786	10	8	16	5	41
1068	11	7	20	8	75
1110	4	3	10	9	80
1132	11	7	5	8	65
1156	5	5	18	6	59
1592	11	7	10	10	42
1656	16	10	8	3	45
2129	7	6	9	5	64
2307	5	7	3	7	60
2663	4	3	22	4	70
3653	8	7	15	11	54
1239	11	19	11	5	52
2115	15	11	4	2	56
2234	12	20	11	5	41
2516	9	11	10	8	35
2543	20	14	12	6	32
2644	23	17	4	3	33
2739	16	13	8	4	34
2877	23	21	4	3	34
2982	13	13	12	5	35
3020	16	15	9	5	43
3235	18	22	10	3	31
3423	15	12	7	6	32
3770	16	16	14	7	43
794	17	15	8	6	53
1070	15	13	12	8	69
1369	16	16	9	4	58
1651	16	9	4	5	62
1831	29	15	7	4	36
2274	16	14	8	8	37
2459	13	3	9	3	68
2596	21	15	7	4	46
2883	18	12	11	4	50
2980	15	22	15	6	38
3161	19	19	5	5	44
3525	15	12	6	3	43

Appendix E (continued). Experimental subjects: prevalence data and selected measurements.

CP#	PPL-PPW	ANS-PNS-V	PCTSKAW
1075	110	141	22.4
1505	122	146	25.4
1829	90	132	19.1
2267	92	130	24.2
2643	102	138	20.7
3122	93	137	16.4
3236	83	138	22.9
3453	106	148	27.5
3476	101	137	17.9
3786	98	149	28.4
1068	103	127	12.2
1110	105	130	10.6
1132	95	123	19.5
1156	117	123	14.1
1592	130	139	14.8
1656	117	139	24.0
2129	111	135	8.8
2307	116	124	9.8
2663	95	129	9.2
3653	105	115	18.5
1239	97	137	30.8
2115	104	128	23.6
2234	114	150	30.1
2516	90	143	22.1
2543	97	153	27.4
2644	90	150	30.8
2739	106	142	26.7
2877	97	144	33.2
2982	86	138	24.5
3020	93	131	34.2
3235	97	133	32.4
3423	104	141	28.2
3770	101	129	33.3
794	96	136	31.3
1070	100	134	28.0
1369	100	132	27.5
1651	102	140	24.6
1831	91	144	37.4
2274	108	146	25.4
2459	88	133	19.6
2596	120	146	28.3
2883	88	142	26.4
2980	110	133	24.6
3161	108	138	37.6
3525	104	142	27.4

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