A DESCRIPTION OF THE TRISOMY 21 PHENOTYPE BASED ON THE STABILITY OF CRANIOFACIAL REFERENCE LINES

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In Partial Fulfillment

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Master of Science

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by

Peter John Porter

Department of Preventive Dental Science

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ABSTRACT

Past cephalometric investigations of individuals affected with trisomy 21 have indicated a general retardation of growth with all linear dimensions being significantly smaller than in a comparable control group. Marked differences in the craniofacial complex have been noted and a distinct phenotype characteristic of the trisomy 21 group has been described.

Studies of maturational development in Down's syndrome have suggested significant differences between trisomy 21 and control groups with little correlation between skeletal ages and chronological ages. Hand-wrist analyses have shown that development of carpal bones progressed normally in the trisomy 21 sample, while epiphyseal maturation did not. Recently, additional support has been accumulating for a possible disturbance in endochondral bone formation. In

view of this evidence, previous methods of cephalometric investigation, utilizing the cranial base as the plane of orientation and with samples grouped by chronological age, require a re-evaluation.

This study was undertaken to investigate the variability and suitability of several craniofacial reference lines for use as the plane of orientation in a comparative study of the trisomy 21 phenotype. Linear and angular dimensions from lateral cephalometric radiographs were then compared by use of a multivariant factorial analysis. Based on the statistical and subjective evaluations, the following conclusions emerged:

1. The angular variability between craniofacial reference lines was found to be significantly greater in the trisomy 21 group than in the control group.
2. No craniofacial reference lines were completely void of changes in shape and position during growth, and the most suitable plane of orientation is one which is closely related to the area under investigation and which demonstrates low variability.

3. Angular variability between craniofacial reference lines was found to have a negative association between the standard deviation and variance of an angle and the means of the distances between the reference points for each of its arms. Other factors affecting variability were found to be the reproducibility of cephalometric landmarks and the biological variation of the skeletal structures involved. The spatial orientation of points defining an angle did not significantly affect angular variation.

4. In spite of recent reports of endochondral growth disturbances in trisomy 21 individuals, the cranial base was shown to be one of the most stable and dependable areas of the craniofacial skeleton in both the trisomy 21 and control samples. Three reference lines defined by cranial base landmarks demonstrated minimal angular variation for the two groups: the anterior cranial base (sella-nasion), the basicranial axis (basion-nasion) and the ethmoidale-sella line.

5. The Frankfort Horizontal also demonstrated low variability for both the trisomy 21 and control groups, when anatomic porion was used as the posterior landmark.
6. In the cephalometric analysis, grouping of the trisomy 21 and control samples by skeletal age rather than chronological age did not eliminate significant differences previously mentioned for most parameters, however, the significance of many of the higher order interactions of group, age and sex were reduced or eliminated altogether. Whether this diminished significance is the result of skeletal age grouping, the natural variability within the groups, or to a combination of the two, is undetermined.
7. Linear measurements involving the cranial base and nasomaxillary complex of the trisomy 21 sample were significantly smaller than the control sample, indicating an underdevelopment of the midfacial region from 3 years to adulthood. When compared to the basicranial axis, the maxilla of the trisomy 21 group was found to be in a normal antero-posterior position.

8. The anterior cranial base of the trisomy 21 group was proportionately shorter in relation to the posterior cranial base, suggesting a greater retardation of growth at the spheno-ethmoidal than sphenoccipital synchondroses.
9. Linear measurements of the mandible were similar for the trisomy 21 and control groups, until the 10-14 year age range suggesting similar growth increments for the two groups. Subsequent mandibular growth in the control sample resulted in a larger absolute size for the mandible of this group.
10. The shape of the mandible at ages 3-5 years in the trisomy 21 group, as well as an underdevelopment of the midfacial region, is believed to be responsible for the prognathic skeletal pattern in young children with Down's syndrome. Postural implications related to mouth breathing also contribute to the trisomy 21 phenotype.
11. When the basicranial axis is used as the plane of orientation, the direction and magnitude of rotation of the cranial base angle are believed to be

involved with the phenotypic appearance of trisomy 21 individuals.

12. The "apparent" mandibular prognathism characteristic of Down's syndrome appears to be the result of a combination of developmental characteristics, including the underdevelopment of the cranial base and nasomaxillary complex, increased convexity of the frontal bone, and the shape and size of the mandible and cranial base.

13. The maxillary incisors were slightly more proclined in the trisomy 21 group relative to the basicranial axis and the mandibular incisors were more proclined relative to the mandibular plane.

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DEDICATION

This thesis is dedicated to my parents whose inspiration has been instrumental in the realization of this achievement.

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INTRODUCTION

CHAPTER 1

INTRODUCTION

Down's syndrome has been the subject of extensive investigation since its initial recognition as a separate clinical entity over 100 years ago. Early studies consisted of subjective appraisals of the various physical abnormalities believed to be characteristic of this condition. In 1959, it was discovered using cytogenetic techniques that Down's syndrome was caused by a trisomy of chromosome number 21. Subsequently, the cytogenetic variability of the condition has become evident with the discovery of translocations, translocation carriers and mosaics. How these imbalances in the karyotype affect the biochemical mechanisms, which in turn may modify the phenotype, are as yet unknown. Recently, several radiographic investigations have contributed significantly to the understanding of the craniofacial abnormalities, characterizing the differences from the accepted norms.

Alteration in the maturational development, both dental and skeletal, of individuals with Down's syndrome has been suggested by several studies. It is presently believed that the rate of skeletal maturation is retarded in younger

age groups, as compared to a control sample, similar during mid-childhood and accelerated in later age groups relative to the control sample.

Considerable evidence has been accumulating that the growth deficiency in Down's syndrome may be associated with disturbed endochondral growth. This evidence includes the analysis of hand ossification centres which indicated an endochondral deficiency in growth, while the intramembranous bones compared well with normal growth (Nevile, 1973). Further support for the hypothesis of endochondral growth disturbance is found in several clinical characteristics of mongolism, as well as in the investigations of Benda (1960), Sommer and Eaton (1970), and Alimchandani (1973).

In view of our present knowledge of craniofacial growth in Down's syndrome, a re-evaluation of presently used methods of investigation would seem to be in order. Previous roentgenographic studies have been cross sectional in nature with the samples, both trisomy and control, divided into groups according to chronological age. Indications that the maturation rates differ between the two groups would suggest that many of the significant differences reported in the literature for the craniofacial dimensions

may be biased due to sampling techniques. It has been suggested that a more accurate depiction of the mongoloid phenotype would be presented if trisomy and control samples were grouped by skeletal and/or dental age (Nevile, 1973).

Similarly, lateral cephalometric studies comparing trisomy and control groups have traditionally used the anterior cranial base as the plane of orientation. The recent evidence supporting endochondral growth disturbances in Down's syndrome would suggest that the cartilagenous anterior cranial base may not be the most suitable plane for comparison. Moss (1967), on evaluating Kisling's templates (1966) of trisomy and control groups, suggested that superimposition on the posterior cranial base provided a more accurate characterization of the mongoloid phenotype.

This study was, therefore, directed firstly at investigating the variability and suitability of several craniofacial planes of orientation for use in a study of the trisomy 21 phenotype. The effect of both biological variability and spatial distribution of the points defining these planes was considered.

Secondly, the trisomy 21 phenotype was investigated,

using lateral cephalometric data, with the following objectives:

(1) to determine the effect of grouping samples by skeletal age on the significant differences in the various craniofacial dimensions previously reported in the literature for trisomy and control samples grouped by chronological age.

(2) to ascertain if a group of individuals confirmed by cytogenetic analysis as having a trisomy 21 karyotype have a distinct craniofacial phenotype.

(3) to observe if a less characteristic appearance would be found in adults with Down's syndrome following growth changes.

(4) to provide insight into the influence of genetic variation on craniofacial morphology and growth by comparing trisomy 21 and control groups.

REVIEW OF THE LITERATURE

CHAPTER II

REVIEW OF THE LITERATURE

I. DOWN'S ANOMALY

Early Investigations of Down's Syndrome

The earliest description of the clinical entity, Down's syndrome, evolved from the investigations of J. Langdon Down at the Eastwood Asylum in England, 1866. He accurately described the more characteristic abnormalities of this condition placing special emphasis on racial degeneration and on the consistent physiognomy of the disease.

Previous to Down, there had been isolated descriptions in the medical literature of patients, who, in retrospect, can be seen to have belonged to the same category (Esquirol, 1838; Sequin, 1846). Sequin, 1866, in his account of cretinism described a furfuraceous type "with milk-white, rosy, and peeling skin; with its shortcomings of all the integuments; with its cracked lips and tongue; with its red ectopic conjunctiva".

After 1866, there were no publications on mongolism until the combined papers of Fraser and Mitchell (1876) which represented the first scientific report on the disease. Although these writers referred to their patients as Kalmuck

idiots, they gave no indication that they knew of Langdon Down's paper. Fraser reported a case and gave an excellent description of an autopsy of the brain and Mitchell drew attention to brachycephalia and increased incidence with increased maternal age.

Many clinical reports followed, notably those of Ireland (1877), Beach (1878), Shuttleworth (1883, 1886) and Shuttleworth and Beach (1899). Shuttleworth, considered to be a leading authority on the subject at the time, referred to mongols as "unfinished children".

Jones (1890) described the brain, Oliver (1891) studied the eyes, Smith (1896) observed the curved little finger as characteristic of mongolism, and Garrod (1894), Thomson (1898), and Fennell (1904) described the association with congenital heart disease.

The next decade was marked by a series of surveys, each emphasizing a different aspect of the condition. Brushfield (1924) was primarily concerned with clinical details and their presence or absence in different cases. Orel (1927) recorded familial data which included notes on ABO blood groups and microsymptoms in relatives. A comprehensive investigation by van der Scheer (1927) surveyed the families of 259 cases and recorded many statistical and genetical data. In Brousseau and Brainerd's

monograph (1928), an extensive review of previous literature was provided.

Such early clinical descriptions of the various physical abnormalities presented in Down's syndrome, proved invaluable in the eventual establishment of definitive diagnostic criteria for this disease.

Clinical Diagnosis

Early diagnostic methods for Down's syndrome consisted entirely of a clinical evaluation of abnormal physical traits. The diagnosis was made by deliberately or unwittingly adding up the points in its favor (Penrose, 1933b). The number of observations required to establish the diagnosis depended on the tests available and on their discriminate efficiency. Some characters, like abnormal facial appearance are easy to observe and highly characteristic but extremely difficult to define. Others, like dermatoglyphic patterns, are definite, but they occur also in other conditions and in "normal" members of the population. Furthermore, measurable characteristics, like head size, stature and birth weight, though they have different mean values in mongols and "normals", have overlapping distributions.

To assist in the clinical diagnosis of mongolism, Oster (1933) described the ten cardinal signs: (1) four-finger line; (2) short, crooked fifth finger; (3) short, broad hands; (4) hyper-flexibility; (5) oblique palpebral fissures; (6) epicanthus; (7) furrowed tongue; (8) irregular and abnormal teeth; (9) high, narrow palate; and (10) flat occiput (brachycephalia). The extreme variability of mongoloid populations led Oster to say that ". . . mental defectives with four or more cardinal signs, in all probability, were mongols."

Supplemental diagnostic signs have been suggested by Levinson et al. (1955), Penrose (1961), Gustavson (1964), and Hall (1964). The diagnostic significance of these traits is limited by the fact that they are not clearly definable and depend on clinical impressions. Hall (1964) gave the frequencies of occurrence of the traits in control groups and these showed that some signs, like flattened features and excessive skin at the back of the neck, have a very high diagnostic value.

Such diagnostic methods can only be logically justified if two rules hold true; first, the traits must all be equally characteristic of the condition concerned; and, secondly, their occurrences should be mutually independent.

Fried (1970) illustrated statistically the ten most informative symptoms of mongolism in the newborn. The most frequent single contributing cause to "mongoloid facies" was found to be the oblique palpebral fissure, occurring in 97.5%. Other significant factors were: (1) abundant skin on neck; (2) mouth corners turned down; (3) general hypotonia; (4) flat face; (5) at least one dysplastic ear; (6) epicanthus; (7) gap between toes one and two; (8) tongue protruding; (9) head circumference at birth not exceeding 32 cm; and (10) simian crease in at least one hand.

Cytogenetic methodology has confirmed the assumption that any infant exhibiting at least five of these signs is, in fact, a mongoloid. In spite of this apparent reliability of clinical diagnostic methodology, chromosome analysis is necessary for complete confirmation.

Incidence

In order to be reliable, figures on the frequency of mongolism among newborns should include those mongoloids who are stillborn and those who die soon after birth (Benda, 1969). Beidleman (1945) reported that in the fourteen years between 1930 and 1944 an average of 3.4 mongoloids

per 1,000 births was found with surprising uniformity. Unfortunately, few hospitals diagnose mongolism at birth and so, if the child dies at birth, the diagnosis is usually congenital heart disease, prematurity or asphyxiation, and seldom mongolism.

Incidences from 0.32 to 3.4 per 1,000 births have been reported by Lilienfeld (1969). Hall (1964) in a population study, and Robinson and Puck (1967) in a hospital study, found incidences of 1.53 and 1.14 respectively. Jacobs (1969), using combined chromosomal surveys from Ontario, New Haven and Edinburgh, reported an incidence of 9.0 per 1,000 births. In "The Manitoba Study", Uchida (1970), the reported incidence of mongolism varied from 0.90 to 1.35 per 1,000 live births. In that study, 96% of the mongoloids were trisomic. Wahrman and Fried (1970) in a four-year study of all hospital births in Jerusalem gave an incidence of 2.19 per 1,000 live births.

The different incidence rates may be caused by population differences or may reflect differences in standards of diagnosis and degree of reporting. However, it would appear that the population incidence ranges between 1 and 2 per 1,000 births, as a mean value for all types of Down's

syndrome and all maternal ages (Mikkelsen, 1971).

The increased prevalence of Down's syndrome with advancing maternal age is well documented (Jenkins, 1933; Penrose, 1933; Oster, 1953, 1956; Collman and Stoller, 1962). A classification of Down's syndrome patients was postulated by Penrose (1963) according to their relative dependency on maternal age. Class A includes all hereditary cases and some hypothetical instances of environmental origin -- age independent cases; Class B includes age dependent cases. Over the last thirty years, there has been a trend towards younger maternal age at childbirth in many countries. Consequently, the proportion of live births to mothers over the age of 35 years has fallen considerably with a corresponding decline in the incidence of Down's syndrome. Richards (1967) reported a slight increase in the number of mongoloids born to young mothers, but a great decrease in the numbers born to elderly mothers. Penrose (1967) found a 9.1% increase in Class A mongoloids and a similar 9.1% decrease in Class B mongoloids in a fifteen year study of England and Wales. Collman and Stoller (1969) observed a decrease in the mean percentage incidence of mongols with diminishing maternal age, while

Uchida (1970) found only a slight fluctuation in the mean maternal age of mongols. Certain environmental factors operating in addition to maternal age were suggested as the cause of this trend.

Mortality

Advances in modern medicine have created a general secular decrease in infant mortality rates, and mongoloids have shared in this. Carter (1958) compared the mortality of mongoloids from birth to ten years of age between the period 1944-48 and 1955-59, and the results suggested a 40% decrease in mortality.

The most common cause of death in mongoloid children is respiratory tract infection (Penrose et al., 1966), with bronchopneumonia being the most lethal complication (Carter, 1958). Pulmonary tuberculosis has been a common cause of death at later ages (Richards, 1970). Congenital heart disease is the second most common cause of death (Record and Smith, 1955; Carter, 1958; Penrose and Smith, 1966).

The mortality during the first year of life, although still high due to lethal congenital malformations and other causes, has been significantly reduced due to

immunization against infectious diseases, the introduction of sulphonamides and antibiotics, and improved general care.

Forssman and Akesson (1965), in a study of 1,263 institutionalized Swedish mongoloids, found the mortality rate for mongols of all ages to be 6% higher than that of the general population. They found no sex differences, unlike Penrose (1964), Record and Smith (1963b) and Collman and Stoller (1963b). Lilienfeld (1969) reported that 25-30% of mongoloids die during the first year of life and about 50 percent during the first five years. Wahrman and Fried (1970) reported that only 60.8% reach the age of six months and by one year 44.7% had died.

There is less information about mortality at later ages. Forssman and Akesson (1965) found an excess mortality of 11% in the one to five age group, and of less than half this excess thereafter, up to age 40 years. Above forty, however, the mortality rate increased sharply, reaching an excess of 30% above the general population. It is not understood why the mortality of mongolism, which is only moderately greater than that of the general population between the ages of five and forty years, then rises steeply. Richards (1970) suggests that the process

of aging that occurs in normal subjects sets in sooner in mongols, or qualitatively different pathological processes occur.

Cytogenetics

Before the chromosomal etiology of mongolism was discovered, twin studies offered strong support for the genetic etiology of the condition. It was noted that all presumed monozygotic twins were concordant for mongolism, while this was not true of dizygotic twins (Oster, 1953; Penrose, 1954; Allen and Kallmann, 1957; Lejeune, 1964). The multiple occurrence of Down's syndrome in families of women with the same condition, lent additional support for a genetic defect.

Waardenburg (1932) was the first to suggest chromosomal abnormality as a causative factor in Down's syndrome. He even suggested nondisjunction as a possible mechanism producing the chromosomal abnormality.

Tijo and Levan (1956) used the hypotonic shock technique (Hsu, 1952) to separate and identify the chromosomes of living fibroblasts from four therapeutically aborted embryos. Their observation that the majority of cells

contained 46 chromosomes was later confirmed by Ford and Hamerton (1956) using human sex cells.

Down's syndrome became the first known example of human aneuploidy and its chromosomal constitution has since been explored more energetically than that of any other condition. Lejeune, Gautier and Turpin (1959) reported that individuals with Down's syndrome had 47 chromosomes and that the supernumary chromosome was one of the small acrocentrics. Shortly afterwards, this was confirmed by Jacobs et al.(1959), Ford et al. (1959), and Book et al. (1959).

The cytogenetic variability of Down's syndrome became evident with the discovery of translocations (Polani et al., 1960; Fraccaro et al., 1960) translocation carriers (Penrose et al., 1970), and mosaics (Clarke et al., 1961; and Blank et al., 1962).

A classification of the cytogenetic entities found in Down's syndrome was established by Hamerton et al. (1965).

I. Primary trisomics result from the phenomenon called "nondisjunction" and constitute the majority of the mongoloid population (94.5%), Hamerton (1971). Non-disjunction implies failure of the homologous chromosomes to

separate during the first of the two meiotic divisions or failure of chromatids to separate during the second meiotic division. The results of nondisjunction were first discovered in plants by Gates (1908), however, the cytological process was not demonstrated until eight years later (Bridges, 1916). This type of aberrant chromosomal behaviour has 47 chromosomes, one of which is an additional chromosome in group G, arbitrarily defined as number 21 (International Study Group, Denver, 1960).

There has been uncertainty about which of the two chromosome pairs numbered 21 and 22 is involved in the trisomy responsible for Down's syndrome. Ordinary staining techniques and autoradiography have not been conclusive (Therman et al., 1961; Yunis et al., 1965; Fraccaro et al., 1967; and Mikkelsen, 1969). By means of the newer technique of fluoroscopy, it has been shown with fair certainty that the trisomic chromosomes are, in fact, the smaller of the two pairs of the G group, therefore, number 22 (Crossen, 1972; Dutrillaux et al., 1972; and Stern, 1973). However, by general consensus, the nomenclature remains trisomy 21.

II. Secondary trisomics result from the phenomenon

"translocation" and constitute about 5.47% of the mongoloid population (Hamerton, 1971). In translocations, a break occurs near the centromeric region of both chromosomes so that the long arm is involved in one of the chromosomes and the short arm in the other. The reorganization leads to two chromosomes, a large translocation chromosome and a micro-chromosome. The large chromosome can be transmitted through several generations, while the small chromosome is lost during cell division (Mikkelsen, 1971).

Several types of translocations have been reported, D/G (DgGg) and G/G (GgGg) being the most common.

The finding of the translocation or secondary trisomy type of Down's syndrome was important in explaining the familial occurrence of mongolism. The translocation chromosome can be carried by a normal person and be transmitted through several generations. Translocations of (DgGg) and (GgGg) type occurred in nearly equal frequencies. Half of the t(DgGg) cases were familial while most of the t(GgGg) arose sporadically (Mikkelsen, 1971).

Translocations are more common among mongols born to young mothers. The first case of translocation trisomy was found when patients born to young mothers were examined cytogenetically (Polani et al., 1960). Mikkelsen (1971)

indicated that about 8% of the mongols born to young mothers showed translocations, while only 1.5% of the mongols born to mothers over 30 years showed this karyotype. About 2.24% of the patients born to young mothers had inherited their translocation from one of their parents, as compared to 0.47% of patients born to elderly mothers.

III. Mixoploid or mosaicism occurs when two or more cell types appear in an individual because of mitotic non-disjunction (Ford, 1969). Mosaics can arise due to non-disjunction during mitosis from a normal zygote with 46 chromosomes, or they can arise from an abnormal zygote with trisomy, due to the loss of the extra chromosome during mitosis.

Mosaics are uncommon in typical cases of Down's syndrome. Hamerton et al. (1965) found frequencies of about 1% in typical cases while the frequency rose to 10% in atypical cases.

Trisomic cells of mosaics have a higher frequency (20%) in skin fibroblasts than in blood (Richards, 1969). No significant difference in the prevalence of mosaics among patients born to young or elderly mothers could be shown by Mikkelsen (1967b); however, Richards (1969) found

a slight excess of mosaics born to young mothers.

Interrelations of Form and Function

Queen (1975), in a cinefluorographic study of deglutition in Down's syndrome using the five stages suggested by Cleall (1965), found significant differences at the rest position for the trisomy and control groups. He felt that both hard and soft tissue compensations were occurring in an attempt to maintain the vital function of respiration and that these compensations were a part of the mongoloid "phenotype".

Upper respiratory obstruction is common in children with Down's syndrome, a fact attributed to decreased size of the nasal cavity and to incomplete involution of the pharyngeal tonsil of the nasopharynx (Queen, 1975). The hard and soft tissues attempt to overcome this obstruction by increasing the 'effective' size of the oral cavity and oropharynx. Low, protruding tongue position and large, obtuse soft palate both appear to be soft tissue adaptations to mouth breathing, and extension of the cervical vertebrae increases the size of the oral cavity and orophyarynx by increasing the distance between the posterior nasal spine

and the anterior tubercle of the atlas.

Local effects of these hard and soft tissue compensations on the remainder of the craniofacial skeleton appear to be minimal; however, correlations with the high incidence of bilateral posterior crossbite (Jensen, 1973), proclined maxillary incisors and openbite tendency, are possible.

Implications of upper respiratory obstruction on general body health can be far-reaching. Menasche et al. (1965) suggested chronic upper respiratory obstruction as a cause of heart failure and this was supported by Noonan (1965), Luke et al. (1966), Massumi et al. (1968) and Clairmont et al. (1975). In all of these cases, substantial improvement was noted after adenoidectomy and/or tonsillectomy.

Luscher (1930) reported that trigeminal nerve stimulation in the nasal mucosa by air currents was involved in the movements of the thorax-lung system. Also, Unno et al. (1969) observed an association between high nasal obstruction and decreased pulmonary function due to a reflex action.

The connection of upper airway obstruction in mongoloid children could have significant effects on the

general health of these individuals, and in particular, on chronic respiratory disease and congenital heart failure -- the two major causes of premature death in Down's syndrome. The surgical procedures of tonsillectomy and/or adenoidectomy have been suggested (Menasche et al., 1965; Cox et al., 1965) and the non-surgical procedure, rapid maxillary expansion, is another possibility (Queen, 1975). Further investigation to determine the most satisfactory approach is required.

Cerebral Metabolism in Down's Syndrome

Diminished cerebral metabolism in early life, whether due to a lack of oxygen or sugar (glucose) could lead to irreversible, pathological changes in cerebral function; changes which persist after the oxygen and sugar again become available to the brain. An example of such a condition is infant hypoglycemia, where glucose deficiency often results in severe mental retardation.

Neuropathological findings are well documented in descriptions of the infant mongoloid brain, which suggest a general lack of development, in particular of the frontal lobes, cerebellum and brain stem (Apert, 1914; Davidoff,

1928; Benda, 1960). The total weight was less than normal and the neuropathological changes were usually diffuse and non-specific (Crome, 1965).

Investigation of cerebral dysfunction in mongoloids involves the analysis of the differential values of oxygen and sugar between arterial and venous cerebral blood (Himwich et al., 1940; Lessen et al., 1966). Technical and human limitations in dealing with mentally retarded patients have created controversy with respect to data collected; for example, the influence of either heavy sedation or general anesthesia on cerebral oxygen intake.

Himwich and Fazekas (1940), with no mention of a general anesthesia, found a diminished utilization of oxygen and sugar for each hundred cubic centimeters of blood passing through the infant mongoloid brain. The oxygen content of cerebral blood was lowest in infants, 14.51 volumes percent, increased to 15.71 volumes percent in children and attained a value within normal limits, 18.49 volumes percent, in adults.

Lessen et al. (1966) studied adult mongoloids using general anesthesia (halothane). They found cerebral oxygen uptake to be within normal limits.

The improvement of cerebral oxygen values with age (Himwich et al., 1940) could have many ramifications. Cerebral dysfunction at infancy would cause irreparable damage regardless of later conditions. Also, the high infant mortality rate in Down's syndrome would tend to eliminate a certain percentage of the population and those who reached adult status would represent a biased sample of the total mongoloid group.

II. CEPHALOMETRIC ANALYSIS

Modern techniques in roentgenographic cephalometry owe their inception to studies of racial types. Anatomists and anthropologists, during the eighteen and nineteen hundreds, utilized craniology (the direct measure of the dry skull) and cephalometry (the direct measure of the living head) to satisfy their preoccupation with race and sex differences in the adult skull. The natural heritor of craniometry and cephalometry, roentgenographic cephalometry, was introduced by the independent efforts of Broadbent (1931) and Hofrath (1931) providing investigators with a practical method of measuring craniofacial growth and development.

Planes of Orientation - Effective utilization of roentgenographic cephalometry in the study of growth and development requires the establishment of a plane of orientation. Little research is reported in the field of cephalometric superimposition due to the difficulty involved in objectively interpreting and comparing the various methods of orientation. Since most methods of orientation presently in use are of untested reliability, it would seem that results of studies dependent upon these methods are of questionable significance.

Superimposition of lateral cephalograms facilitates the analysis of local changes within a very limited area and analysis of more general areas or relations between different regions. A basic problem is the difficulty in locating any particular point or area that is without modification in shape due to growth and development. For ideal superimposition, it is necessary to locate a reference plane void of changes not only in shape, but also in position, during all stages of growth. The fact that different areas grow at different rates, which are not proportional, suggests that a completely acceptable method of orientation will never be found. With this in mind, the

best method would be to use that linear dimension which best describes the particular area of interest and which, at the same time, demonstrates relatively low variability within the craniofacial complex.

Minimal biological variation is critical to a plane of orientation. Schmidt (1876) studied the variability of horizontal craniometric planes and ranked the planes according to the ranges of the angles between them. His results indicated that the Gottingen plane and His plane were the least variable. Koski and Virolainen (1956) investigated the angular relationships between six lines of reference. They concluded that each of the lines covering the whole sagittal length of the skull had a more constant relationship to the other lines of reference than those which covered only part of the skull base or face. They recommended the His line for studies involving the facial area.

Bergersen (1961) studied the adaptability of several superimposition techniques to longitudinal cephalometric research. He introduced "the intersection point method" which superimposes on the posterior extensions of the incremental growth vectors of nasion and anterior nasal

spine, when the calvarial outlines are concentrically centred upon one another. He found that the intersection point method described facial changes more accurately during growth than the more conventional methods which utilize sella-nasion (Bjork, 1941, 1947, Riedel, 1952) or the registration point of Broadbent (1931, 1937).

Wei (1968) studied five commonly used reference lines and demonstrated that although all the lines showed considerable variation, the nasion-sella line was the least variable, followed by the Frankfort Horizontal and the ethmoid-sella line.

Solow (1966), in a study of the patterns of cranio-facial associations, demonstrated that the variability of angular measurements between different reference lines followed a definte relationship based on the geometrical distribution of the landmarks defining these lines. He confirmed a negative association between the standard deviations of the angles and the means of the reference point distances of the angle arms. Thus, biological factors alone were not responsible for the variability of most reference lines. Henry and Cleall (1974) confirmed these findings in a repeated orientation study on monkey

cephalograms.

Reproducibility of Cephalometric Landmarks - The reproducibility of the anatomical landmarks defining a plane of orientation is of the utmost importance. Bjork (1947) mentioned that studies of the reliability of cephalometric landmarks were directed towards the error of the method, which he differentiated into:

(i) differences between two films of the same subject

(ii) observed differences in locating the points and

(iii) variations in measuring the distance between two marked points.

His analysis of the error of the method revealed large differences in precision when localizing different cranial landmarks. However, with easily identified landmarks, only minor errors were found and these ranged from 0.3 mm to 1.4 mm in linear measurements and from 0.3 degrees to 1.6 degrees in angular measurements. Richardson (1966) found that most cranial landmarks had a margin of error of less than $\pm$ 1.0 mm and he found that all angular

measurements followed the variation tendency of the landmarks. Vertical deviations rose when anatomical curves were involved (subspinale and supramentale) and horizontal deviations rose when menton, anterior nasal spine or the pterygomaxillary fissure were used.

Baumrind and Frantz (1971) found that each landmark had its own characteristic pattern of errors and that landmarks placed on curves with wide radii were difficult to locate, while those located on anatomically formed edges or creases were easy to identify.

Midtgärd, Bjork and Sten-Linder-Aronson (1974) studied the reproducibility of fifteen landmarks and the errors of measurement in seven cranial distances. They found that errors caused by the radiography were slight, while those created by the uncertainty of the observer in placing the landmark were greater. The reproducibility was good for all landmarks, except orbitale.

The correct interpretation of bone structure has been studied by Yen (1960) and Van der Linden (1971). Van der Linden, using sixty-four Asiatic Indian skulls, found that a number of landmarks deviated from their generally accepted defintions (prosthion, infradentale, menton and gnathion). He also concluded that individual local

variations in skeletal structure played a role in the location of sella, nasion, prosthion, infradentale, menton, gnathion, and, especially, point A.

Recent advances have been made in the method of quantifying data from cephalometric radiography in an attempt to reduce the error of the method in order to identify subtle change. Actual tracing of radiographs has been eliminated by the use of the strip chart digitizer and key punch equipment and the use of computer programming for geometric and mathematical calculations (e.g. coordinate analysis system - Cleall and Chebib, 1971).

Horizontal Planes of Orientation

Krogman and Sassouni (1957) pointed out that because roentgenographic cephalometry developed from craniometry, many of the points and planes of reference adopted for use were those devised by craniologists for comparing adult dry skulls. Krogman (1951) published a historical survey of the many planes used in both craniometry and cephalometry. He particularly liked the use of Frankfort Horizontal because it made no difference whether craniometry or

cephalometry were used. Prior to "the x-ray era", the Frankfort Horizontal was the most commonly used horizontal plane of reference. It was defined at the anthropological congress in Frankfort am Main (1882) as passing through the upper perifery of the external auricular canal and the lowest point of the left orbit. Some authors have chosen to use the cephalometric, or anatomic porion (Blair, 1954; Craig, 1951; Higley, 1954; Williams, 1955), while others have used machine porion (Bjork, 1947; Moorrees, 1954; Ricketts, 1952; Graber, 1952). Frankfort Horizontal has the advantage of being fairly accessible and well defined, as well as coinciding with the true horizontal plane through the cranium. Lüthy (1948) reported a median deviation of about 5.0 degrees, while Downs (1952) found the mean position deviated + 0.9 degrees from level. Cleall (1966) found Frankfort Horizontal to be close to the true horizontal (90.1 degrees) at the normal resting posture.

Broadbent (1931, 1937) was among the first to recognize the problems of interpreting cephalometric radiographs on a longitudinal basis. He found the cranial base to be a relatively stable region and used this as a

basis for orientation.

McDowell (1941) used several reference points (lambda, bregma and Bolton point) to orient successive calvarial outlines.

Krogman (1951) suggested four major classifications for craniofacial planes:

(i) Resting Horizontal Planes which were defined by the external anatomy of the skull and mandible and included Blumenback's Plane and Von Baer's Plane.

(ii) Planes using Craniometric Points which corrected the deficiency of the first classification by having precise defintion of endpoints. This group included: Broca's Plane, His' Plane (His, 1864; Koski, 1953, 1956; Koski et al., 1955;Silversten and Hasund, 1970), Martin's Plane, Huxley's Plane, or the basicranial axis (Welcher, 1868; Lindegard, 1951), Hamy's Plane, Schwalb's Plane, Schmidt's Plane, and the plane from glabella to opisthion.

(iii) Planes Centering Upon the External Auditory Meatus, which included six planes: Camper's Plane, Von Ihring's Plane, Pycraft's Plane, Montaqu's Plane, Frankfort Horizontal and the Krogman "Nasion-Parallel".

(iv) Roentgenographic Cephalometric Planes which included the Broadbent Plane, the Broadbent-Bolton Plane, the Margolis Plane, and the Bjork Plane.

The cranial base represents a phylogenetically stable area of the skull (Moss and Greenberg, 1955; Ford, 1958; Scott, 1967; Moss and Salentyn, 1969; Sicher, 1970). Brodie (1941, 1953) made use of the sella to nasion line registered on sella as a method of orientation because it served as a division between the cranial vault and face, and provided a stable reference base against which sutural facial growth could take place. The use of this plane was supported by Bjork (1941, 1947), Riedel (1952) Steiner (1953), and Bjern (1957). The use of sella turcica and nasion as reliable fixed reference points has been criticized in recent studies. Baume (1957) felt that the active growth of the sphenoccipital synchondrosis and the pituitary gland caused variation in the position of the reference points and Scott (1956) found superior migration of the landmark nasion. Moore (1949) used vital staining techniques on monkeys and found evidence of appositional bone growth at nasion.

DeCoster (1951, 1953) reported that the cribiform

plate and planum sphenoidale completed growth at about seven years and suggested the use of the cribiform plane as a superior method of superimposition. Ford (1958) substantiated this constancy on dried skull material. Richardson (1966) found this area difficult to reproduce.

According to the German school, the most conservative portion, phylogenetically and ontogenetically, of the neural mass is the brain stem and, therefore, the most conservative portion of the cranial base is the cerebral surface of the postsella portion of the skull base which supports the immediately overlying brain stem. Moss (1967) suggested that when comparing trisomy 21 and control populations, registration on the posterior cranial base provided a more accurate characterization of certain features of the trisomy 21 phenotype.

Vertical Planes of Orientation

The use of a vertical plane of orientation has been suggested by several investigators. Broadbent (1931) suggested a vertical axis of growth which extended from the coronal suture to the anterior border of the pterygomaxillary fissure and crossed the mandible close to the antigonial notch.

Perez and Beauvieux (1922) investigated the horizontal semicircular canal and the petrous bone. As the semicircular canals were involved with the sense of equilibrium, they felt that an axis based on these canals would have a meaningful relation to postural orientation. Beauvieux, Autissiere and Beltrami (1949, 1951) felt that the axis of the semicircular canal was parallel to the nasion-opisthion line. Delattre and Daile (1950) disagreed and Delattre and Fenart (1955) demonstrated variation with age and species.

Enlow (1969, 1973) investigated the P.M. Vertical Plane (posterior nasomaxilla) which was defined superiorly by the point of intersection of the greater wings of the sphenoid with the cranial floor and inferiorly by the lowermost point of the pterygomaxillary fissure. This plane was said to be approximately perpendicular to the line of vision and so represented a reference line consistent with the anatomically "neutral" position of the head. Feuer (1974) found the P.M. Vertical Plane to have an average inclination of 9.0 degrees to the vertical, with a standard deviation of 4.4 degrees. The reproducibility of the landmarks for this vertical line was 0.2 degrees with

standard deviation of 0.9 degrees.

III. MATURITY INDICATORS

The scientific investigation of dentofacial deformities is dependent upon an accurate interpretation of the facioskeletal growth pattern. Physical growth and developmental manifestations can provide useful criteria for such an interpretation. Such parameters as weight, height, dental development and skeletal development are frequently used in evaluating the growth and maturational status of subjects.

Hereditary, functional, environmental, sexual, nutritional and metabolic factors influence growth and development. Although the proportional effects of each of these factors is subject to controversy, their collective input tends to introduce significant variation both within an individual and between individuals.

Height and weight are the physical manifestations of growth and development which are probably used most in diagnostic procedures, and in the assessment of growth and development. Body weight is probably the best index of nutrition and growth because it sums up all increments in

size (Ausubel, 1958; Stuart et al., 1946; Watson and Lowry, 1954).

The development and eruption of teeth are a part of the child's total development. Dental developmental schedules are used as indices of growth and maturation during childhood since teeth develop and erupt in characteristic sequences and within predictable age ranges (Massler et al., 1941; Nelson, 1959; Schour et al., 1941; and Watson and Lowry, 1954).

Of the various methods of expressing growth time that have been suggested as substitutes for, or adjuncts to, chronological age, the progressive maturation of the skeleton is the most widely used (Greulich, 1950; Johnston, 1963). The appearance and union of different skeletal centres of ossification follows a fairly definite pattern and time schedule from birth to maturity and a roentgenographic study of these skeletal maturational processes provides a valuable criterion of the child's level of osseous maturation (Nelson, 1959; Watson and Lowry, 1954). The carpal area provides a useful index of skeletal maturation and is frequently utilized because it is easily accessible and radiographs can be taken at a minimum of expense and

time (Nelson, 1960).

Skeletal maturation assessments are made by comparing the individual's hand-wrist radiographs with a series of films typical of various age groups. Such pictorial standards have been published by Wilms (1902), Rotch (1909), Flory (1936), Greulich and Pyle (1950), and Mackay (1952).

More recently, a series of standard stages through which each bone passes, has been established (Acheson, 1954, 1966; Tanner and Whitehouse, 1959; Tanner, Whitehouse and Healy, 1962). Each bone in the radiograph is matched with the standard stages, each of which has a numerical score associated with it, and the hand and wrist thus scores a total of so many maturity points. This procedure is termed the Oxford method.

The significance of this "skeletal yardstick" in assessing the time of achievement of maturity was investigated by Green (1961). He studied the correlation between the various maturity indicators (dental age, skeletal age, weight age, height age and chronological age) and found positive correlations between each, suggesting that maturation and growth go "hand-in-hand". Thus parameters, such as skeletal development, are used

in comparative studies to illustrate the true relationship between the samples.

Sex differences are apparent in skeletal maturation (Pryor, 1905, 1923, 1925; Menghi, 1954; Tanner, 1962) presumably related to the genes on the Y chromosome (Tanner and others, 1959) or to the genes on the X chromosome (Garn and McCreery, 1970). At birth girls are ahead by a matter of weeks, at midgrowth by months, and at adolescence by two years (Tanner, 1962).

The Greulich and Pyle method for assessing skeletal maturation tends to rule out sex difference by using a separate set of standards for each sex. In contrast, the Oxford Method, having one set of standards for both male and female subjects, reveals differences in maturation rates related to sex.

IV. SKELETAL MATURATION IN DOWN'S SYNDROME

Individuals with Down's syndrome present a fairly consistent alteration of growth, in both timing and resultant morphology. Shuttleworth (1886) concluded that mongoloids were "unfinished children" and Benda (1960) suggested that they represented a deceleration of prenatal growth. Presumably

these abnormalities were produced, either directly or indirectly, by the additional genetic material found in chromosome 21.

Alteration in the skeletal development of mongoloids has been supported by previous studies. Ballard (1911) examined 25 children with mongolism and found delayed skeletal age to be general. Hefke (1940) and Engler (1949) reported that bone maturation in mongolism approximated the normal rate. Benda (1960) stated that the appearance of ossification centres was frequently retarded and irregular among mongoloid children. Watson and Lowry (1958, 1973) asserted that delayed osseous development was characteristic in mongolism. Menghi (1954) found delayed bone development, especially among male mongoloids.

Poszonyi et al. (1964), using the Greulich and Pyle standards to investigate hand-wrist radiographs of 100 mongoloid children, found delayed skeletal age present until about 8 years of chonrological age, followed by an acceleration of bone development until the theoretical norm was surpassed. Like Benda (1960), these investigators found osseous maturation to terminate well in advance of the theoretical normal. Their findings suggested an

intrinsic rate of aging which was unique to the mongoloid and advanced of the norm.

Roche (1964), in a longitudinal study of osseous development in Down's syndrome, supported the findings of Poszonyi et al. (1964). Using Greulich and Pyle standards, he found a definite difference between early and late skeletal maturation rates.

Nevile (1973), in a cross sectional study of maturation in Down's syndrome, found skeletal maturation to be retarded in the youngest age groups, not different from the control group in mid-childhood, and accelerated in later age groups.

Developmental differences between round and long bones have been reported for both normal children (Robinow, 1942; Garn and Rohmann, 1959; Pyle and Sontag, 1943) and mongoloids (Nevile, 1973). Nevile found that carpal development in Down's syndrome was almost normal, while epiphyseal development was greatly delayed. This could suggest deficiency in endochondral bone growth, a theme which has been supported by Benda (1960), who demonstrated disorganized endochondral bone growth and early fusion of the synchondroses, and by Sommer and Eaton (1970),

who described a case of trisomy 21 where achondroplasia was the most prominent feature. Alimchandani (1973), in a cross sectional study of Down's syndrome using postero-anterior radiographs, found interorbital width, height of the nasal cavity and width of the maxilla to be smaller in the trisomy 21 group than in the control group. These areas of the craniofacial complex were believed to be largely influenced by growth of cartilage.

Clinical evidence is also supportive for the hypothesis of disturbed and deficient endochondral bone growth, with features such as decreased height, brachycephalic head, short, blunted fingers and toes, relative protrusion of the mandible and decreased distance between the vertebrae and posterior aspect of the maxilla.

V. GROWTH OF THE CRANIOFACIAL SKELETON

Bone and cartilage, being readily associated with skeletal growth and maturation, are intimately involved with the development of skeletal abnormalities. A clear appreciation of their differences and respective mechanisms of growth is imperative for an understanding of the different reactions in different parts of the craniofacial complex.

Bone

Bone structure and bone growth are dictated by variations in the distribution of the component parts - bone cells, vascular canals, and lamellae. These complex factors emphasize the marked lability and the dynamic adaptability of bone as a tissue to the many different circumstances involved in skeletal growth and physiology. Rate and extent of growth relate directly to the type of structural patterns produced during bone deposition.

All parts of the growing bone are directly involved in the total growth process. Enlow (1968) described the process in a 'neat package' when he suggested two mechanisms of bone enlargement -- the addition of new bone at the major growth sites (sutures, synchondroses and alveolar margins), and remodelling of the remaining parts of the bone to provide structural adjustments necessary for the overall growth process.

Bone formation in cartilage (endochondral ossification) or membranous connective tissue (intramembranous ossification) is accomplished by apposition rather than by interstitial production of additional substance. Enlow (1968) concluded that the calcified nature of bone matrix created fundamental

differences in the growth mechanisms of bone and cartilage.

Cartilage

Cartilage is a tissue readily associated with the process of skeletal growth and with the development of craniofacial abnormalities. Enlow (1968) suggested that the structure and function of cartilage, like any connective tissue, are associated with the proportions in which its component parts -- cells, intercellular matrix and ground substance -- are combined.

Durkin (1968, 1971, 1973), in a study of the normal maturational changes of cartilage, found striking similarities in the basic morphohistologic features of the "embryonic cartilages". The cartilaginous anlage of the rat long bone and the epiphyseal and condylar cartilages were found to have an inherent embryonic character, as well as, similar responses to changes in the relationship of their surrounding structures during development by a process of adaptive remodelling. In contrast, growth plate cartilage was found to be highly specialized and a unique type of cartilage specifically adapted to meet the demands of the primary growth requirements of an area. Rather than being a model for comparison of all other cartilages, the

growth plate cartilage was to be considered "atypical".

The normal growth and adaptive capabilities of cartilage have also been studied in a series of transplantation studies. In vivo and in vitro transplants have shown that synchondroses and the condylar growth centre respond differently from other cartilaginous growth sites (Koski, 1960, 1968; Koski and Ronning, 1965, 1969, 1971; Ronning, 1966).

Sarnat (1968) has shown that the mandibular condyle is a unique structure in the body, in that it has a fibrous covering under which the proliferating fibroblasts provide a reservoir of cells for the chondroblasts, which in turn will complete the endochondral growth process.

Petrovic and his associates have demonstrated conclusively that it is the fibroblasts, which form a layer beneath the fibrous covering of the condyle, that in turn form what is known as a prechondroblastic layer (Charlier and Petrovic, 1967; Charlier et al., 1968, 1969a, 1969b; Petrovic et al., 1968, 1973; Petrovic, 1970, 1972, 1974). It is this prechondroblastic layer that is different in its response to extrinsic forces. Petrovic (1972, 1974) and Meikle (1973a, 1973b) demonstrated that under certain

conditions, the fibrous capsule covering the condyle could form either osteocytes or chondrocytes.

Petrovic et al. (1973) subjected young rats to chincap therapy for periods up to four weeks and showed that the pressure brought about a retardation of growth of the mandibular condylar cartilage by inhibiting the cell proliferation of the prechondroblastic zone. He found that the articular disc of the temporomandibular joint and the articular zone of the condyle were not affected by the chincap and, thus, he felt that the extrinsic force, to be successful, had to operate on a particular tissue at a particular stage of development. This would agree with Durkin's (1971, 1973) findings of an immature (hypertrophic) form of cartilage which undergoes adaptive remodelling and a more mature (non-hypertrophic) form of cartilage which is less susceptible to environmental changes.

That there is a maturational level which seems to be of significance in the response of cartilage to extrinsic and intrinsic forces is found in the contradicting results of studies dealing with the adaptability of the temporomandibular joint. Colico (1958), Hiniker and Ramfjord (1966) and Ramfjord and Enlow (1971), utilizing non-growing animals,

found that the temporomandibular joints were extremely stable and resistant to occlusal change and trauma. On the other hand, Breitner (1930, 1933, 1940), Haupl and Psansky (1939), Hoffer and Colico (1958), Baume and Derichsweiler (1961), Stockli and Willert (1971), Moyers et al. (1970) and Elgoyhen et al. (1972), using growing animals, demonstrated that compensatory tissue changes occurred in the condylar cartilage following altered mandibular functional position.

Petrovic et al. (1973) cut the external pterygoid muscle, unilaterally, in rats and found a reduction of fibroblasts in the prechondroblastic zone. This implied the role of extrinsic functional forces in the development of the condyle. Petrovic, Gasson and Oudet (1973) used the combined therapy of growth hormone (somatomedin) and mandibular hyperpropulsion on rats, to increase the prechondroblastic zone to almost twice that of a control. According to Petrovic (1974), the administration of the growth hormone stimulated the differentiation of the prechondroblast into the chondroblast and, hence, was most effective at a particular stage of development.

Cranial Base

The cranial base, made up of the ethmoid, sphenoid and occipital bones, represents the junctional region between the cranium and face and might be expected to show a growth rate intermediate between the neural pattern of the cranium and the general skeletal rate typical of the face. Ford (1958) suggested that this was true of the base as a whole, but that its individual parts had either the neural or the general growth rate, not an intermediate one. The area from nasion to foramen caecum and from sella trucica to basion exhibit the general growth rate, while that from foramen caecum to sella and from the anterior margin of the foramen magnum to the posterior margin of the foramen magnum have a neural growth pattern. Wilkinson (1940) suggested the importance of the sphenoid bone as a controlling factor in facial development and Enlow (1973) suggested an interrelationship between neural mass growth and cranial base growth with a controlling effect being initiated on facial growth.

Schuller (1918) and Keith and Campion (1922) suggested that cranial base growth occurred at the sphenoccipital, sphenoethmoidal and frontal sutures, while

Bjork (1955) pointed out that, while the sphenoccipital synchondrosis was a prime growth centre, the development of the base as a whole was dependent on growth of the four cranial fossae.

Most researchers, such as DeCoster (1952), Ford (1958), Scott (1954, 1958) Bjork (1955) and Sassouni (1962), agreed that anterior cranial base growth, per se, was usually terminated with closure of the sphenoethmoidal and frontoethmoidal synchondroses by the end of the first decade. Bjork (1955), Sassouni (1958) and Scott (1958) suggested that any elongation of the anterior cranial base after the first decade was due to appositional bone growth at the glabellar region of the frontal bone, simultaneous with pneumatization of the frontal sinuses.

Sassouni (1958) suggested that since the sphenoccipital synchondrosis was active until adolescence, angular and linear changes in the posterior cranial base could alter the relationship between the lower face and midface. Ricketts (1955) and Bjork (1955) agreed that cranial base rotation could affect the positioning of the temporomandibular joint.

The cranial base in humans demonstrates a higher degree of flexure of the cranial base angle than any other species.

Senneville et al.(1950) found the cranial base angle to remain constant from three months inrauterine to birth. Moss (1955) also found the angle to remain constant at different levels. Bjork (1955), using the pituitary fossa and the meeting of the anterior and posterior cranial axial lines, gave a mean value of the angle as 130.8° at 12 years and 131.6° at 20 years. He stated that in some individuals the angle increased, while in others it decreased. Ford (1956) showed that during fetal life, the cranial base angle increased from 131.5° at 10 weeks to 150.5° at birth. Scott (1958) felt that most of the change in cranial base angle occurred during fetal life and probably did so at the post and presphenoid synchondroses. Changes that occurred in later life were due to positional changes in nasion and the sphenoccipital synchondrosis.

Roche and Lewis (1974) found elongation of all cranial base measurements continuing into adolescence. They attributed this to five possible mechanisms:

(1) apposition at basion - this must be accompanied by resorption at or near opisthion and repositioning of foramen magnum because its antero-posterior dimension does not change after childhood (Ford, 1958; Koski, 1960).

(2) repositioning of sella - in either a posterior or superior position by remodelling.

(3) repositioning of nasion - the usual pattern is apposition (Enlow, 1968; Ford, 1958; Koski, 1960).

(4) change in the saddle angle.

(5) apposition at the sphenoccipital synchondrosis - bony fusion of the synchondrosis occurs at about 15-16$\frac{1}{2}$ years in boys and 11-14 years in girls (Nelson, 1969; Powell et al., 1963; Nelson, 1972). The age of fusion was found to be closely associated with skeletal age (Konie, 1964).

Down's Syndrome:

Early investigations by Benda (1940), using histological data, and Rezk (1964), Kisling (1966) and Ghiz (1969), using lateral cephalometric measurements, indicated that the sphenoccipital synchondrosis closed prematurely in Down's syndrome. All of these authors observed that the cranial base was considerably shorter in Down's syndrome than in normals, and Kisling (1966), and Ghiz (1969) showed that the anterior cranial base was shortened more than the posterior cranial base.

Rezk (1964), Kisling (1966) and Ghiz (1969) found

greater flexion of the cranial base angle in mongoloids. Sassouni et al. (1964) and Kisling (1966) found this to be associated with a lowering of sella, while Ghiz (1969) suggested it could also be due to a change in direction of growth of the sphenoccipital synchondrosis and the appositional growth patterns. Kisling (1966) found much more flattening of the central and lateral parts of the cranial base while at the site of the mandibular condylar head, the flattening was hardly discernible. Thus, the posterior positioning of the middle and lower face, which would normally be expected in increased cranial base flexion did not occur in Down's syndrome.

The shape and size of the sella turcica in mongoloids has been investigated by several authors; for example Clift (1923) noticed a characteristic recess under the anterior clinoid process. Engler (1949) found the size of sella to be smaller in trisomy 21, while Schiffer (1951) found sella to be small and similar in size and appearance to that of the normal father. Kisling (1966) found the height of sella to be greater in the mongoloid group, while the maximum diameter and the entry were smaller.

Nasomaxillary Complex

The nasomaxillary complex, made up of the maxillae, the nasal bones, the laryngeal turbinates and palatine bones and their associated soft tissue elements, forms part of the craniofacial region. As a result of growth, and in general terms when considered from the lateral aspect, this group of structures seems to be translated in a downward and forward direction relative to the cranial base.

Massler and Schour (1944) and Moore (1946), using vital staining techniques with monkeys, concluded that the oblique facial sutures were the primary agents of growth. Wienmann and Sicher (1947) concurred with this hypothesis.

Scott (1954) felt that the primary growth stimulus for the midface was the cartilage of the nasal septum which translated the nasomaxillary complex downward and forward thus separating the facial bones at the sutures and initiating a secondary growth stimulus at these sites. Scott (1958) pointed out that the circummaxillary suture system allowed the maxillary complex to grow forward away from the sphenoid bone. This system was active until age seven years after which time the sutures closed. Future

growth changes were attributed to apposition in conjunction with internal resorption to allow for an increase in size of the nasal cavity, the air sinuses and the oral cavity. Sarnat (1966) extirpated the septovomeral region in rabbits and found severe facial demformation.

Moss (1962) considered the "functional matrix" as the primary growth site, an interpretation based on the concept of "functional cranial components" conceived by Klaauw (1946, 1948-52). According to Moss, the orbital, nasal and oral cavities and their viscera must be considered as the functional matrix for the nasomaxillary complex.

Enlow (1968) described nasomaxillary growth as "a composite process involving bone additions at sutures, extensive surface deposition in specific regions and, at the same time remodelling growth on all inside and outside surfaces". His histological description of the various remodelling sites agrees with the results of animal studies (Baume, 1962; Bjork, 1955; Cleall, 1968, 1971; Craven, 1956; Moore, 1949).

Ricketts (1961) found that the maxilla grew forward at a similar rate as nasion. In 100 non-orthodontically treated children observed over a three year period, this relation-

ship changed very little. He specified that the maxilla drops vertically about one-third of the total face height increase. Lande (1952) noted that development of the subnasal region generally kept pace with development of nasion. Bergersøn (1966) demonstrated that nasion, anterior nasal spine and A point had growth directions closely resembling straight line trends.

Brodie (1946) showed a high degree of constancy in nasal height, and he found nasal height (nasion to anterior nasal spine) to be 43 percent of total face height. Wylie (1947) concurred with these findings. Savarra (1968) described the height dimension as having the most rapid growth rate in the maxillary complex, followed by length and width.

Down's Syndrome:

Sassouni et al. (1964) and Rezk (1964) found the midface to be markedly underdeveloped in mongoloids, both in the vertical and antero-posterior dimensions. Kisling (1966) and Ghiz (1969) observed a shorter maxilla, however, one that was positioned normally relative to the anterior cranial base. Frostad (1970), in a subjective

appraisal of cephalometric radiographs, suggested that although the anterior nasal spine, A point, and the dentition appear to be in a normal relationship, the frontal process of the maxilla appeared to be underdeveloped. in an antero-posterior relationship, helping to give the middle face a retruded appearance. Fink et al. (1975) found a deficiency in the mongoloid midface, both in gross area and in relation to the endocranial area. This deficiency became progressively greater with age.

Benda (1956), Spitzer et al. (1961), Rezk (1964), Kisling (1966), Ghiz (1969), and Frostad (1970) all found the maxilla to be considerably smaller in Down's syndrome. Kisling and Ghiz found the maxilla to be slightly more inclined to the anterior cranial base than the upper occlusal plane (Kisling, 1966). This was interpreted to mean that the intergroup differences in the dental and alveolar heights were greater anteriorly than posteriorly - possibly due to atypical tongue position. Frostad (1970) found that vertical growth of the maxilla occurred with an almost parallel lowering of the palatal plane from the anterior cranial base, similar to the condition found in the control group. Frostad (1970) found a tendency for a

more rapid descent of the maxilla at the anterior end in the males of his study. Unlike Kisling (1966), he did not believe this was caused by abnormal tongue function, because the same was not observed in females.

Kisling (1966), Ghiz (1969) and Frostad (1970) found the anterior and posterior and dentofacial heights to be underdeveloped in mongolism, however, growth occurred at a normal rate and appeared to accommodate the changing facial prognathism and occlusal plane.

Mandible

The classical concept of craniofacial growth suggested that the mandible was comparable to the long bone, and that the condylar cartilage and growth plate cartilage had a similar structure and function. A corollary of this belief was that the condylar cartilage of the mandible was a major growth centre for that bone.

Brodie (1941) demonstrated a posterior direction of condylar growth and suggested that the resulting forward projection of the mandible was a direct result of the condylar movement. Massler and Schour (1944), using alizarine red, concluded that the condylar cartilage was

a major growth site. Moore (1949), also using vital staining techniques, suggested that a parallel could be drawn between the growth plate and condylar cartilages. This idea was supported by the work of Jarabak et al. (1953), using autoradiographic techniques, and Levy and Gorlin (1953), in a histological study.

Robinson and Sarnat (1955) described the condyle as one of the most proliferate sites of growth resulting in increased ramal height and that the condylar cartilage was the most important growth centre in the mandible. This view was coincident with the thinking of Weinmann and Sicher (1955), Craven (1956) and Sarnat (1957).

More recently, a new line of thought has developed concerning growth of the mandible. Moss (1960, 1962) advanced the functional matrix theory and suggested that condylar growth was required to maintain the functional unity of the temporomandibular joint.

As early as 1922, Keith and Campion, by means of osteometry on human skulls, suggested that growth of the upper face acted as a pace maker to which mandibular growth adapted. Scott (1953) stated that growth of the condyle was upward and backward, so as to maintain contact

at the temporomandibular joint. Baume et al. (1959, 1961) and Koski and Mäkinen (1963) supported this hypothesis.

Bjork (1963), using metallic implants, found that the mandibular base curved with growth decreasing the gonial angle and that the direction of condylar growth curved. Much of this was suggested to be purely adaptive, adding little to the length of the mandibular body.

Enlow (1963) concluded that the condylar growth mechanism was not the primary centre for growth of the entire mandible and was not responsible for regulating overall mandibular growth. He suggested that its primary role was to provide articulation with the cranium and that its upward and backward growth was coordinated with remodelling activities in the neck and ramus of the mandible.

Enlow (1963) described the mandible as a bone that was "remodelled, reworked, reshaped and resized." The constant remodelling during the increase in size of the mandible was explained by the "V" principle, the precise direction of changes being dependent on the structural interpretation of cortical zones and by the identification of various endosteal and periosteal bone deposits.

Moss et al. (1974), in an extension of his functional

matrix hypothesis, described mandibular growth as being allometric and thus capable of graphic presentation as a unitary logarithmic spiral. Also, he described this growth as being gnomonic in that it maintains its original shape while increasing in size.

Down's Syndrome:

Spitzer and Robinson (1955), Sassouni et al. (1964) Kisling (1966), and Ghiz (1969) found that the mandible was underdeveloped in Down's syndrome, and that the body and ramal lengths were smaller dimensions. Frostad (1970) found mandibular size to be more variable with ranges from a smaller than normal mandible to one exhibiting extreme prognathism. He suggested that such variability could have a hereditary basis.

The "apparent" mandibular prognathism characteristic of Down's syndrome has been a source of controversy among investigators. Brown et al. (1961) suggested that a severe midfacial deficiency makes the mandible appear prognathic. Sassouni et al. (1964) found the mandible to be normally positioned relative to the anterior cranial base. Kanar (1971) reported that the body and ramus of the mandible

were not significantly different from the control subjects in form, but that the labial and linqual contours of the mandibular symphysis were significantly different in the mongoloid subjects giving them the prominent chin point. Kisling (1966) and Ghiz (1969) found the mandible to be in a protrusive position relative to the anterior cranial base. Raison, Le Poivre and Ackermann (1966) suggested an alveolar rather than basal mandibular prognathism. Fink et al. (1975) found the mongoloid mandible to be relatively and absolutely smaller than the control group. They suggested that the magnitude of the deficiency, both in gross area and in relation to the endocranial area, remained nearly constant with age.

In summary, an understanding of the factors which determine the phenotype is a major area of interest in modern medicine. Trisomy 21 presents a unique opportunity to examine the abnormalities in the development of humans by the addition of a small but specific amount of genetic material. As a result, investigations are being conducted in a variety of disciplines.

The integration of cytogenetic, biochemical, physiological and morphological studies will augment understanding of the controlling mechanisms in the growth and development of the craniofacial complex.

METHODS AND MATERIALS

CHAPTER III

METHODS AND MATERIALS

The sample under investigation consisted of 117 trisomy 21 individuals, which included 62 males and 55 females. Each subject had been karyotyped and found to have an extra chromosome number 21, and hence, a cytogentically confirmed trisomy 21 sample was obtained. All mosaics and translocations were eliminated. The sample was drawn from a group of 512 mongoloids studied by the Department of Medical Genetics, Winnipeg Children's Hospital, Winnipeg, Manitoba, Canada, (Uchida, 1970).

The trisomy 21 sample resided in the Province of Manitoba where 65.1 per cent were institutionalized and 34.9 per cent lived at home. No attempt was made to analyze the data on an institutional or non-institutional basis. Selection of the sample was entirely determined by the cooperation in obtaining the necessary radiographic records.

The sample ranged in age from 3 to 55 years. The age and sex distribution can be found in Table I.

A control sample of normal caucasian individuals matching, as closely as possible, the trisomy 21 sample in

age and sex was collected by the Department of Preventive Dental Science, the University of Manitoba. This group consisted of 100 individuals, which included 48 males and 52 females. They were randomly selected and included students from the University of Manitoba and individuals residing in the Metropolitan Winnipeg area. The age and sex distribution of the control sample is shown in Table I.

Ethnic background, economic status and other regional differences were not considered between the trisomy and control groups, however, it was felt that a similarity in backgrounds existed between the two groups.

The records obtained included hand-wrist radiographs and lateral cephalometric radiographs.

SAMPLE SIZE						
SKELETAL AGE GROUP IN YEARS	TRISOMY 21			CONTROL		
	TOTAL	MALE	FEMALE	TOTAL	MALE	FEMALE
3 – 5	9	6	3	15	9	6
6 – 9	10	4	6	20	8	12
10 – 14	15	9	6	12	6	6
15 – 18	17	10	7	14	6	8
ADULT	66	33	33	39	19	20
TOTAL	117	62	55	100	48	52

TABLE I

AGE AND SEX DISTRIBUTION OF SUBJECTS

I. RECORDS

A. Hand-Wrist Radiographs

Hand-wrist radiographs and subsequent assessments of skeletal maturation, determined for both trisomy 21 and control groups by Nevile (1973), were used in this study.

Left hand and wrist radiographs were taken using the techniques suggested by Tanner and Whitehouse (1959). The Oxford method (Tanner and Whitehouse, 1959; Tanner, Whitehouse and Healy, 1962) was used for the actual assessment of skeletal development because of its accuracy and the fact that it differentiates between round bones and long bones.

The radiographic images of each of the twenty bones of the hand and wrist were compared with pictorial and verbal descriptions of the developmental stages for that particular bone, as published by Tanner and Whitehouse, 1959. The relative importance of each stage of a specific bone had been previously assessed statistically to derive a score for each stage of the individual bone, by Tanner, Whitehouse and Healy, 1962. These scores were self-weighted and the overall score was arrived at by adding the scores of the individual bones. The long bone score and the carpal score

each contributed equally to the total score (Nevile, 1973).

Determination of total Oxford scores for individuals in the trisomy 21 and control groups (Nevile, 1973) made it possible to group the sample by skeletal age, rather than chronological age.

B. Lateral Cephalometric Radiographs

The lateral cephalometric radiographs were obtained from the orthodontic files of the Department of Preventive Dental Science, the University of Manitoba. The radiographs were taken using the now conventional technique first developed independently by Broadbent (1931) and Hofrath (1931). Three cephalometric x-ray machines were used. A Broadbent-Bolton cephalometer was used on a portion of the trisomy 21 group living in private homes. A Cephalometrix* cephalometer was used on the control group and a portion of the trisomy 21 group. Some of the trisomy group residing in institutions were radiographed with a specially built portable cephalometer. This latter machine was built along the lines of a conventional cephalometer utilizing a General Electric** 90 Kv. x-ray head and control panel, a standard

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* Moss Corporation, Chicago, Illinois, U.S.A.
** General Electric of Canada Limited, Toronto, Ontario, Canada

cephalostat, and an easily dismantled plywood base. These three sections were constructed to faciliate easy transportation, erection and dismantling of the machine.

All machines had an approximate focal point to film distance of 5 feet, 6 inches. Magnification factors for each of the machines had been previously established (Frostad, 1969). The magnification averaged 7 per cent on the Broadbent-Bolton and portable cephalometers between individuals. On the Cephalometrix cephalometer, the magnification averaged 9 per cent between individuals. All linear dimensions were corrected for the magnification to absolute units. Therefore, the linear dimensions for the three machines were comparable. Angular measurements were not influenced by magnification and, therefore, could be used as absolute units of measurement.

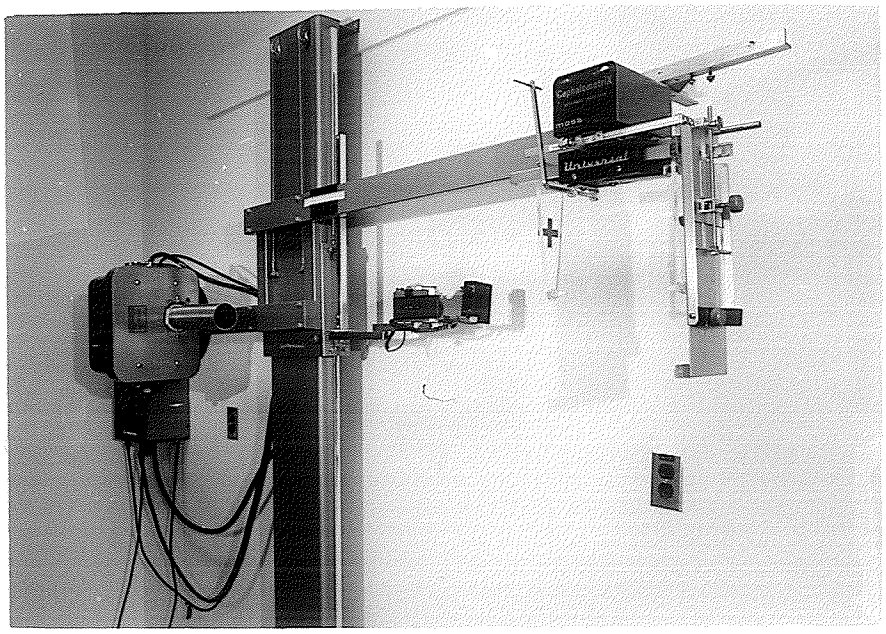

Figure 1. Cephalometrix Cephalometer used in this study.

II. SELECTION OF LANDMARKS

A total of 61 landmarks were selected to be digitized from the radiographs of the trisomy 21 and control samples. These landmarks are illustrated in Figure 4. A detailed description of the landmarks is found in the Glossary.

The X and Y coordinates of each landmark were recorded in a predetermined order and transferred to IBM* 80 column computer punch cards, by means of a Ruscom** logistics strip chart digitizer. Information from the punch cards was then loaded into the University of Manitoba IBM 360-65 computer system which mathematically computed all the linear and angular measurements used in this study, according to the method described by Cleall and Chebib (1971).

Paired landmarks not superimposed were bisected, thereby effectively reducing lateral landmarks to the same value as midsagittal structures, where error is the least. When any landmarks could not be accurately identified, they were not recorded. Similarly, mandibular landmarks were excluded when the radiograph was not recorded in centric occlusion.

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* IBM, Don Mills, Ontario, Canada
** Ruscom Logics Limited, Rexdale, Ontario, Canada

The error of the measurement had been previously calculated to range from 1-2 per cent (Ghiz, 1969; Frostad, 1970). Certain landmarks known to be variable, such as anterior nasal spine, posterior nasal spine, orbitale and maxillary and mandibular molars, ranged from 2-3 per cent. This degree of error was considered to be within the range of experimental error and so no correction was attempted in the statistical analysis.

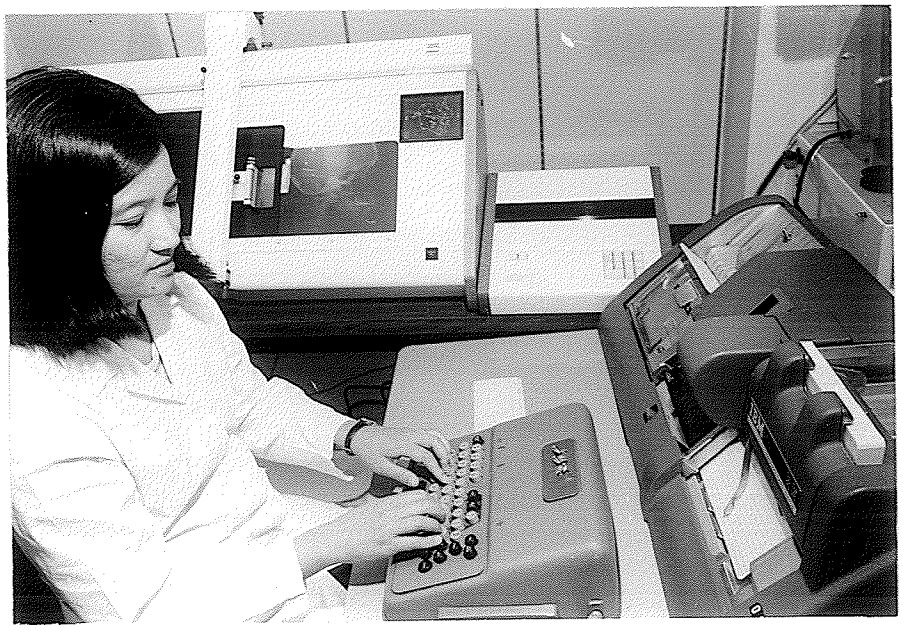

Figure 2. Digitizer and IBM Key Punch* used to record the coordinates of the landmarks from the lateral cephalometric radiographs.

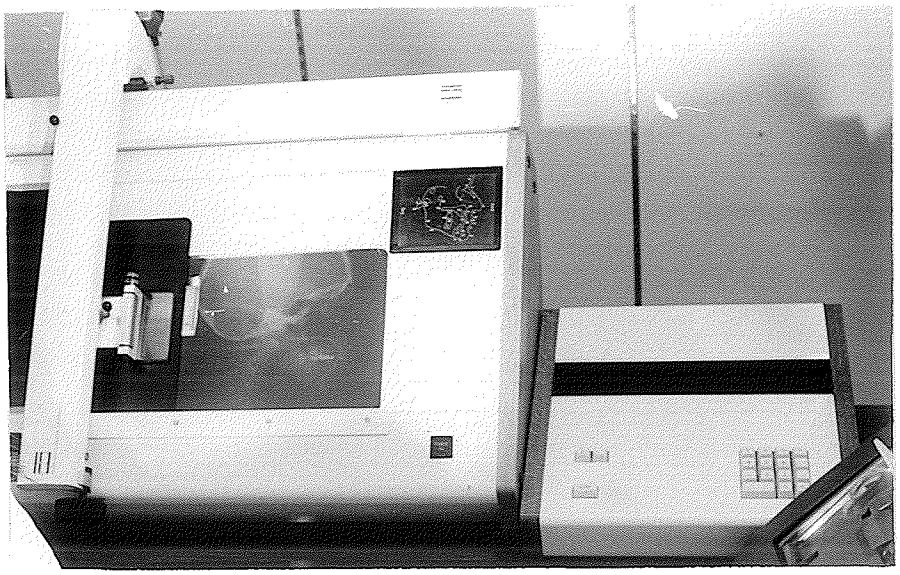

Figure 3. Ruscom logistics strip chart digitizer.

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* IBM, Don Mills, Ontario, Canada

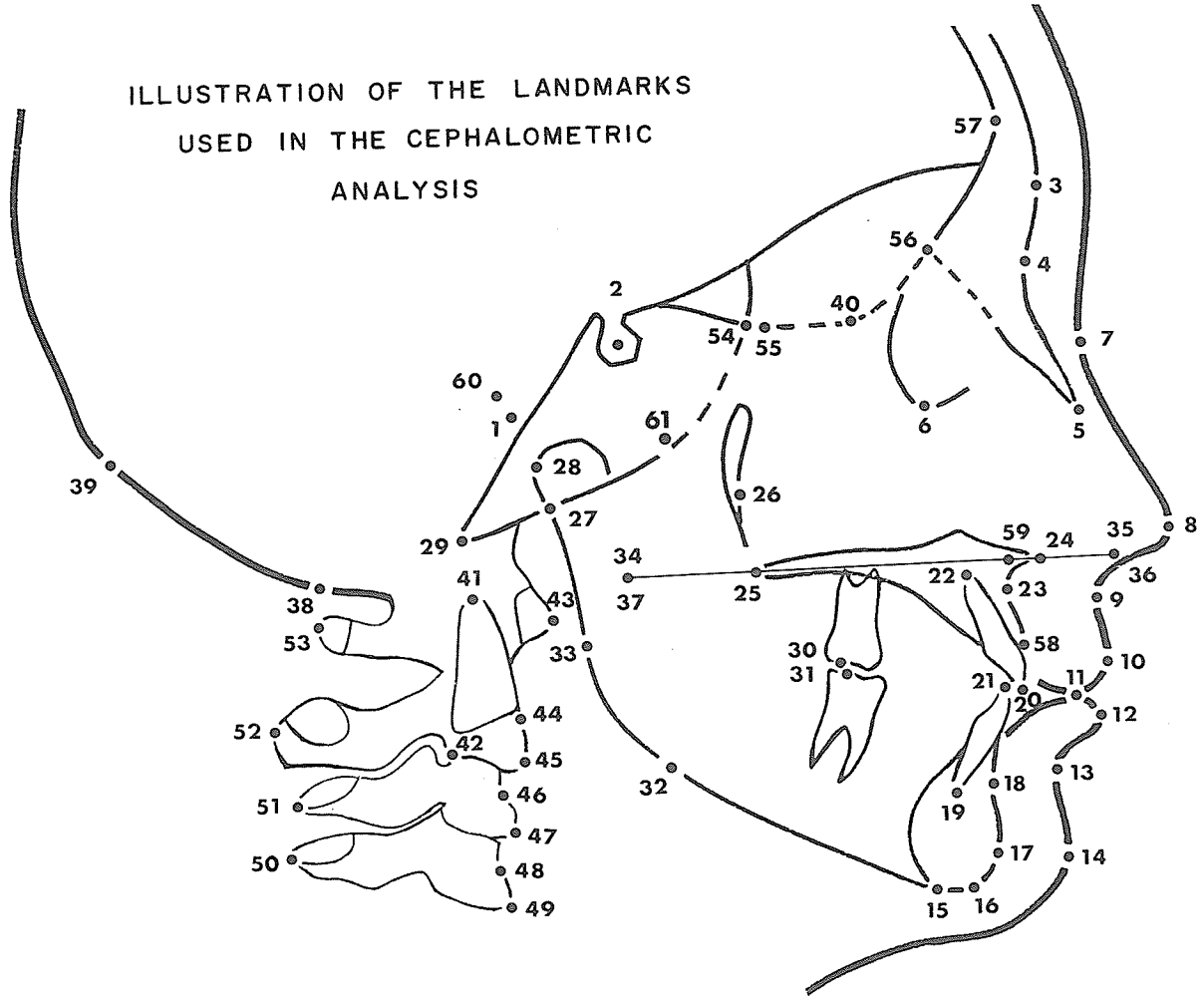


Figure 4. An illustration of the 61 points used in the cephalometric analysis.

III. INVESTIGATION OF THE VARIABILITY OF CRANIOFACIAL PLANES

The investigation of craniofacial growth and development using roentgenographic cephalometry requires the selection of a plane of orientation that demonstrates minimal variability - both biologically and geometrically. To facilitate the selection of such a plane suitable for use in a cephalometric study of the trisomy 21 phenotype, the pattern of association between various components of the craniofacial complex was studied.

Eleven lines, representing various craniofacial dimensions, were selected and their interactions investigated. Six of the lines were defined by cranial base landmarks, as illustrated in Figures 5 and 6, while the remaining five lines were defined by facial and/or cranial landmarks, as illustrated in Figures 7 and 8. Some of these lines covered the whole sagittal length of the skull base, while others covered only a part of the skull base or face.

The methodology used in evaluating the relative variability of the eleven linear dimensions was similar to that of Koski and Virolainen (1956) and Wei (1968). The assumption was made that the stability of craniofacial lines can be assessed by determining the variability of

the angles formed by their intersection points. This variability can be recorded as angle standard deviation and, by summing these values, an estimation of the relative stability of each plane can be obtained.

In this study, the eleven lines of orientation being investigated provided 55 angular combinations. The standard deviations of the 55 angles were determined for the individuals within each age and sex subgrouping of trisomy 21 and control samples. These subgroup values were then pooled for each group - trisomy 21 and control - to give representative angle standard deviations that eliminated any age/sex effects. Subsequently, the pooled angle standard deviations for each linear dimension were summed to provide an indication of the relative stability of that dimension in trisomy 21 and control groups. These results can be found in the Appendix.

Solow (1966), however, suggested that the standard deviation of the angles formed by the intersection of various craniofacial dimensions had an inverse relationship to the length of the arms forming the angles. Thus, biological variability is not the only factor involved and geometric distribution of the defining landmarks is

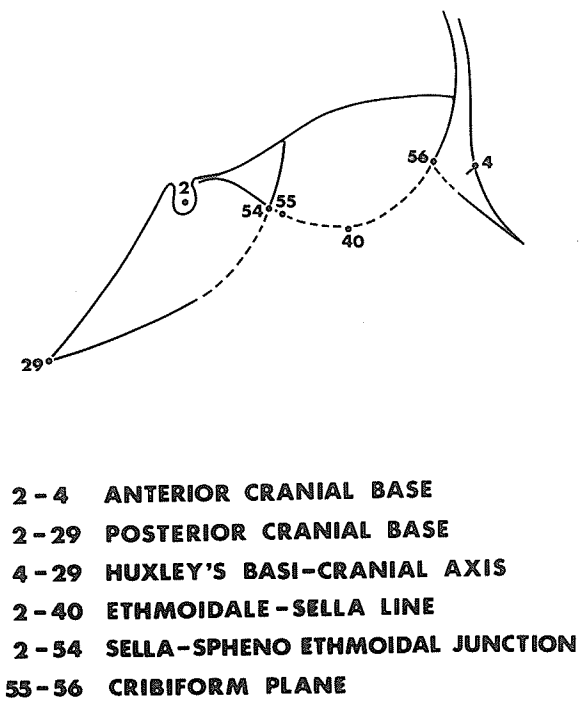


Figure 5. A diagrammatic illustration of the cephalometric points describing the six cranial base planes of orientation.

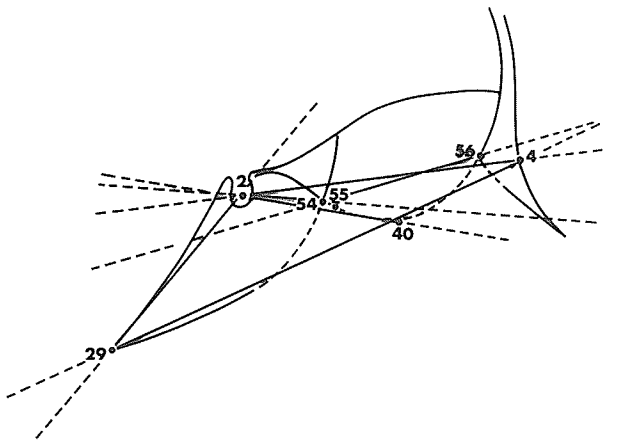


Figure 6. A diagrammatic illustration of the six cranial base planes of orientation.

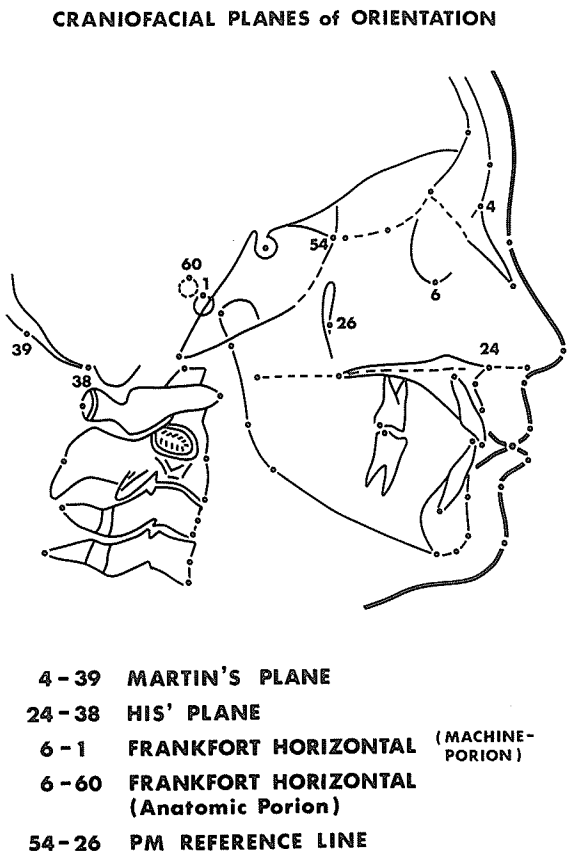


Figure 7. A diagrammatic illustration of the cephalometric points describing the five craniofacial planes of orientation.

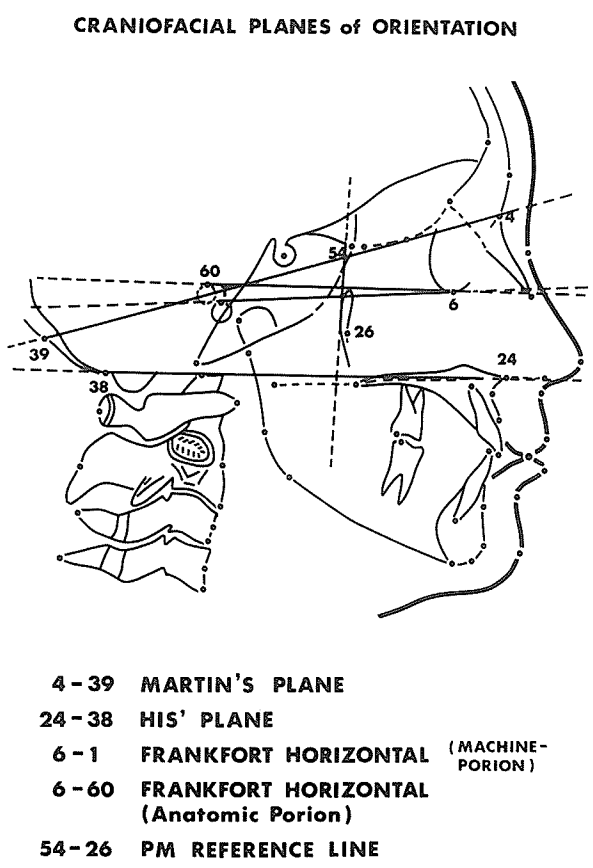


Figure 8. A diagrammatic illustration of the five craniofacial planes of orientation.

of significance. This assumption would suggest that the previously mentioned method of assessing stability is questionable and, at best, biased by the spatial arrangement of the landmarks describing the angle arms. With this in mind, the effect of arm length on the standard deviation and/or variance of an angle was investigated. An angle arm length is defined as the linear distance between two craniofacial landmarks that define one arm of an angle. For both trisomy 21 and control groups, average angle arm length and the corresponding pooled angle standard deviation and variance for each of the 55 angles were collected and subjected to regression analysis. These distances and their corresponding angle standard deviations/variances are listed in the Appendix.

The regression analysis was used to determine the relationship between the two variables - the dependent variable, standard deviation or variance, and the independent variable, the average reference point distance. This independent variable is described by the formula:

$$\bar{l} = \frac{l_1 + l_2}{2}$$

where:

$\bar{l}$ = the average reference point distance, or average arm length

l_1 = the length of one angle arm

l_2 = the length of the second angle arm

Regression analysis was also performed on log angle variances with respect to average arm length to test for the possibility of a curvilinear relationship rather than a straight line relationship.

i) 3 and 4 Point Angles

To test the hypothesis that angles with a common point (3 point angles) would demonstrate a somewhat different relationship with respect to arm length than angles formed by two completely independent lines (4 point angles), the 55 angles were divided into those described by 3 and 4 points and a regression analysis was performed. Average arm lengths, with the corresponding standard deviations and variances, for 3 and 4 point angles are found in the Appendix.

ii) Corrected Standard Deviations

Finding that angle standard deviation was related to the arm lengths defining the angle, pooled standard deviations were adjusted to eliminate this arm length influence. This was done by re-calculating each standard deviation to a common average arm length, using the formula:

$$S_i \text{ adj} = S_i - b(\bar{l}_i - \bar{\bar{l}})$$

where:

S_i adj = the corrected standard deviation

S_i = angle standard deviation of angle i

b = slope

$\bar{l}_i$ = average arm length for angle i

$\bar{\bar{l}}$ = mean average arm length

Subsequent to the adjustment of the trisomy 21 and control pooled angle standard deviations, the corrected values were summed for each of the eleven linear dimensions providing a more accurate stability index describing their natural or biological variability in the two groups. Tables for corrected standard deviations, variances and log variances are found in the Appendix.

iii) Statistical Analysis

In order to test for significance of differences between the stability indices for the eleven lines within each trisomy 21 and control group, a complete block analysis of variance was performed on the 11 x 11 orientation plane intersection matrix (see Figure 9), each element representing the pooled log variance of the angle between two lines. This same matrix was used to calculate the stability indexes, each index being the sum of one column. The results of the analysis of variance for the two groups are found in the Appendix.

To test for significant differences between the stability indexes of the trisomy 21 and control groups, a paired t-test was performed on each of the eleven linear dimensions.

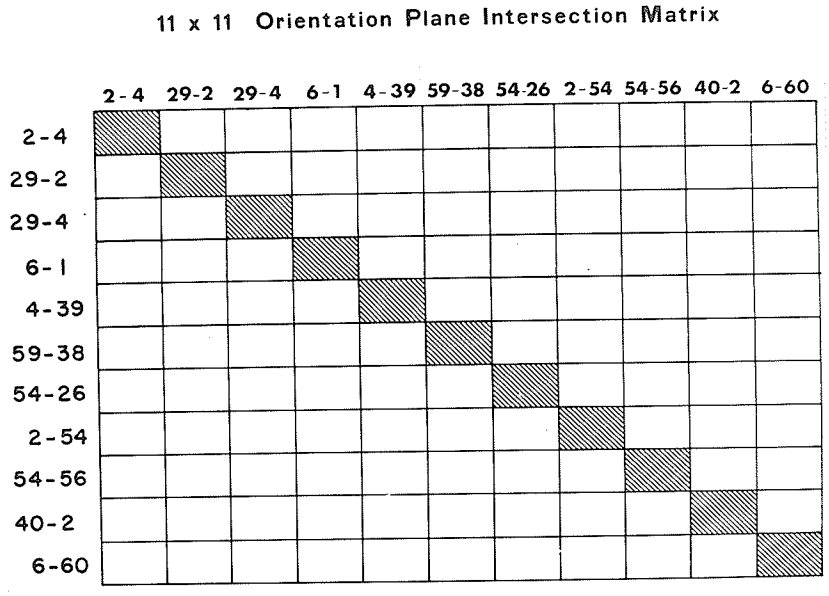


Figure 9. The 11 x 11 orientation plane intersection matrix used in the investigation of the variability of craniofacial reference lines.

IV. CEPHALOMETRIC ANALYSIS

A cephalometric analysis was used to evaluate, both quantitatively and qualitatively, the morphologic configuration and developmental changes associated with Down's syndrome. A total of 23 measurements were recorded from each cephalogram, 13 angular and 10 linear. Both angular and linear dimensions are illustrated in Figures 10 and 11 respectively.

The selection of a suitable plane of reference is extremely important in cephalometric analysis and, as mentioned earlier, should involve minimal variability and maximal stability - both from a biological and a geometrical standpoint. The very nature of craniofacial growth makes the selection of such an "ideal" plane impossible and our only recourse is to choose that dimension which best fulfills this description and which best describes the particular area of interest.

This study is primarily concerned with the facial region and its relationship to the underlying cranial base morphology. The basion-nasion line (Ba-N line), also referred to as Huxley's basicranial axis, represents a plane to which both upper and lower facial areas are

intimately related. This line is a reflection of the "total" cranial base region and its geometrical relationship to both the anterior and posterior portions of the cranial base (diagrammatically it represents the hypotenuse of the cranial base triangle defined by points nasion, basion and sella turcica) is such that cartilagenous growth disturbances in any area of the cranial base would be minimized in the Ba-N line.

The origin for the cephalometric coordinate analysis was formed by dropping a perpendicular from sella to the Ba-N line (point 61) and the direction was to nasion (point 4).

The following are the various angular measurements used in evaluating the facial region, with basion-nasion used as the plane of orientation:

Lateral Cephalometric Angular Measurements

These measurements are illustrated in Figure 10.

Angle 1 - the angle formed from basion-nasion to point B

Angle 2 - the angle formed from basion-nasion to point A

Angle 3 - the angle formed from basion-nasion to pogonion

Angle 4 - the angle formed by the intersection of the long axis of maxillary central incisor to the basion-nasion plane.

Angle 5 - the angle formed by the intersection of the Y-axis with the basion-nasion plane

Angle 6 - the angle formed from basion-sella to nasion

Angle 7 - the angle formed by the intersection of the tangent to the posterior border of the ramus with the basion-nasion plane

Angle 8 - the angle formed by the intersection of the palatal plane with the basion-nasion plane

Angle 9 - the angle formed by the intersection of the mandibular plane with the basion-nasion plane

Angle 10 - the angle formed by the intersection of the mandibular plane with the tangent to the posterior border of the ramus

Angle 11 - the angle formed by the intersection of the long axis of the mandibular central incisor to the mandibular plane

Angle 12 - the angle formed by the intersection of the long axis of the maxillary and mandibular central incisors

Angle 13 - the angle formed from point A-nasion to point B

Although the basion-nasion line is useful in analyzing facial areas, its value in the study of the

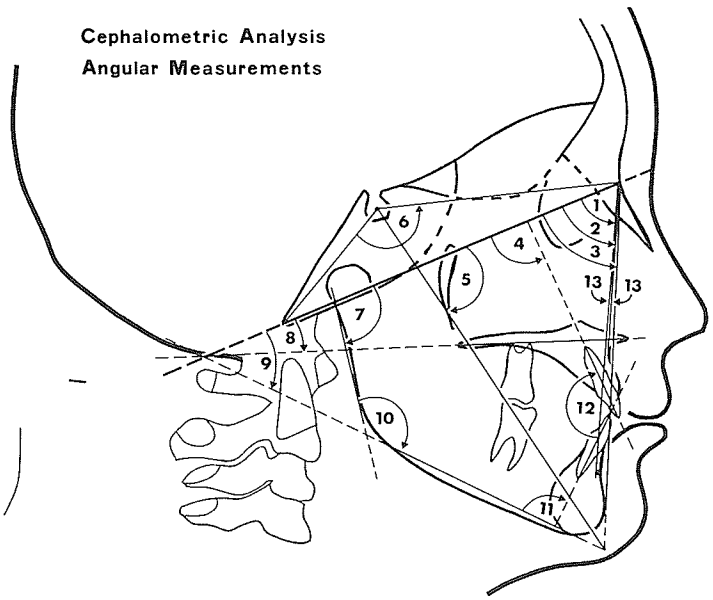


Figure 10. A diagrammatic illustration of the lateral cephalometric angular measurements.

cranial base itself is questionable in that it involves cartilage and thus would not be suitable for measuring alterations in the posterior and anterior cranial base. To assist in correlating facial morphology with that of the cranial base, a second linear dimension - the posterior nasomaxilla (PM) vertical plane (Enlow, 1969, 1973) - was selected. This vertical line extends inferiorly from a point located by the intersection of the greater wings of the sphenoid with the floor of the anterior cranial fossa to the inferior point of pterygomaxillary fissure (PTM). The plane is approximately perpendicular to the line of vision (Feuer, 1974), regardless of the rotational positions of various other planes, and is consistent with the anatomically "neutral" position of the head.

The following are the various linear measurements used in correlating facial growth and morphology with cranial base growth and morphology:

Lateral Cephalometric Linear Measurements

These measurements are illustrated in Figure 11.

Linear Horiz. 1 - the perpendicular distance from nasion to the vertical P.M. line

Linear Horiz. 2 - the perpendicular distance from sella to the vertical P.M. line

Linear Horiz. 3 - the perpendicular distance from articulare to the vertical P.M. line

Linear Horiz. 4 - the perpendicular distance from basion to the vertical P.M. line

Linear Horiz. 5 - the perpendicular distance from point A to the vertical P.M. line

Linear Horiz. 6 - the perpendicular distance from the maxillary incisal tip to the vertical P.M. lin

Linear Horiz. 7 - the perpendicular distance from the mandibular incisal tip to the vertical P.M. line

Linear Horiz. 8 - the perpendicular distance from the most posterior-inferior point on the ramus to the vertical P.M. line

Linear Horiz. 9 - the perpendicular distance from point B to the vertical P.M. line

Linear Horiz. 10 - the perpendicular distance from pogonion to the vertical P.M. line

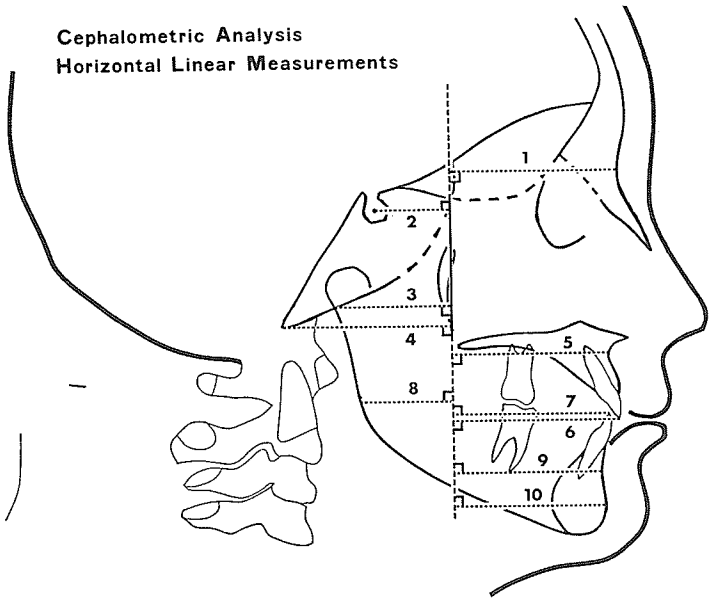


Figure 11. A diagrammatic illustration of the lateral cephalometric horizontal linear measurements.

Statistical Analysis of the Data

Values for each of the selected angles and distances were calculated for individuals in the trisomy 21 and control groups, using a coordinate analysis program (Cleall and Chebib, 1971), and the means and standard deviations were produced according to group, sex and age.

To investigate the differences due to each of these three factors, the data for each variable was subjected to a 3-factor factorial analysis of variance, the factors being group, sex and age.

The 216 degrees of freedom among the 217 subjects were allocated as shown in Table II. All the main effects and interactions were tested for significance by the variance ratio "F" tables (Snedecor, 1946). The significant variables were then subjected to further statistical analysis using the multiple range test.

Degrees of Freedom for Eight
Sources of Variation for 217 Subjects.

Source of Variation	Degrees of Freedom
Between Groups	1
Between Sexes	1
Among Age Groups	4
Group X Sex	1
Group X Age	4
Sex X Age	4
Group X Sex X Age	4
Error (within cells)	197
Total	216

TABLE II

Polygonal Profiles

Mean values obtained from the statistical data were used to construct facial polygons comparing the growth and development of the craniofacial complex in the trisomy 21 and controls groups, at each of the five age ranges studied. This method of comparison is similar to that used by Bjork (1954), Ghiz (1967) and Frostad (1970). Growth trends were determined by superimposing the polygons on the line basion-nasion, with registration at the point of intersection of a perpendicular from sella to the basion-nasion line.

RESULTS

CHAPTER IV

RESULTS

I. INVESTIGATION OF CRANIOFACIAL REFERENCE LINES

i) Influence of Craniofacial Reference Lines

The effect of angle arm length on the relative variability, i.e. standard deviation and/or variance, of an angle defined by two craniofacial reference lines is shown in Figures 12 and 13.

Linear regression analysis, with standard deviation as the dependent variable, revealed a multiple R value of 0.64 and an F value of 37.1 for the control group and a multiple R value of 0.65 and an F value of 39.0 for the trisomy 21 group.

Similarly, the regression analysis, using variance as the dependent variable, demonstrated a multiple R value and F value of 0.61 and 31.7 respectively for the control group and 0.65 and 38.7 respectively for the trisomy group.

These results, with reasonably high multiple R and F values significant at the 0.1% level, suggested a negative correlation between the two dependent variables, standard deviation and variance, and the independent variable,

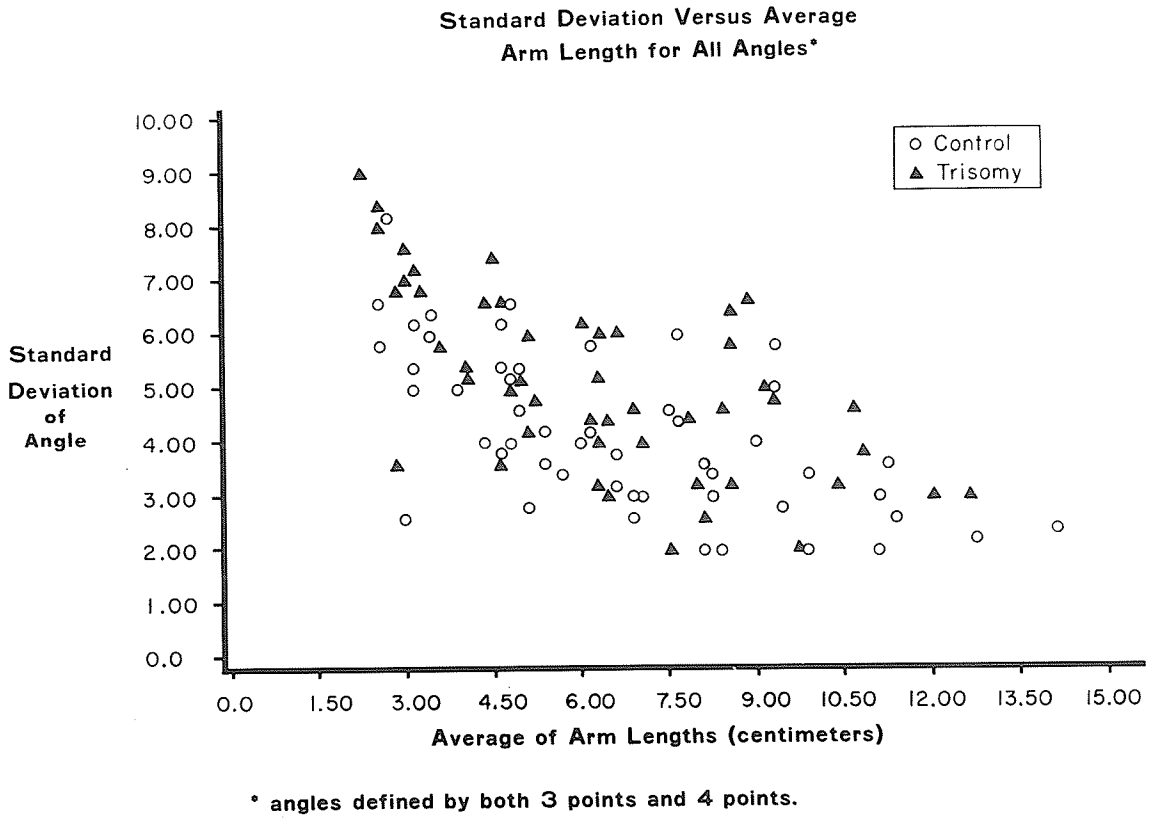


Figure 12. Graphic illustration of the effect of angle arm length on the standard deviation of angles defined by eleven craniofacial reference lines.

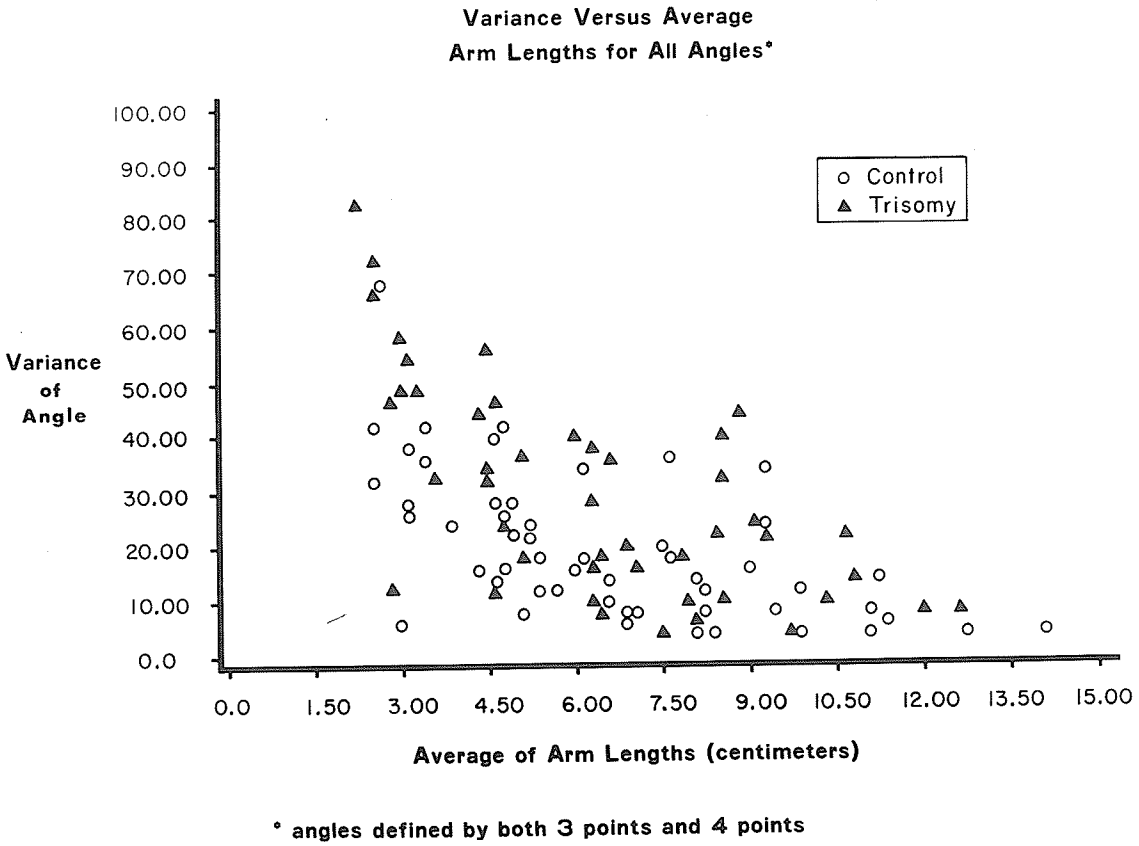


Figure 13. Graphic illustration of the effect of angle arm length on the variance of angles defined by eleven craniofacial reference lines.

average angle arm length. As the arm length increased, the angle variability, i.e. standard deviation or variance, decreased.

ii) Influence of the Spatial Arrangement of Points Defining an Angle - (3 and 4 point angles)

The effect of the spatial arrangement of the points defining an angle on the variability, as indicated by either standard deviation or variance, was investigated by dividing the 55 angles into those defined by 3 and 4 points. The results are shown graphically in Figures 14,15 16 and 17.

For the 3 point angles, the regression analysis, using standard deviation as the dependent variable, revealed a multiple R and an F value of 0.68 and 10.5 respectively for the control group, and 0.71 and 12.5 respectively for the trisomy group. With variance as the dependent variable, multiple R and F values of 0.62 and 7.6 respectively were found for the control group, and 0.68 and 10.3 respectively for the trisomy group.

For the 4 point angles, the linear regression analysis revealed a multiple R and an F value of 0.65 and 28.6 respectively for the control group, and 0.66 and 29.6

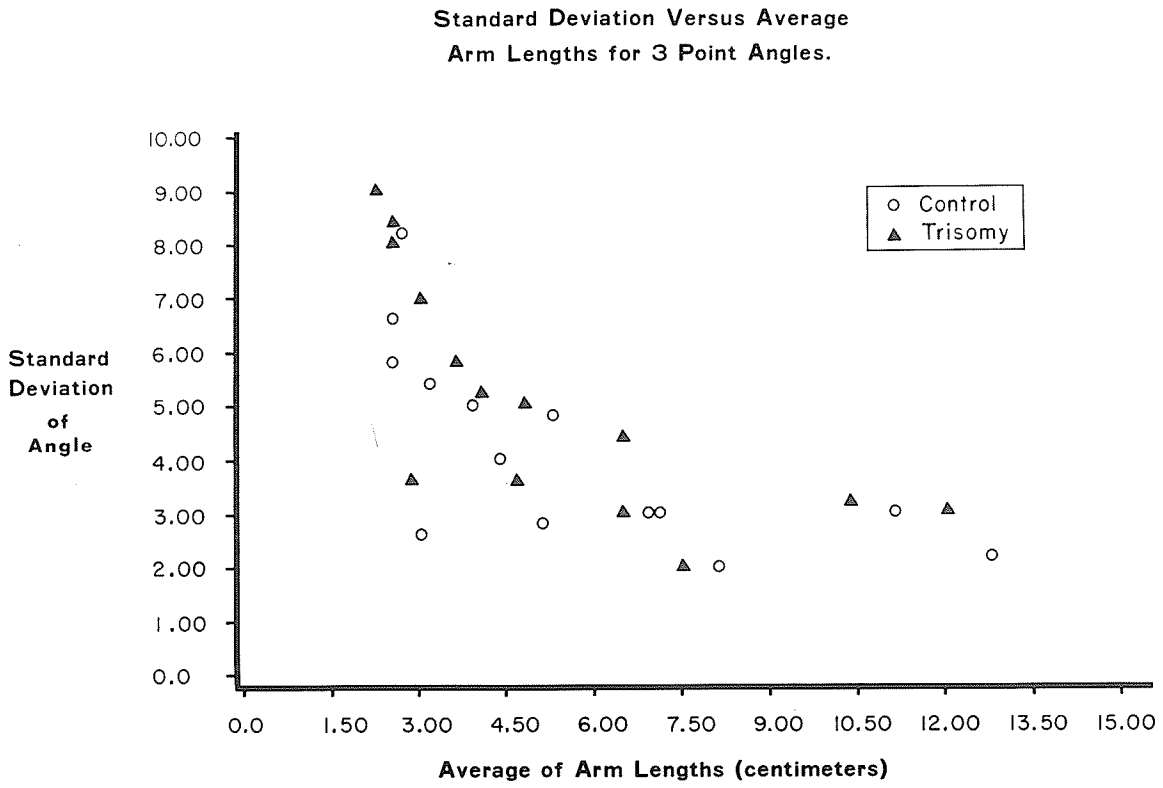


Figure 14. Graphic illustration of the effect of angle arm length on the standard deviation of angles defined by craniofacial reference lines with a common reference point (3 point angles).

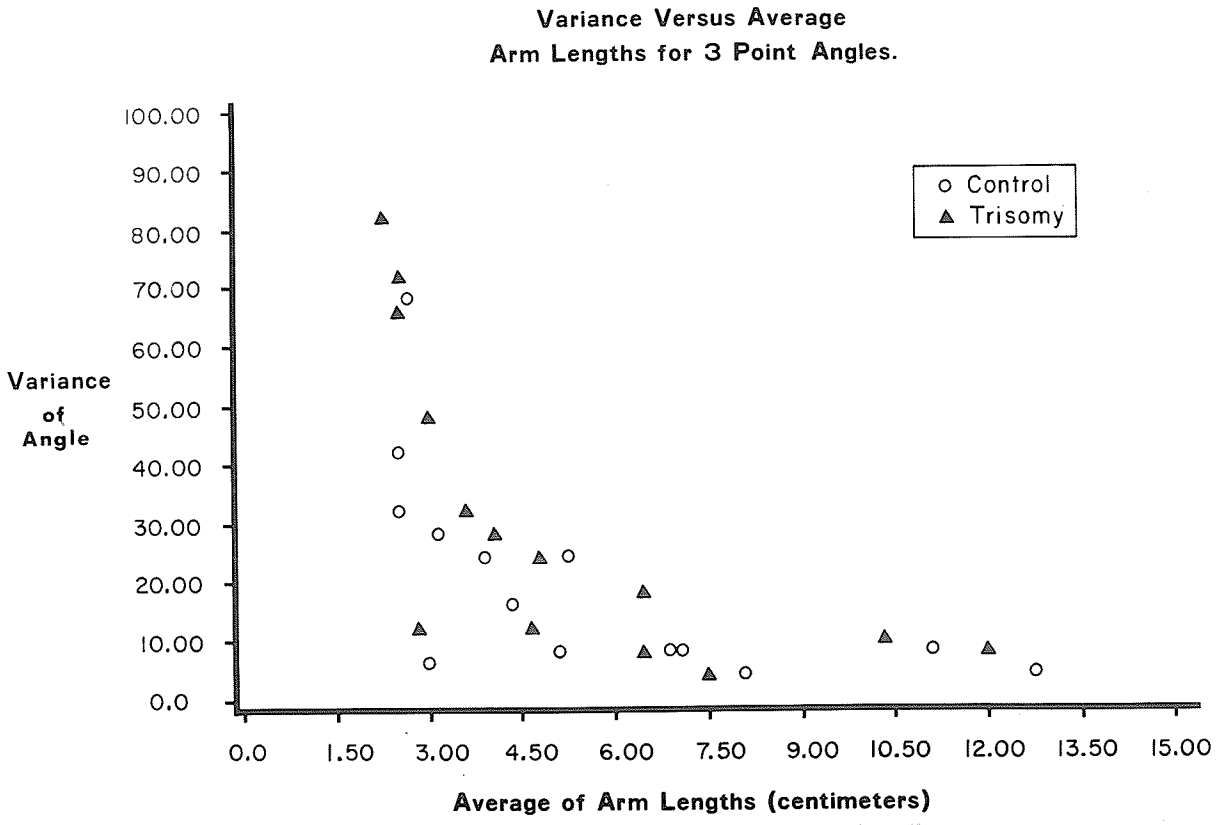


Figure 15. Graphic illustration of the effect of angle arm length on the variance of angles defined by craniofacial reference lines with a common reference point (3 point angles).

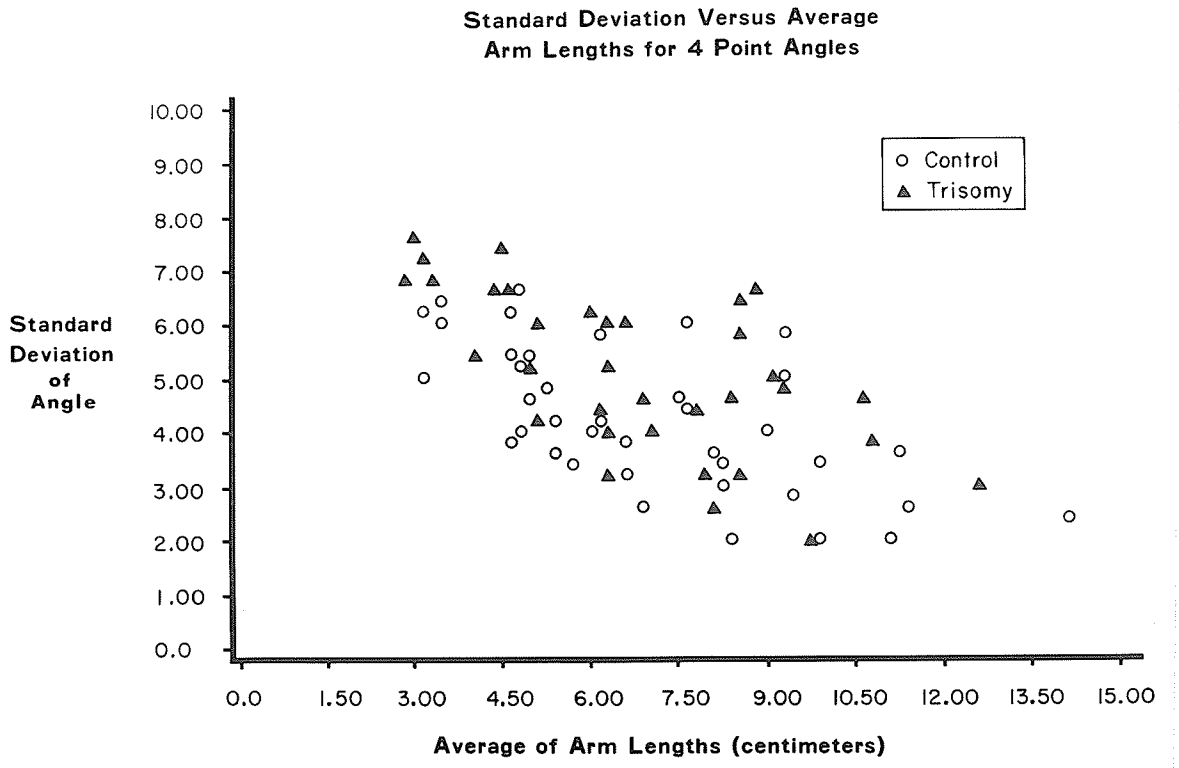


Figure 16. Graphic illustration of the effect of angle arm length on the standard deviation of angles defined by four separate craniofacial landmarks (4 point angles).

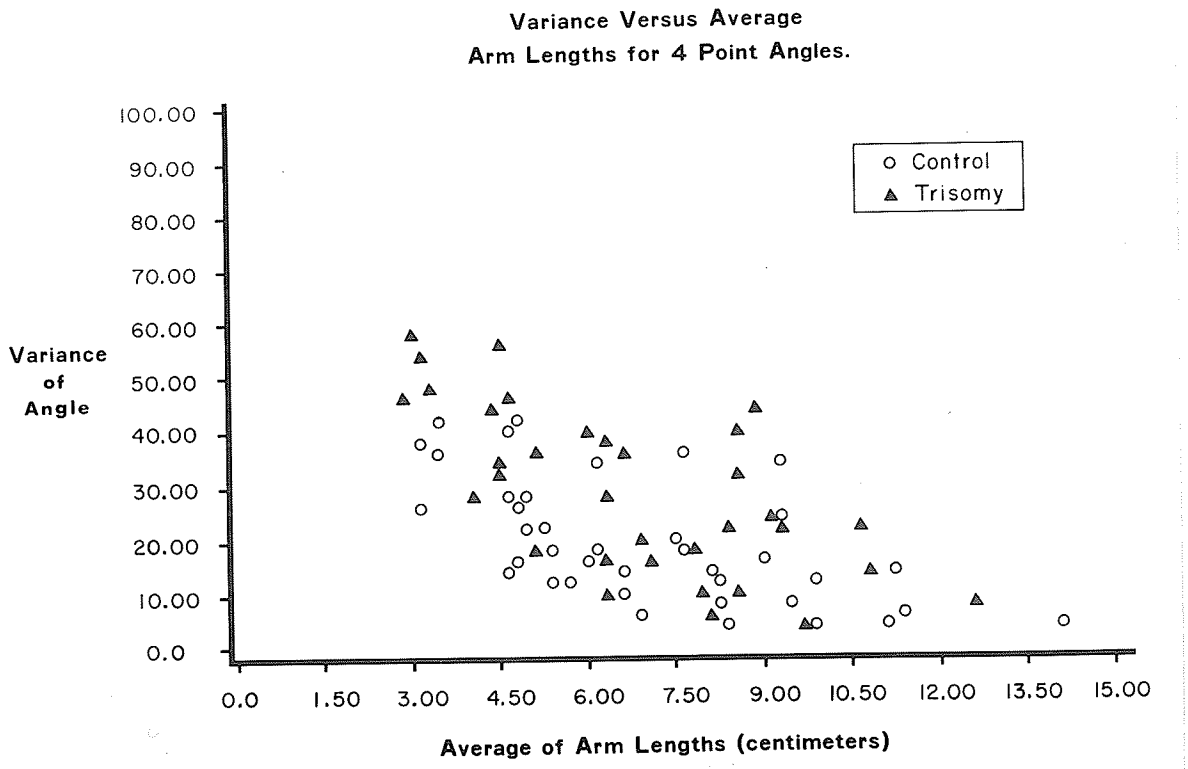


Figure 17. Graphic illustration of the effect of angle arm length on the variance of angles defined by four separate craniofacial landmarks (4 point angles).

respectively for the trisomy group, when standard deviation was used as the dependent variable. When variance was the dependent variable, values of 0.63 and 25.1 were found for the control group, and 0.66 and 30.0 for the trisomy group.

As noted previously, an inverse relationship was demonstrated between the independent and dependent variables. The multiple R and the F values indicated that the inverse relationship was slightly better defined in 3 point angles than in 4 point angles, however, these differences were not statistically significant.

iii) Curve Fitting

A comparison of the various curves, e.g. log, exponential, etc., indicated that the linear equation $Y = AX + B$ had the best "goodness of fit" for the mean curve representing both control and trisomy groups for the dependent variables, standard deviation and variance, and the independent variable, average arm length. The following mathematical formulas were obtained as shown in the four equations:

Control Group	Trisomy Group
S = -0.64 L - 0.32	S = -0.65 L - 0.42
with multiple R = 0.64	with multiple R = 0.65
F = 37.1	F = 39.0
V = -0.61 L - 2.88	V = -0.65 L - 4.54
with multiple R = 0.61	with multiple R = 0.65
F = 31.7	F = 38.7

where:

S = the angle standard deviation

V = the angle variance (or S^2)

L = the average reference point distance or average arm length

It should be noted that a multiple R value between 0.61 and 0.65 demonstrates that the mean mathematical curves have fitted the sample reasonably well. More specifically it means that R^2 or about 40% of the angle variability is due to variation in arm length.

iv) Adjusted Values for the Variability of Craniofacial Reference Lines

The variability of the angles formed by the craniofacial reference lines was used as an indication of their stability

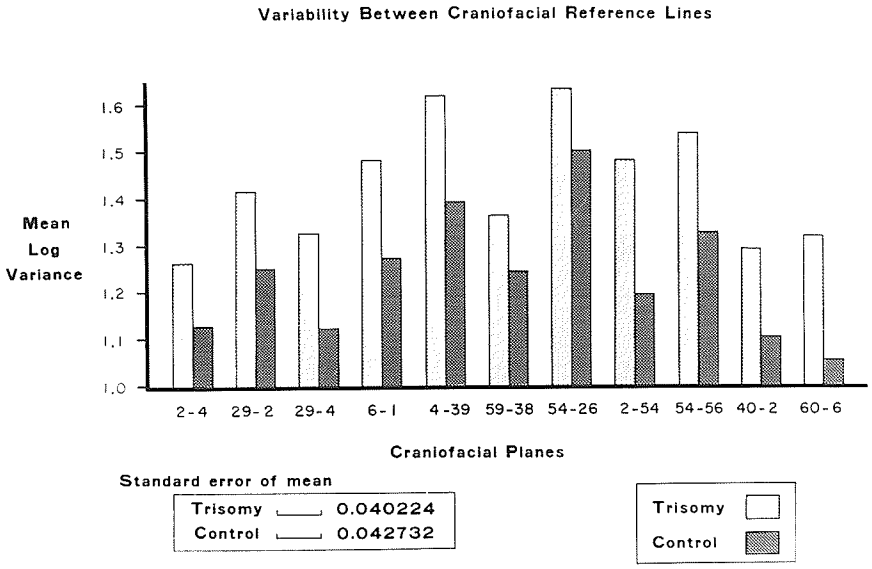
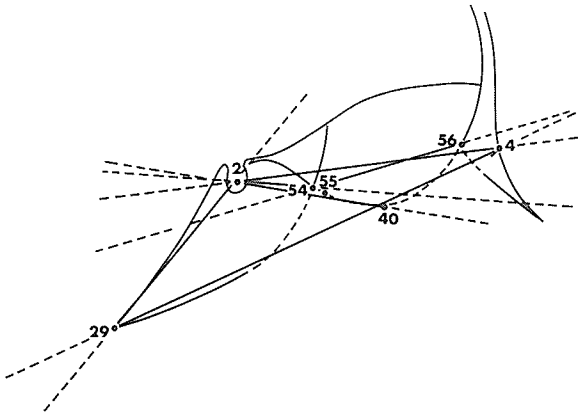


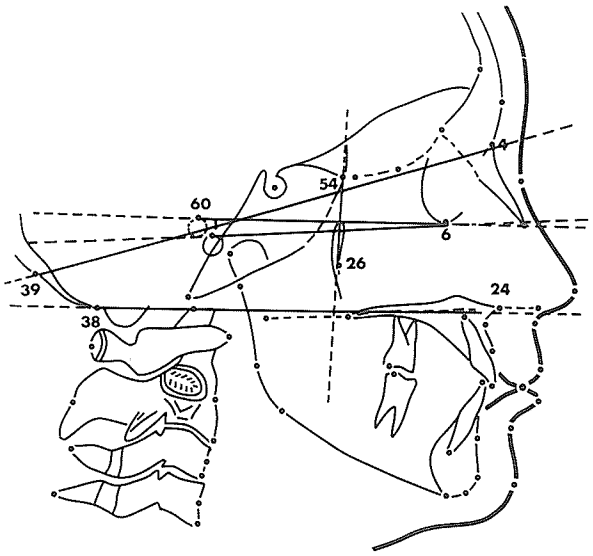
Figure 18. Graphic illustration comparing the variability of eleven craniofacial reference lines in the trisomy 21 and control groups.

CRANIAL BASE PLANES of ORIENTATION



2 - 4 ANTERIOR CRANIAL BASE
2 - 29 POSTERIOR CRANIAL BASE
4 - 29 HUXLEY'S BASI-CRANIAL AXIS
2 - 40 ETHMOIDALE - SELLA LINE
2 - 54 SELLA - SPHENO ETHMOIDAL JUNCTION
55 - 56 CRIBIFORM PLANE

CRANIOFACIAL PLANES of ORIENTATION



4 - 39 MARTIN'S PLANE
24 - 38 HIS' PLANE
6 - 1 FRANKFORT HORIZONTAL (MACHINE-PORION)
6 - 60 FRANKFORT HORIZONTAL (Anatomic Porion)
54 - 26 PM REFERENCE LINE

and suitability for superimposition. Adjusted values can be found in the Appendix. Significant differences at the 0.1% confidence level were noted between the trisomy and control groups for all of the lines under investigation.

Using angle log variance as the measure of variability, a within group analysis of variance demonstrated significant differences in the stability of the 11 lines (Figure 18). For the control group, minimal variation was found to be characteristic of lines 29-04, 40-02, and 60-06, while in the trisomy 21 group, minimal variation was characteristic of lines 29-04, 40-02, 60-06 and 02-04. Differences in the variability between these lines and the other lines under consideration were significant at the 0.1% level of confidence.

II. SKELETAL ANALYSIS

Developmental changes and the resulting craniofacial morphology found in both trisomy 21 and control samples were evaluated in the skeletal analysis. The osseous facial structures, the nasomaxillary complex and the mandible, were studied using the basion-nasion (29-04) line as the plane of superimposition, with registration

at the point of intersection of a perpendicular from sella (02) to the basion-nasion line. Horizontal linear measurements to the vertical P.M. line from both cranial base and facial landmarks were subsequently used to interrelate the growth and developmental processes of these two areas of the craniofacial complex.

Results of the skeletal analysis will be discussed under the following general headings:

A) cranial base

B) nasomaxillary complex

C) mandible

The means and standard errors for all the variables used in the skeletal analysis can be found in the Appendix in Tables XIX to XLIII. Statistical data is provided for the five age ranges, corresponding to the subgrouping of the trisomy 21 and control samples by skeletal age.

A) Cranial Base

i) Anterior Cranial Base

This linear dimension was measured as the distance between the anatomic points sella and nasion. The trisomy 21 group was found to be significantly smaller than

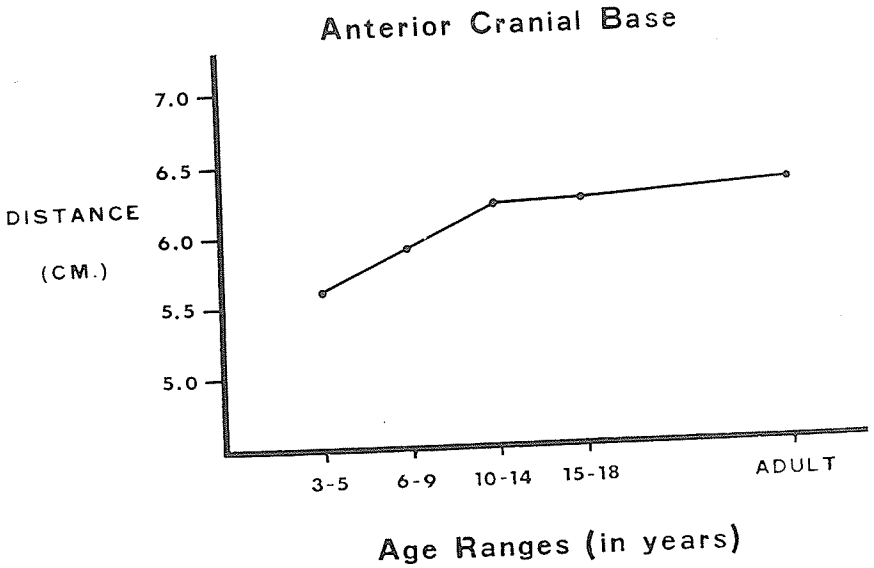


Figure 19. Main effect of age on the linear dimension Anterior Cranial Base (Sella-Nasion).

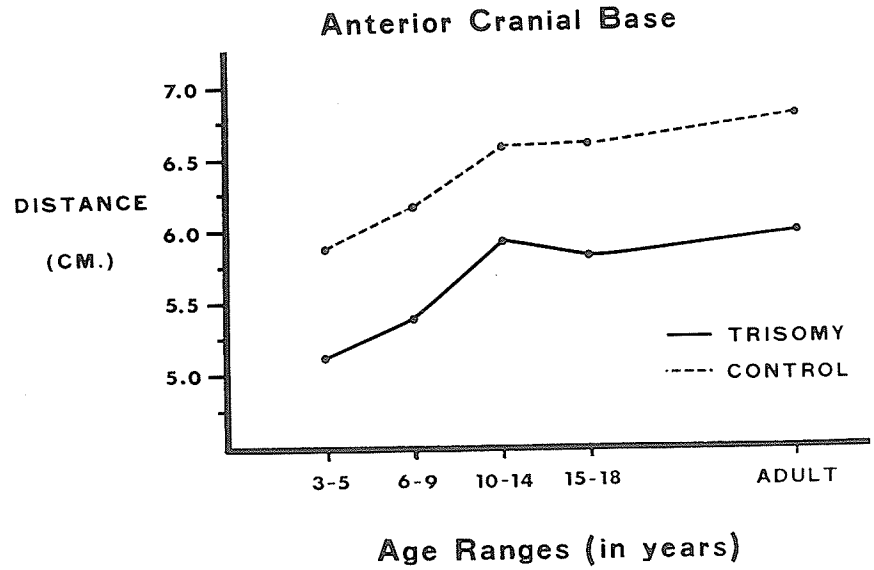


Figure 20. Effect of age on the linear dimension Anterior Cranial Base (Sella-Nasion) for the trisomy 21 and control groups.

the control group at the 1% level of confidence. The means for the trisomy and control groups were 5.9 cm. and 6.5 cm., respectively. Significant differences, at the 1% level, were also noted between the sexes, with mean values being 6.3 cm. for males and 6.0 cm. for females.

Among the age ranges, a significant difference at the 1% level was found, as shown in Figure 19. An incremental growth pattern was demonstrated by both populations up to 10-14 years ($P < 0.01$) and this was followed by a diminished incremental growth in the older age ranges. No significant group X age interaction was detected implying that this measurement behaved the same in both groups (Figure 20).

ii) Posterior Cranial Base

This linear measurement represented the distance between anatomical points basion and sella. The trisomy 21 group was significantly smaller at the 1% level with means for the trisomy and control groups being 3.8 cm. and 4.0 cm., respectively. Sex differences were significant at the 1% level of confidence with females being smaller than the males.

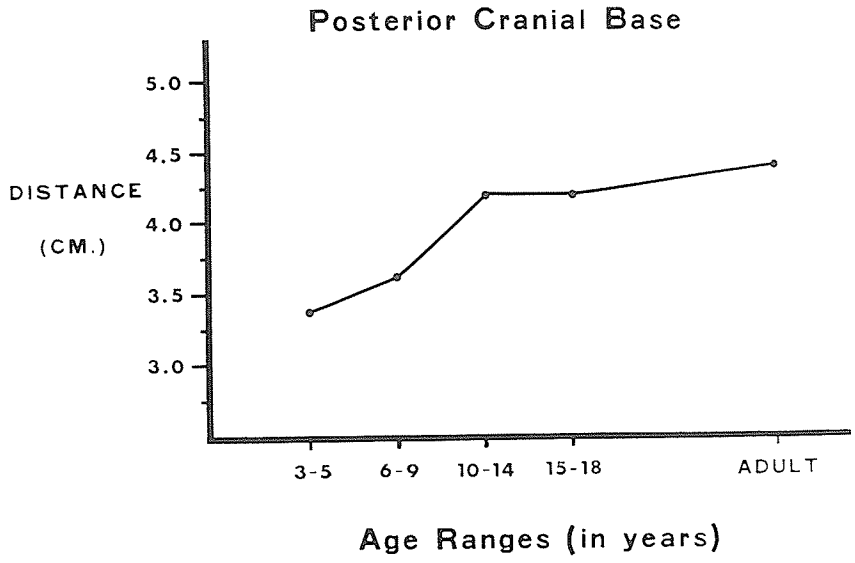


Figure 21. Main effect of age on the linear dimension Posterior Cranial Base (Basion-Sella).

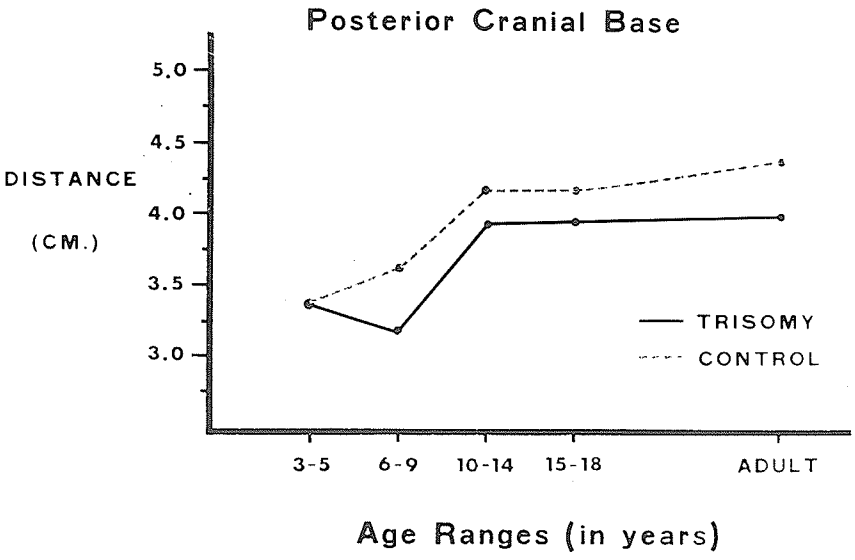


Figure 22. Effect of age on the linear dimension Posterior Cranial Base (Basion-Sella) for the trisomy 21 and control groups.

As shown in Figure 21, significant differences at the 1% level were found among the age ranges. Maximum increase in the length of the posterior cranial base occurred up to 10-14 years, after which there was little noticeable change.

A group X age interaction, significant at the 5% level of confidence, is shown in Figure 22. Increases in posterior cranial base occurred as early as 6-9 years in the control group and continued to ages 10-14 years. In the trisomy group, increase in this dimension was delayed until ages 6-9 years and continued to ages 10-14 years. Continued growth in the control sample resulted in adult differences between the groups being significant at the 1% level.

iii) Basicranial Axis or Ba-N Plane

This linear dimension was defined as the distance between points basion and nasion, and its length is representative of both the length and the degree and direction of flexure of the cranial base. Differences between groups were significant at the 1% level of confidence, with mean values being 9.2 cm. for the trisomy sample and 9.7 cm. for the control sample. Females were found to be

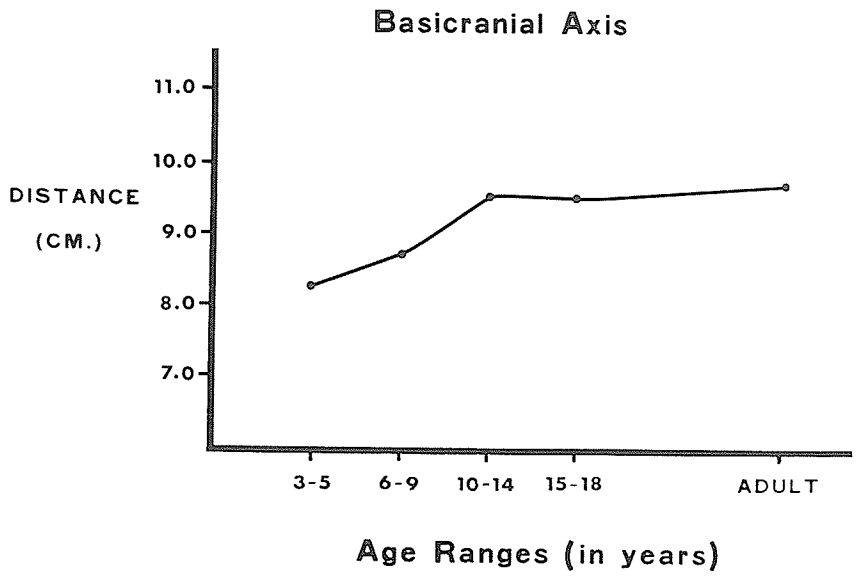


Figure 23. Main effect of age on the linear dimension Basicranial Axis (Basion-Nasion).

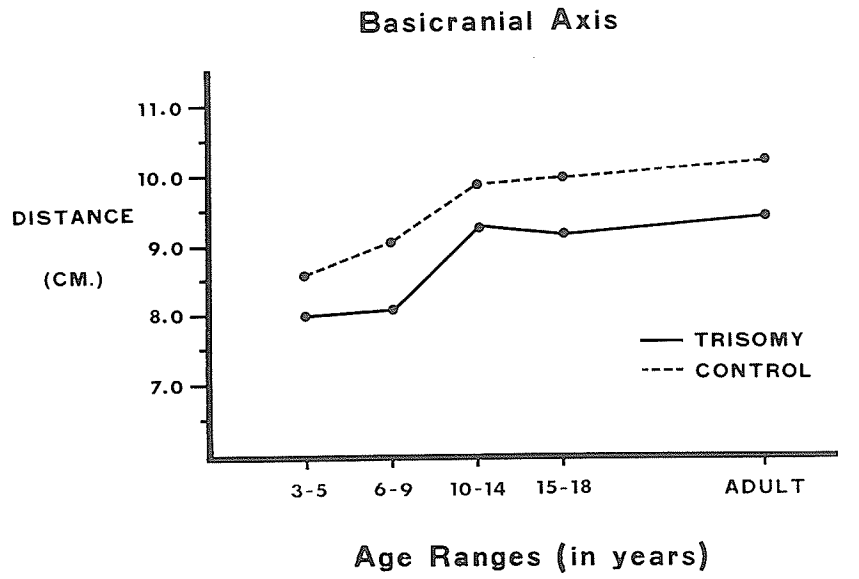


Figure 24. Effect of age on the linear dimension Basicranial Axis (Basion-Nasion) for the trisomy 21 and control groups.

smaller than the males, significant at the 1% level.

Significant differences at the 1% level were found among the age ranges, as illustrated in Figure 23. Changes in the length of the basicranial axis occurred up to the age range 10-14 years, after which were was no significant increase or decrease in this parameter.

No significant higher order interactions were found and the group X age interaction, shown in Figure 24, illustrated that this measurement behaved the same in both groups.

iv) Sella to the P.M. Vertical Line

This linear dimension was defined as the perpendicular distance from sella to the posterior nasomaxilla (P.M.) vertical line. Significant differences for this distance, at the 1% level of confidence, were found between the trisomy 21 group, mean value 2.1 cm., and the control group, mean value 2.2 cm. Males were found to be larger than females -- significant at the 1% confidence level.

Among the age ranges a significant difference at the 1% level was found, as shown in Figure 25. Increases in this parameter were observed between ages 6-9 to 10-14 years ($P < 0.05$) and between ages 15-18 to adult ($P < 0.01$).

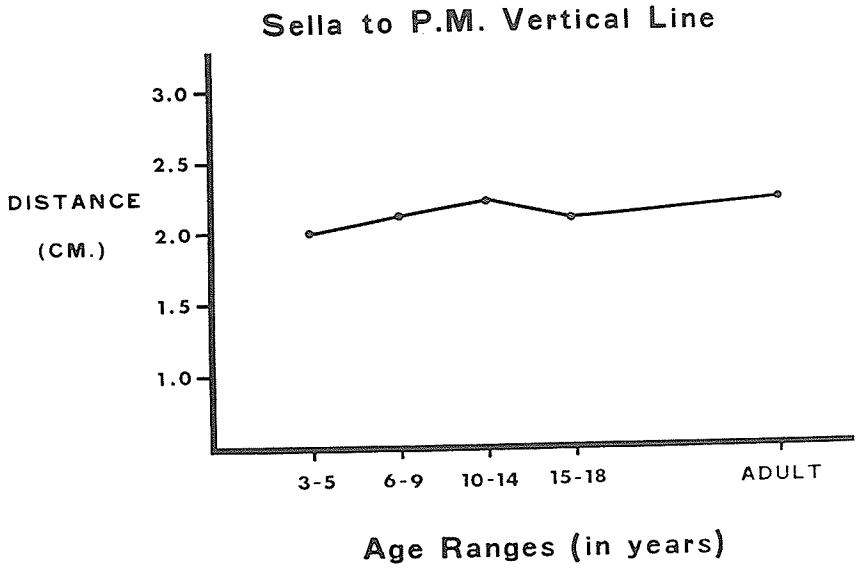


Figure 25. Main effect of age on the linear dimension Sella to the P.M. vertical line.

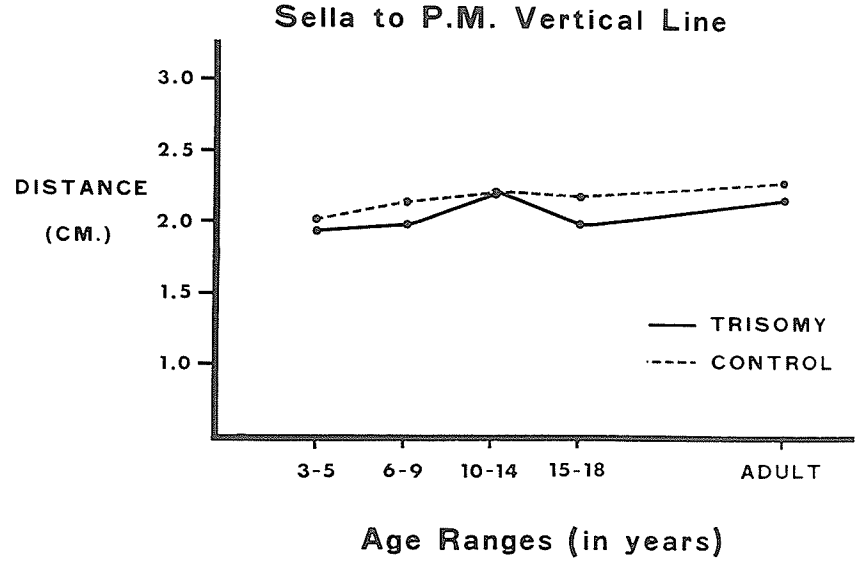


Figure 26. Effect of age on the linear dimension Sella to the P.M. vertical line for the trisomy and control groups.

The group X age interaction was not found to be statistically significant suggesting a relative parallelism in growth changes for this parameter (Figure 26).

v) Nasion to the P.M. Vertical Line

This measurement represented the perpendicular distance from nasion to the vertical P.M. line. Differences between the trisomy and control groups were significant at the 1% level with mean values being 3.3 cm. and 3.9 cm., respectively. Males were found to be larger than the females at the 1% level of confidence.

Among the age ranges, a significant difference at the 1% level was found, as shown in Figure 27. An incremental growth pattern was demonstrated by both populations up to 10-14 years, after which there was a diminished incremental growth into the older age ranges.

A group X age interaction, significant at the 5% level, was found, as illustrated in Figure 28. Examination of the mean measurements at the five age ranges indicated that the trisomy 21 sample showed a smaller value for this parameter at all age ranges.

vi) Basion to the P.M. Vertical Line

This linear dimension was represented by the

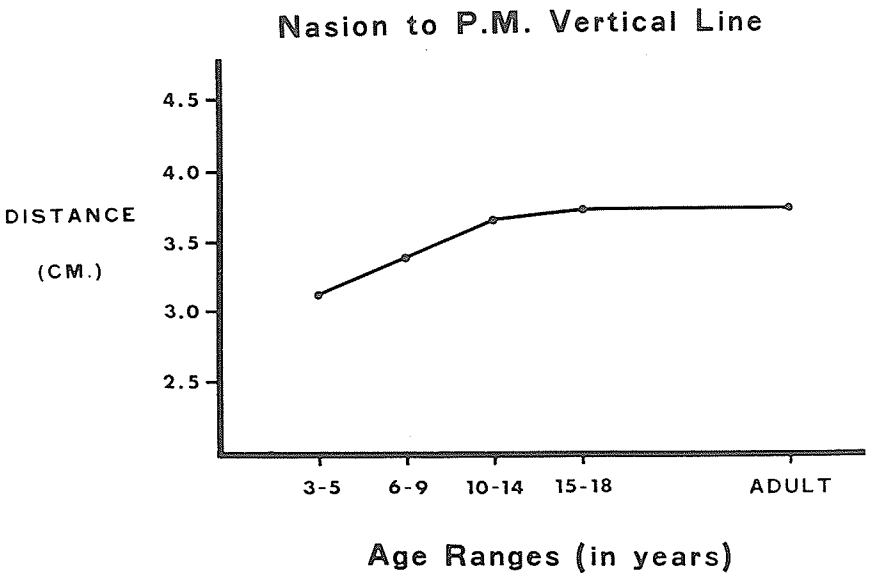


Figure 27. Main effect of age on the linear dimension Nasion to the P.M. vertical line.

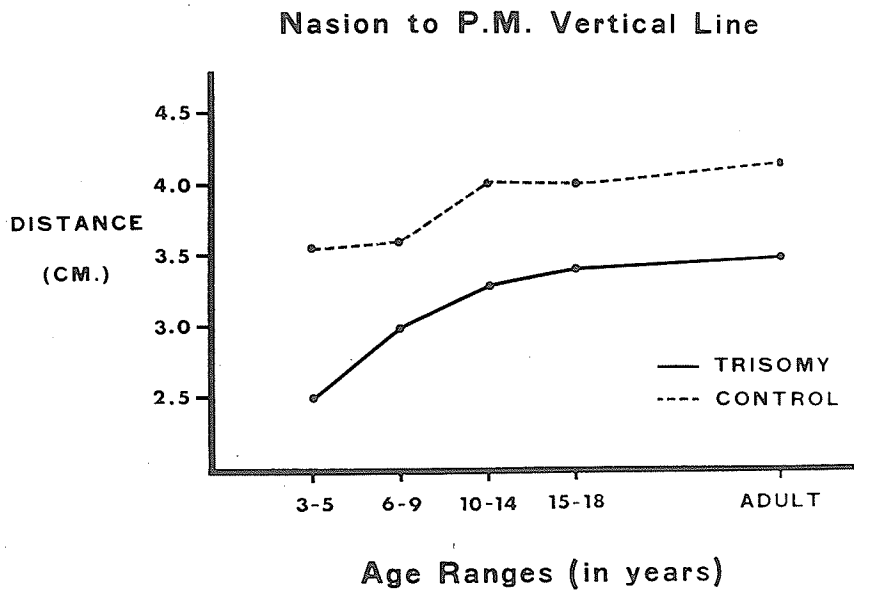


Figure 28. Effect of age on the linear dimension Nasion to the P.M. vertical line for the trisomy 21 and control groups.

perpendicular distance from the anatomic point, basion, to the vertical P.M. line. Differences between groups were not found to be significant, however, sex differences, significant at the 1% level, were found indicating that males were larger than females.

A significant difference at the 1% level of confidence was found among the age ranges, as shown in Figure 29. Maximum increases in this dimension were found between the age ranges 6-9 and 10-14 years.

A group X age interaction was found to be significant at the 1% level, as shown in Figure 30. The multiple range tests indicated that differences between the trisomy and control groups at each of the five age ranges were not statistically significant. Significant increases in this dimension were observed for both the trisomy ($P < 0.01$) and control ($P < 0.05$) groups between the age ranges 6-9 and 10-14 years.

The group X age X sex interaction was found to be significant at the 5% confidence level (Figure 31) and illustrated the changes found in each of the male and female subgroups for this parameter. The limited sample size of trisomy 21 males, aged 3-5 years, necessitated the

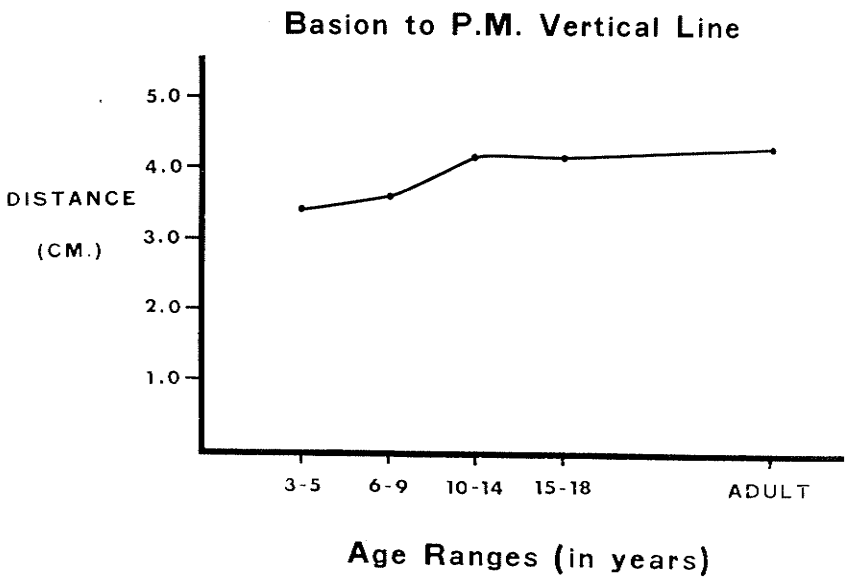


Figure 29. Main effect of age on the linear dimension Basion to the P.M. vertical line.

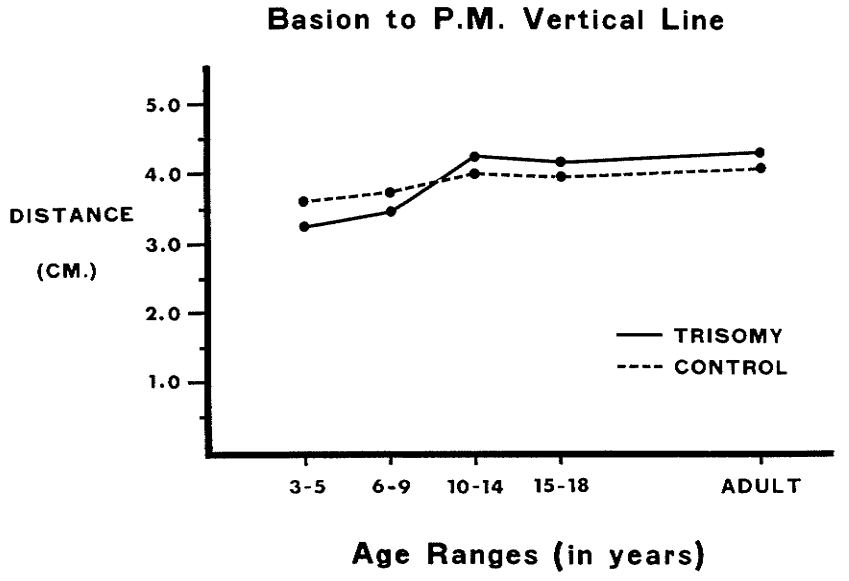


Figure 30. Effect of age on the linear dimension Basion to the P.M. vertical line for the trisomy 21 and control groups.

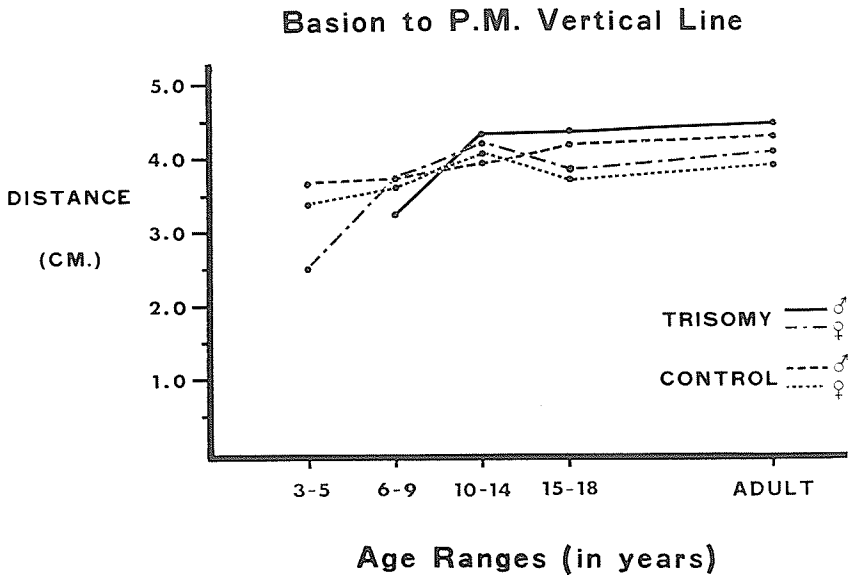


Figure 31. Effect of age on the linear dimension Basion to the P.M. vertical line for the trisomy 21 and control, males and females.

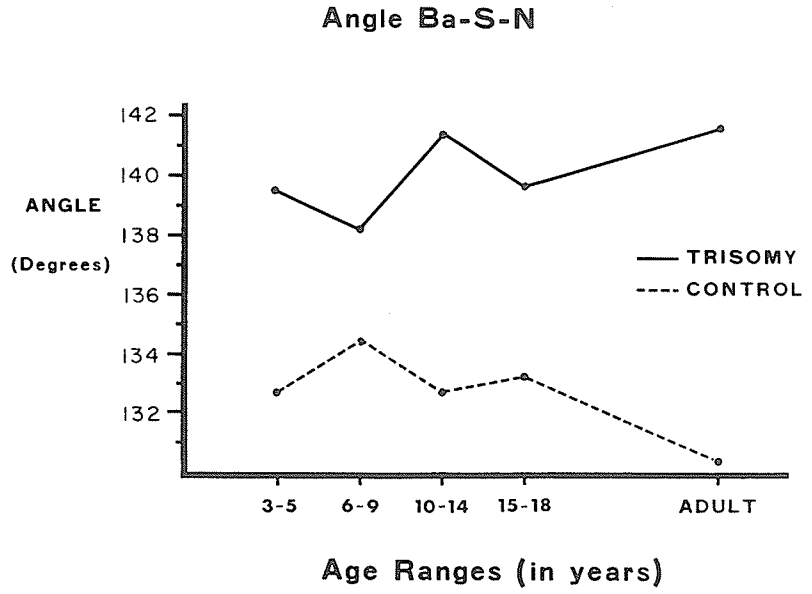


Figure 32. Effect of age on the angular dimension Ba-S-N for the trisomy 21 and control groups.

elimination of this value.

vii) Cranial Base Angle

The cranial base angle was defined by points basion, sella and nasion and represented the angle formed by the anterior and posterior components of the cranial base. The trisomy 21 group was found to be significantly larger, at the 1% level, than the control group, with mean values being 140.6 degrees and 132.2 degrees, respectively.

The group X age interaction was not found to be statistically significant, however, examination of the mean measurements at the five age ranges indicated that the trisomy 21 group showed a considerably larger value for the cranial base angle at all age ranges (Figure 32).

B) Nasomaxillary Complex

i) Point A to the P.M. Vertical Line

This linear measurement, recorded as the perpendicular distance from point "A" to the vertical P.M. line, represented the antero-posterior length of the maxilla. Significant differences, at the 1% level, were found between trisomy and control groups, their mean lengths being 4.2 cm. and 4.8 cm., respectively.

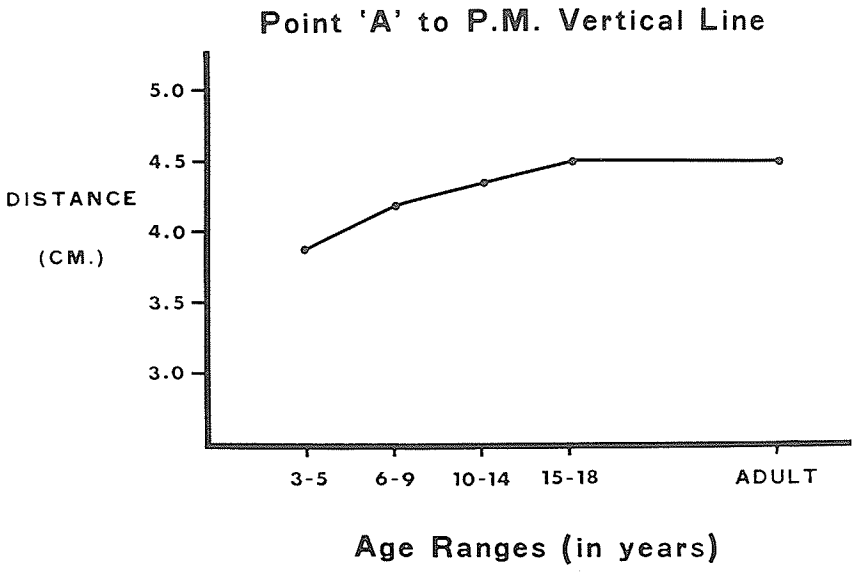


Figure 33. Main effect of age on the linear dimension Point "A" to the P.M. vertical line.

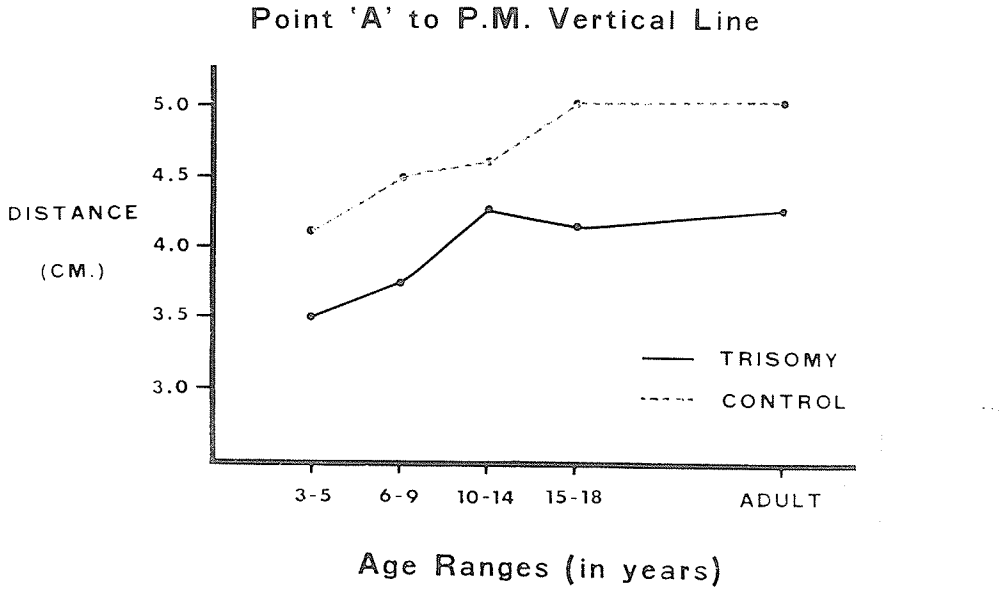


Figure 34. Effect of age on the linear dimension Point "A" to the P.M. vertical line for trisomy 21 and control groups.

Among the age ranges, a significant difference at the 1% level of confidence, was found (Figure 33). An incremental growth pattern was shown by both trisomy and control samples up to 10-14 years. Beyond this age, no significant changes occurred in the antero-posterior length of the maxilla.

The group X age interaction, significant at the 1% level, was found, as illustrated in Figure 34. Examination of the mean measurements at the five age ranges indicated that the trisomy 21 group was smaller for this parameter at all age ranges.

ii) Angle Ba-N-A

This angular measurement was recorded as the angle described by lines joining points basion-nasion and point "A"-nasion. The group analysis demonstrated that this parameter was significantly larger in the trisomy 21 group than in the control group ($P < 0.01$), with mean values being 65.0 degrees and 63.8 degrees, respectively.

Sex and age differences were not found to be significantly different. Similarly, the various interactions of group, age and sex were not statistically significant, a situation due, in part, to the large variation in each of

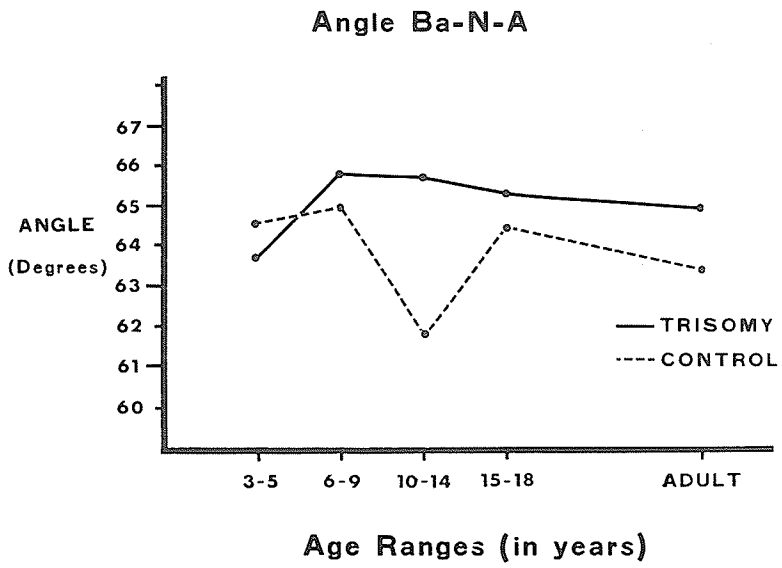


Figure 35. Effect of age on the angular dimension Ba-N-A for the trisomy and control groups.

the groups for the angular dimension. The group X age interaction, illustrated in Figure 35, demonstrated the growth patterns of each of the two groups. Multiple range tests indicated no significant change in this angle at any of the five age ranges for the trisomy 21 sample, while the control sample showed a decrease, significant at the 5% level, between the ages 6-9 and 10-14 years. This corresponded to the period of maximum flexure of the cranial base in the control group. Trisomy and control values for the Ba-N-A angle were significanlty different only at ages 6-9 and 10-14 years.

iii) Palatal Plane to the Ba-N Plane

This angular measurement, described by the intersection of lines joining nasion to basion and the anterior nasal spine to the posterior nasal spine, demonstrated the inclination of the palatal plane, or maxilla, to the cranial base. The differences found between groups and between sexes were not statistically significant.

Differences among the age ranges were significant at the 5% confidence level, as shown in Figure 36. An incremental growth pattern was demonstrated by both populations until 10-14 years and this was followed by a

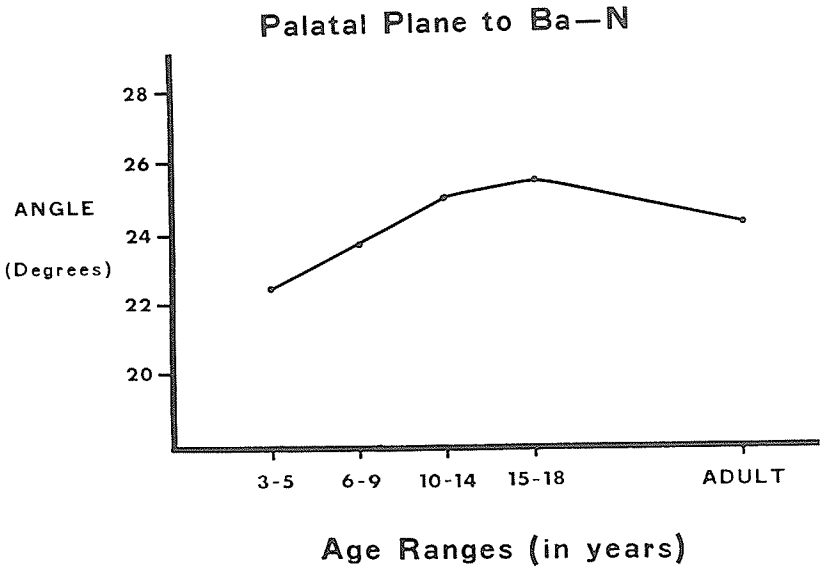


Figure 36. Main effect of age on the angular dimension palatal plane to the Ba-N line.

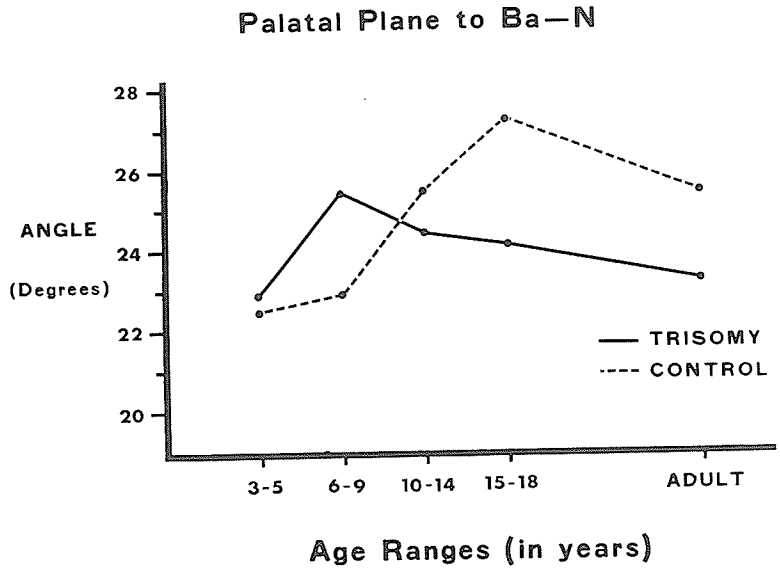


Figure 37. Effect of age on the angular dimension palatal plane to the Ba-N line for the trisomy 21 and control groups.

diminished growth pattern in the older age ranges.

The group X age interaction (Figure 37) was found to be significant at the 5% level of confidence. The multiple range tests demonstrated significantly higher values ($P < 0.05$) for this parameter in the control group from ages 15-18 years to adult.

iv) Upper Incisor to the P.M. Vertical Line

This horizontal linear distance was measured as the perpendicular from the maxillary incisal tip to the vertical P.M. line. Between group differences were found to be significant at the 1% level, with mean distances for the trisomy and control samples being 4.8 cm. and 5.3 cm., respectively.

Significant differences at the 1% level of confidence were also found among the age ranges, as illustrated in Figure 38. Increases in the dimension were observed through age ranges 6-9 and 10-14 years, after which, any further changes were not found to be statistically significant.

The group X age interaction was found to be significant at the 1% level and is shown in Figure 39. Significant increases in this distance occurred in the control group up to ages 15-18 years, after which little

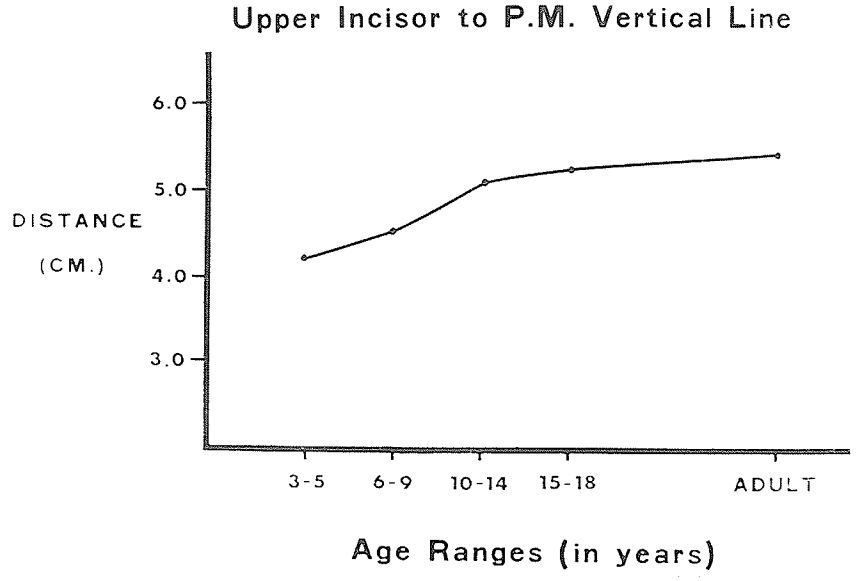


Figure 38. Main effect of age on the linear dimension upper incisor to the P.M. vertical line.

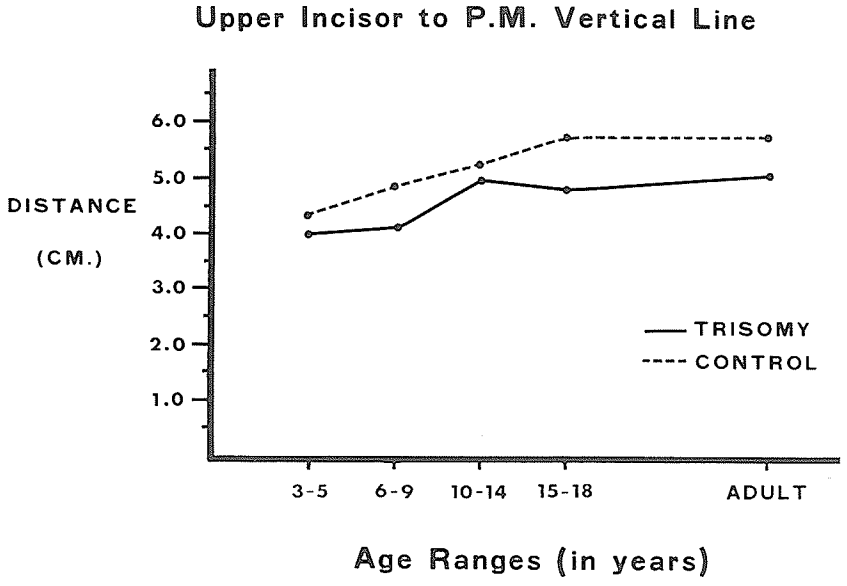


Figure 39. Effect of age on the linear dimension upper incisor to the P.M. vertical line for the trisomy 21 and control groups.

change took place. The trisomy 21 sample underwent a rapid increase in this dimension between the age ranges 6-9 and 10-14 years beyond which no significant changes occurred.

v) Upper Incisor to the Ba-N Plane

This angle, formed by the intersection of a line representing the long axis of the maxillary central incisors and the basion-nasion line, described the relative proclination of the maxillary incisors to the basicranial axis. Differences between groups were found to be significant at the 1% level of confidence. Mean values for the trisomy 21 sample were 91.0 degrees and for the control sample were 82.7 degrees.

Differences among the age ranges were found to be significant at the 1% level, as shown in Figure 40. The largest increase in this parameter occurred between the age ranges 6-9 and 10-14 years.

The higher order group X age interaction, shown in Figure 41, was found to be significant at the 1% level of confidence. Changes in the proclination of the maxillary incisors were not found to be significant at any of the five age ranges for the control sample. An increase,

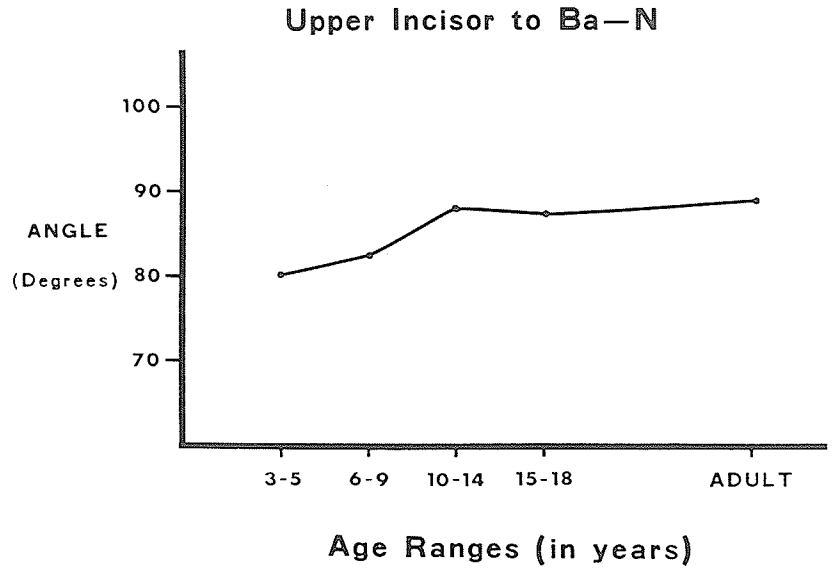


Figure 40 . Main effect of age on the angular dimension Upper Incisor to the Ba-N line.

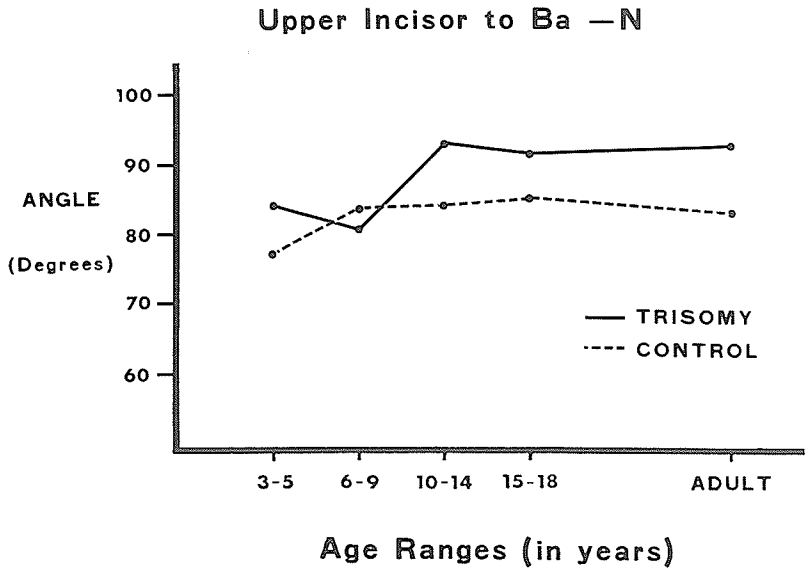


Figure 41. Effect of age on the angular dimension Upper Incisor to the Ba-N line for the trisomy 21 and control groups.

significant at the 1% level, was found between the age ranges 6-9 and 10-14 years for the trisomy 21 sample, resulting in larger values for this parameter ($P < 0.01$) in the trisomy group from 10-14 years to adult ages.

The increased proclination of trisomy maxillary incisors corresponded in time to their eruption time and to the period of maximum cranial base flexure in the trisomy group.

C. Mandible

i) Mandibular Plane Angle

This angle was recorded as the angle formed by a tangent to the lower border of the mandible and the basicranial axis (Ba-N line). Significant differences, at the 1% level of confidence, were found between the trisomy and control groups, with mean values being 47.5 degrees and 51.0 degrees, respectively.

Differences, significant at the 5% level, were found among the age ranges, as shown in Figure 42. Multiple range tests comparing age groups indicated little change in this variable until the 15-18 year age range. Subsequent to this, a significant decrease at the 1% level of

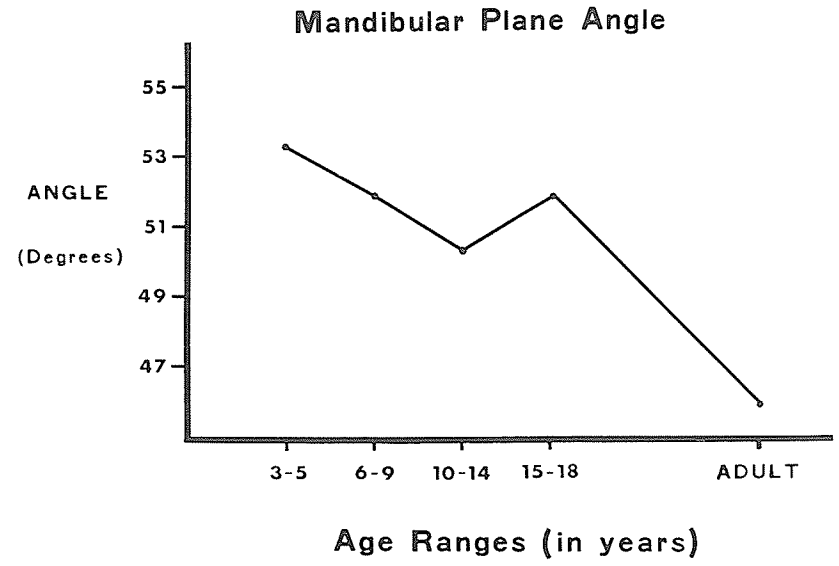


Figure 42. Main effect of age on the angular dimension Mandibular Plane Angle.

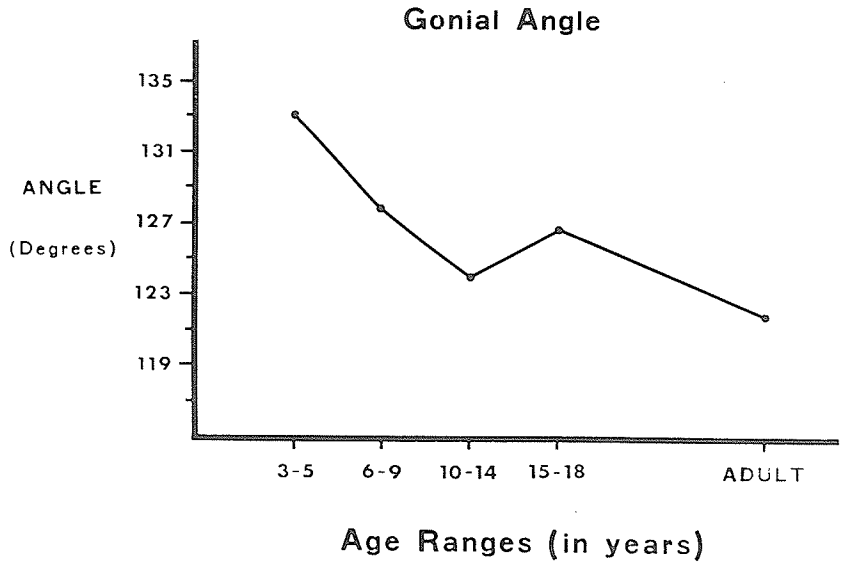


Figure 43. Main effect of age on the angular dimension Gonial Angle.

confidence was noted.

None of the higher order interactions for the mandibular plane angle were statistically significant.

ii) Gonial Angle

This angle was measured as the angle defined by the tangent to the lower border of the mandible and the tangent to the posterior border of the ramus. A significant difference, at the 1% confidence level, was found between the trisomy 21 and control groups -- their means being 123.4 degrees and 126.3 degrees, respectively. Males were found to have a more obtuse gonial angle than females with mean values being 125.8 degrees and 124.2 degrees, respectively, and significant at the 5% level.

Significant differences were noted in the gonial angle for the various age ranges, at the 1% confidence level. As illustrated in Figure 43, a slight decrease in this variable was noted between age ranges 3-5 years and 6-9 years. The only other significant difference occurred in the adult age range when the gonial angle significantly decreased at a confidence level of 1%.

The gonial angle demonstrated no significant interaction for groups, age and sex.

iii) Angle Ba-N-B

This angular measurement was defined by the three anatomical landmarks - basion, nasion and point "B". The group analysis demonstrated that this parameter was significantly larger in the trisomy 21 subjects ($P < 0.01$). Mean value for the trisomy 21 group was 64.8 degrees and for the control group was 60.2 degrees.

Sex and age differences were not found to be statistically significant. Similarly, the higher order interactions of group, age and sex were not significant, a fact attributable to the wide variation of this angular measurement in the two groups.

The group X age interaction, shown in Figure 44, illustrated the trend followed by the two groups at the various age ranges. Multiple range tests among the five age ranges, indicated no significant changes in this angle for the control group, while the trisomy 21 group experienced a significant increase in the angle ($P < 0.05$) between the 6-9 and 10-14 year age ranges. This corresponded with the period of maximum flexure of the cranial base in the trisomy group.

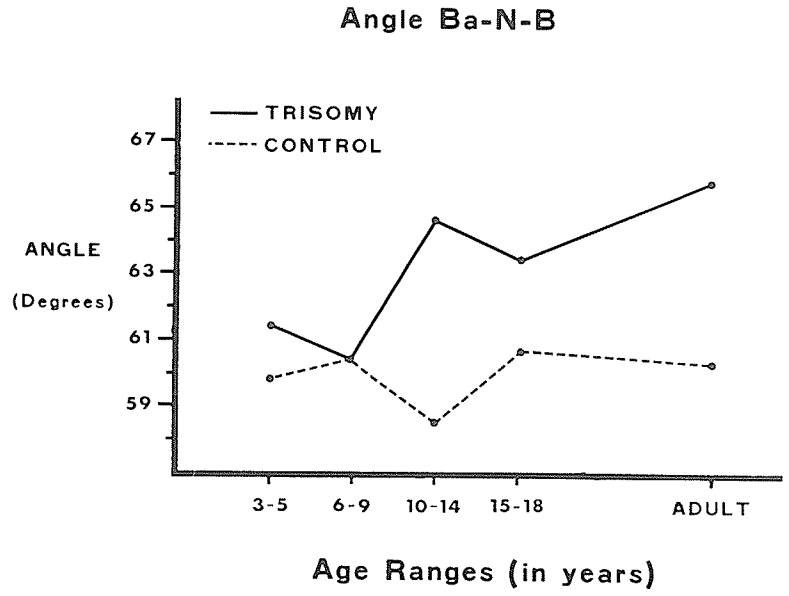


Figure 44. Main effect of age on the angular dimension Ba-N-B for the trisomy 21 and control groups.

iv) Point "B" to the P.M. Vertical Line

The relationship of point "B" to the P.M. vertical line was studied by measuring the perpendicular distance from point "B" to this vertical line. No significant differences were found when comparing groups and when comparing sex differences.

The analysis of variance indicated a significant difference at the 1% level among the age ranges, as shown in Figure 45. However, the multiple range tests detected significant differences only between the age ranges 6-9 and 10-14 years, at which time an increase significant at the 5% confidence level was noted.

The interaction of group X age was found to be significant at the 1% level of confidence, and is illustrated in Figure 46. This distance was found to be greater in the trisomy group at ages 3-5 years. The trisomy and control samples did not differ significantly at ages 10-14 years, however, the increase of this variable between age ranges 10-14 and 15-18 years, significant at 5%, resulted in significant differences being noted between trisomy and control groups for the adult age range.

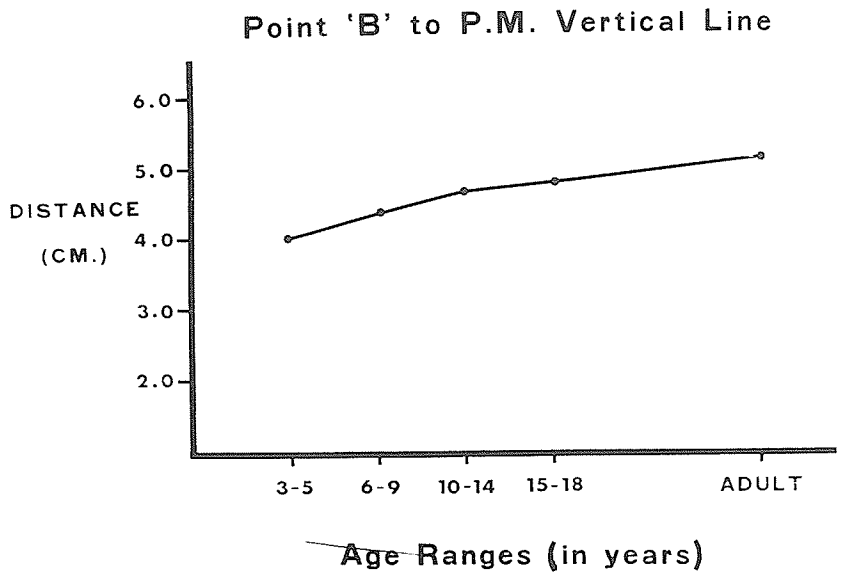


Figure 45. Main effect of age on the linear dimension Point "B" to the P.M. vertical line.

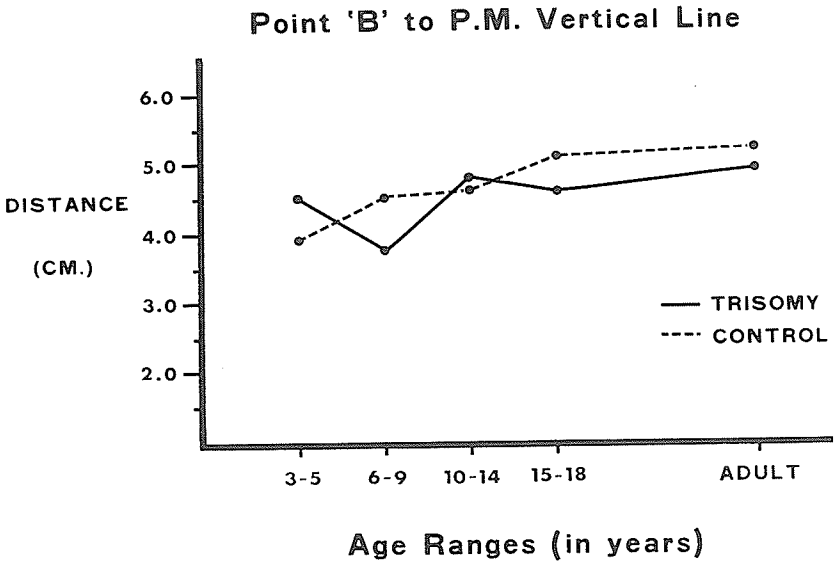


Figure 46. Effect of age on the linear dimension Point "B" to the P.M. vertical line for the trisomy 21 and control groups.

v) Pogonion to the P.M. Vertical Line

This linear dimension, measured as the perpendicular distance from the anatomical point pogonion to the vertical line, was not significantly different either between groups or between sexes.

Differences among the age ranges were found to be significant at the 1% level of confidence. The most substantial increases in length occurred between the age ranges 6-9 to 10-14 years ($P < 0.05$) and 15-18 to adult ($P < 0.05$), as shown in Figure 47.

The group X age interaction was found to be significant at the 1% level of confidence, as illustrated in Figure 48. This interaction was similar to that of point "B" to the vertical P.M. line. Initially this dimension was larger in the trisomy sample, however, increases during the 15-18 year age range resulted in the control sample having larger values at adult ages.

The higher order interaction of group X age X sex, shown in Figure 49, further clarified the changes that occurred with age for each group and sex. The limited sample size of trisomy 21 females, ages 3-5 years, necessitated the elimination of this value. It was noted that females -- both trisomy and control -- underwent greater increases of

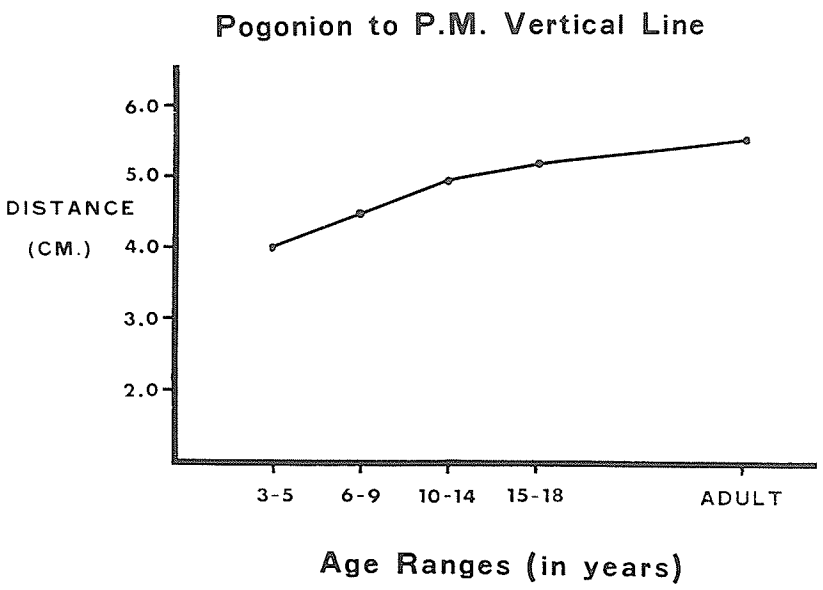


Figure 47. Main effect of age on the linear dimension Pogonion to the P.M. vertical line.

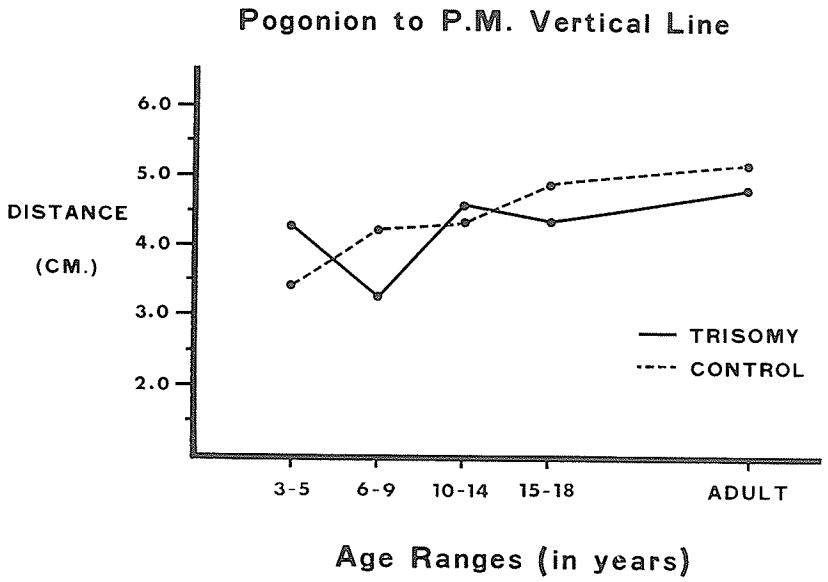


Figure 48. Effect of age on the linear dimension Pogonion to the P.M. vertical line for the trisomy 21 and control groups.

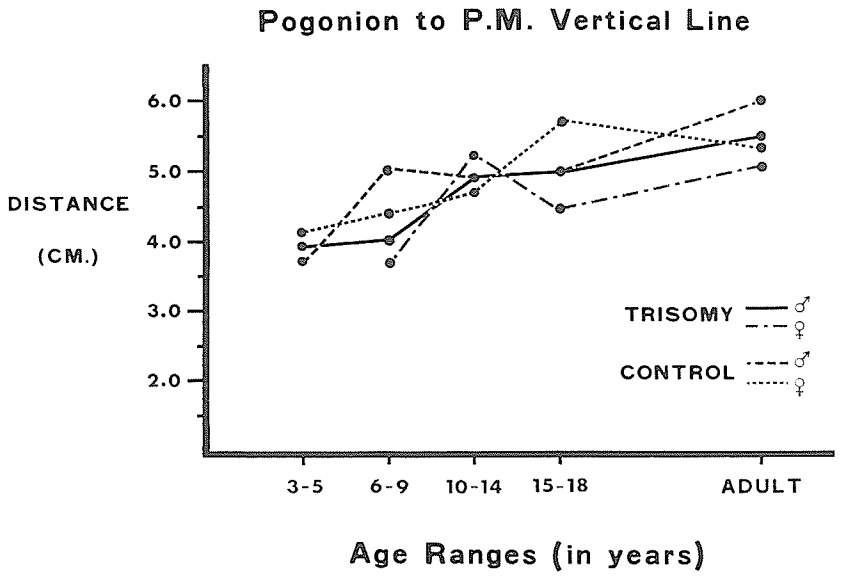


Figure 49. Effect of age on the linear dimension Pogonion to the P.M. vertical line for the trisomy 21 and control groups, males and females.

this dimension between age groupings 10-14 and 15-18 years than their male counterparts. However, greater increases in the male samples at later age groupings resulted in higher values for this variable in adult males.

vi) Articulare to the P.M. Vertical Line

This horizontal linear measurement was recorded as the perpendicular distance from articulare to the P.M. vertical line. Differences between the two groups were found significant at the 1% level of confidence, with mean values being 2.9 cm. for the trisomy group and 3.1 cm. for the control group. Males, with a mean value of 3.1 cm., were found to be larger than females, with a mean value of 2.9 cm. ($P < 0.01$).

Among the age ranges a significant difference of 1% was observed, as seen in Figure 50. This linear distance was found to increase significantly, at the 1% confidence level between the age ranges 6-9 and 10-14 years.

The interaction of group X age X sex was found to be significant at the 1% level, as shown in Figure 51. Trisomy values, both male and female, were initially less than control values. Increases occurred between the ages 6-9 and 10-14 years, and continued in the trisomy males to the

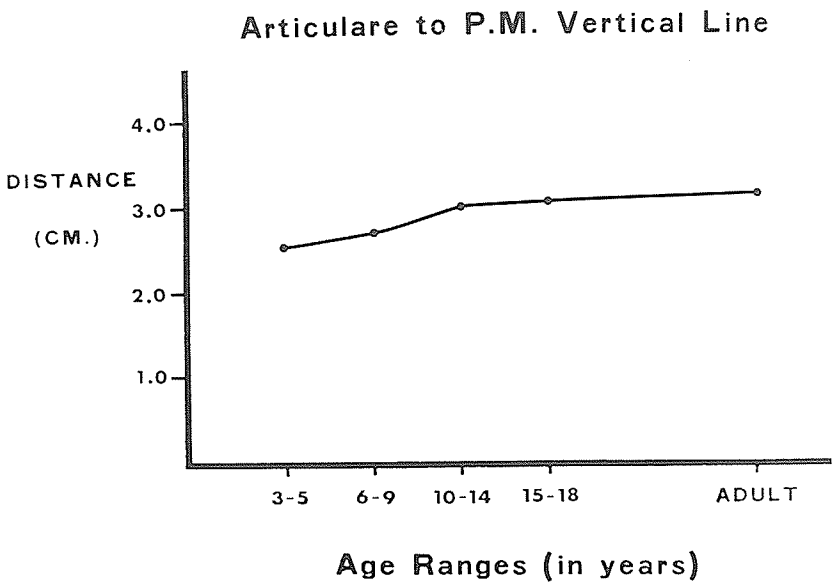


Figure 50. Main effect of age on the linear dimension Articulare to the P.M. vertical line.

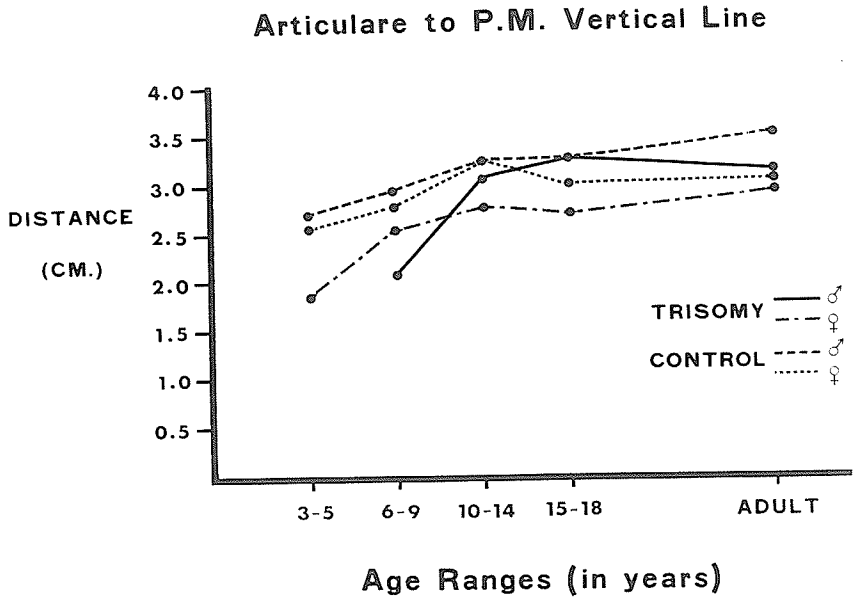


Figure 51. Effect of age on the linear dimension Articulare to the P.M. vertical line for the trisomy 21 and control groups, males and females.

15-18 age range where they surpassed control female values.

vii) Gonion to the P.M. Vertical Line

This horizontal linear measurement was recorded as the perpendicular distance from the most inferior and posterior part of the ramus of the mandible to the vertical P.M. line. This distance was not found to be significantly different between the trisomy and control groups, however, sex differences were found at the 1% confidence level, with males (mean value 2.1 cm.) being larger than females (mean value 1.9 cm.).

As illustrated in Figure 52, significant differences at the 1% level were found among the various age ranges. Significant increases were demonstrated between the age ranges 6-9 and 10-14 years.

The higher order interactions of group, age and sex were not found to be statistically significant and Figure 53 shows the relative parallelism of changes recorded in this parameter for each group.

viii) Lower Incisor to the P.M. Vertical Line

This horizontal linear measurement was recorded as the perpendicular distance from the incisal edge of the mandibular central incisor to the vertical P.M. line.

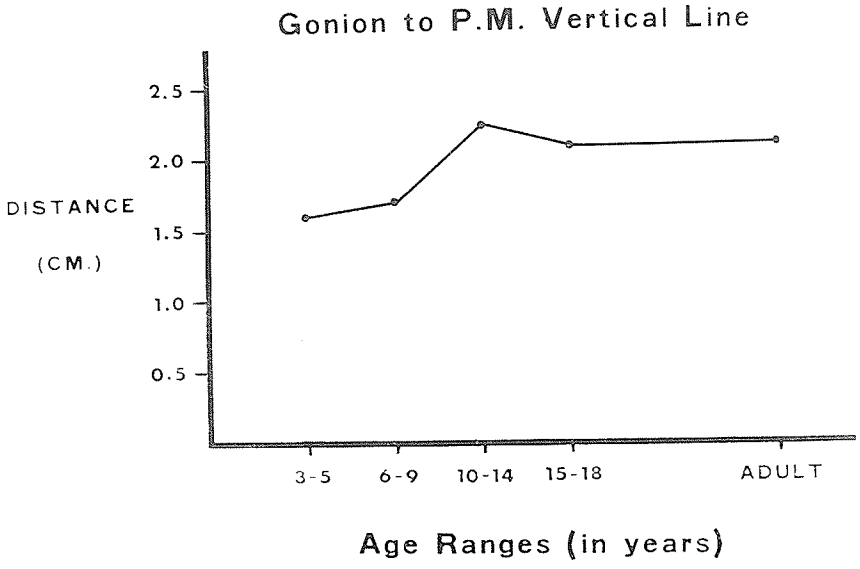


Figure 52. Main effect of age on the linear dimension Gonion to the P.M. vertical line.

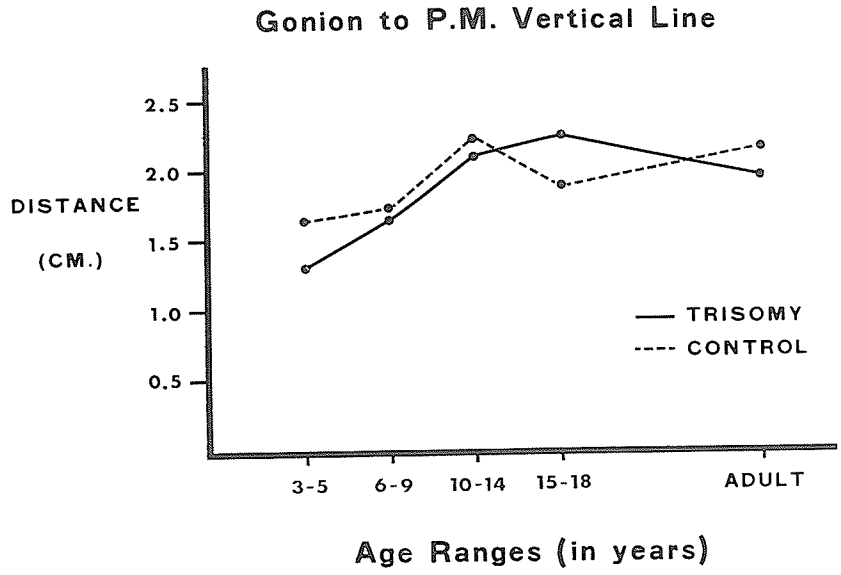


Figure 53. Effect of age on the linear dimension Gonion to the P.M. vertical line for the trisomy 21 and control groups.

Differences found between groups and between sexes were not statistically significant.

A significant difference, at the 1% confidence level, was found among the age ranges, as shown in Figure 54. Significant increases were observed between the age ranges 3-5 to 6-9 years ($P < 0.05$) and 6-9 to 10-14 years ($P < 0.01$).

The group X age interaction for this variable, as illustrated in Figure 55, was significant at the 1% level of confidence. The multiple range tests indicated significant increases in this linear dimension during the age range 3-5 to 6-9 years in the control sample and from 6-9 to 10-14 years in the trisomy sample ($P < 0.01$). Continued increases for the control group resulted in larger values for this variable during the adult age range ($P < 0.01$).

ix) Lower Incisor to the Mandibular Plane

The relationship between the lower incisors and the mandibular plane was studied by measuring the angle formed by the long axis of the mandibular central incisor and the tangent to the lower border of the mandible. This variable was found to be significantly different ($P < 0.05$) between the trisomy and control groups, with mean values of 94.1 degrees and 93.5 degrees, respectively. Significant differences were also found between the sexes ($P < 0.01$), with females, mean value 95.9 degrees, being larger than

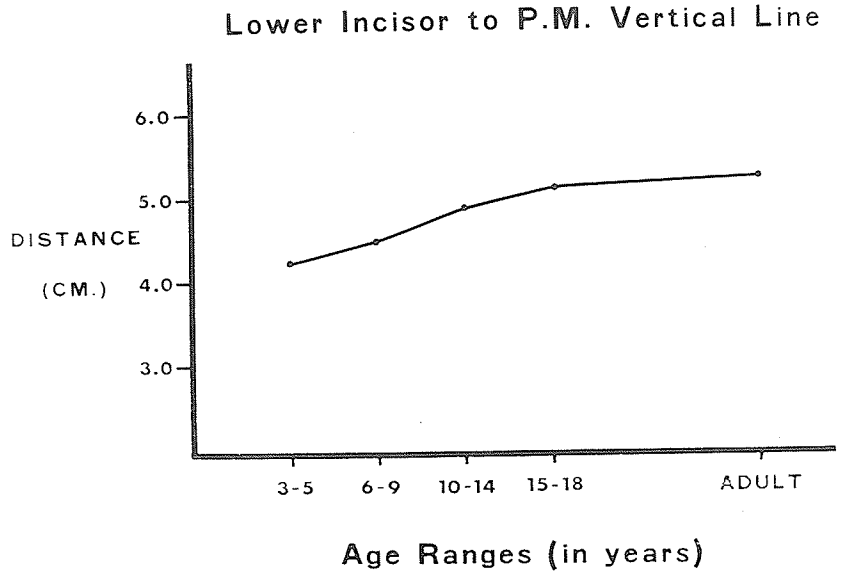


Figure 54. Main effect of age on the linear dimension Lower Incisor to the P.M. vertical line.

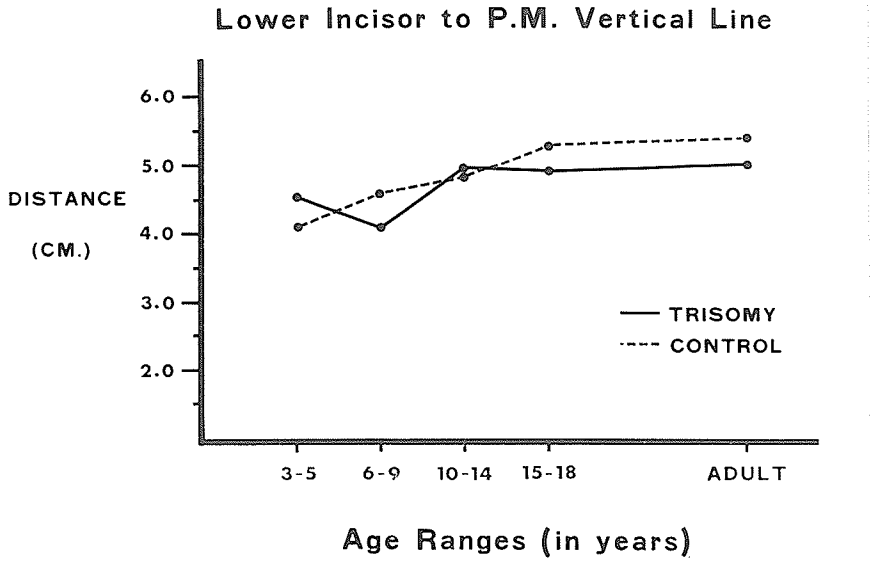


Figure 55. Effect of age on the linear dimension Lower Incisor to the P.M. vertical line for the trisomy 21 and control groups.

males, mean value 92.0 degrees.

x) Angle ANB

This angular measurement, described by lines joining point "A" to nasion and point "B" to nasion, demonstrated the antero-posterior relationship of the maxilla to the mandible. Differences between the trisomy and control groups were found to be significant at the 1% level of confidence the mean values being 1.3 degrees and 3.6 degrees, respectively.

Differences among the age ranges (Figure 56) were found significant at the 1% confidence level. A substantial decrease in this angle was found between the age ranges 6-9 and 10-14 years ($P < 0.01$).

The higher order interactions were not found to be statistically significant, a finding that corresponded to the findings of angles Ba-N-A and Ba-N-B. For each of these angular dimensions, the absence of significant 2nd and 3rd order interactions was attributed to the wide variation found in the two groups. The multiple range tests among the five age ranges indicated no significant changes in angle ANB for the control group, while the trisomy 21 group demonstrated a significant decrease ($P < 0.01$) between the 6-9 and 10-14 year age ranges. Significant differences, at the 1% level were found between the two groups from the 10-14 to the adult age ranges (Figure 57).

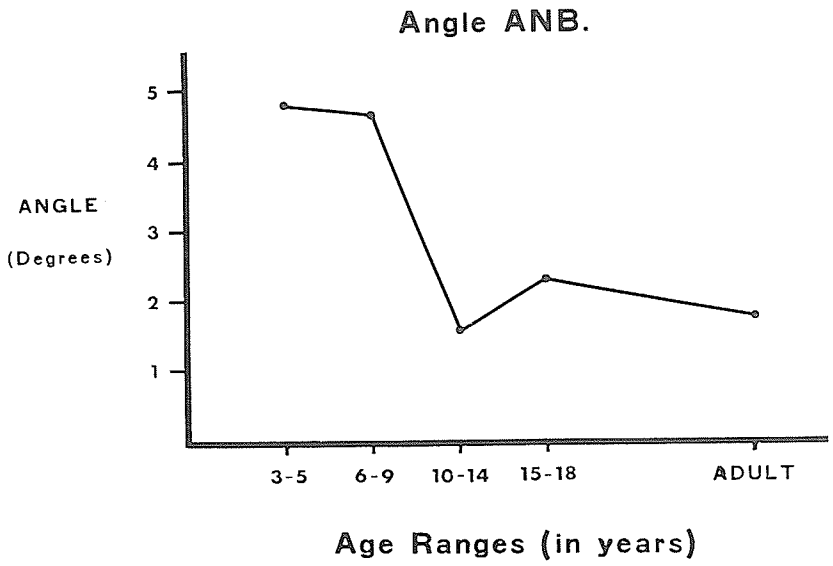


Figure 56. Main effects of age on the angular dimension A-N-B.

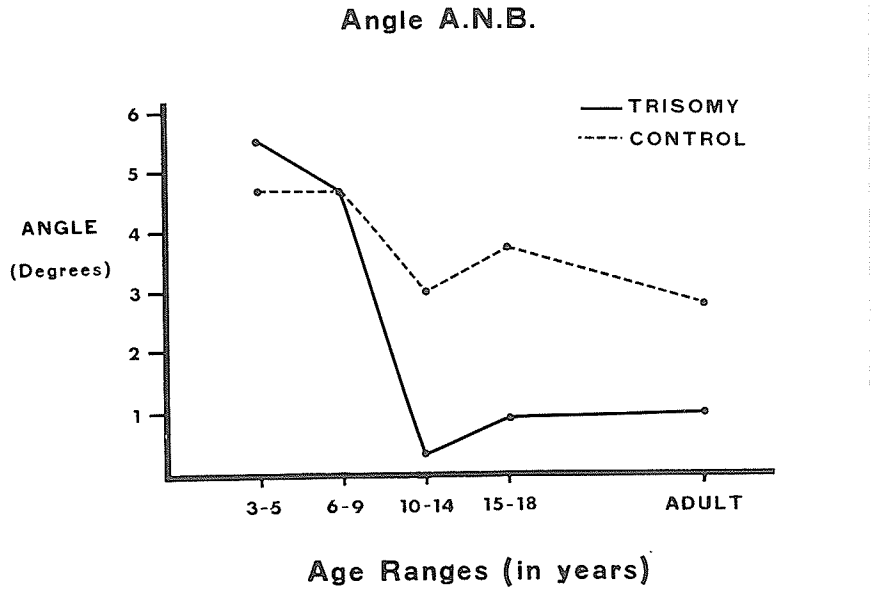


Figure 57. Effect of age on the angular dimension A-N-B for the trisomy 21 and control groups.

DISCUSSION

CHAPTER V

DISCUSSION

Past investigations of Down's syndrome, using roentgenographic cephalometry, have contributed much to our understanding of the mongoloid phenotype. These studies have been primarily concerned with morphological descriptions and the findings of most parameters have illustrated significant differences from accepted norms. Most of the linear measurements for these subjects have been found to be significantly smaller than control subjects indicating that the overall size of the craniofacial complex was smaller than that found in "normal" individuals from ages four years to adulthood. This fact, coupled with other findings, indicates that trisomy 21 subjects present a distinct phenotype.

Early investigations of lateral cephalometric radiographs, traditionally used the anterior cranial base as the plane of orientation for comparisons between trisomy and control groups. The studies were characterized by cross sectional samples grouped according to chronological age. The recent evidence of Nevile (1973) suggesting

different maturation rates in trisomy and control groups and the findings of Sommer and Eaton (1970), Alimchandani (1973), and Nevile (1973), among others, supporting the findings of endochondral growth disturbances in Down's syndrome have suggested a re-evaluation of past methods of cephalometric investigation and, as well, have questioned the significance of findings from previous studies.

I. INVESTIGATION OF CRANIOFACIAL REFERENCE LINES

Solow (1966) suggested that when two variables involved a common reference point, a correlation between them could be expected with the magnitude of this correlation being determined from the means and variabilities of the distances between the reference points. Similar correlations occurred between variables that did not involve a common reference point, but did involve a common reference structure. Thus, correlation between variables involving common reference points did not necessarily indicate the presence of biological coordination. It was suggested that angular variability between different reference lines followed a definite relationship based on the geometrical distribution of the landmarks defining these lines.

The results of the present investigation of eleven

craniofacial reference lines, support the findings of Solow (1966) and Henry and Cleall (1974) and confirm a negative association between the angular variables, standard deviation and variance, and the reference point distances of the angle arms. These results are also supported by the studies of Koski and Virolainen (1956). About 40% of the variation in angle variability was found to be due to variation in the arm length.

The investigation into the effect of the spatial arrangement of reference points defining an angle formed by two reference lines included the division of angles into those defined by 3 points, with a common reference point, and those defined by 4 points. Angular variability was not found to differ significantly between the two groups, although the inverse relationship between variation and angle arm length was slightly better defined in the 3 point angles. The results of this study would suggest that the spatial arrangement of points defining an angle is not one of the factors responsible for craniofacial associations.

Assessment of the biological stability of craniofacial planes must, therefore, attempt to factor out the extraneous effects of the geometrical distribution of the landmarks

defining the lines. Adjusted values must be computed for angular variability that provide an accurate indication of the biologic variability of the craniofacial planes.

Since the introduction of roentgenographic cephalometry in 1931, numerous investigators have attempted to establish the "ideal" plane of orientation for describing craniofacial form. As early as 1876, Schmidt had realized the importance of minimal biologic variation to a plane of orientation and, with this concept in mind, many different planes have been suggested for use in the study of growth and development.

The findings of this investigation suggest that several craniofacial reference lines demonstrate consistently low variability for both trisomy 21 and control groups. Three planes, closely associated with the cranial base, were included lending support to the suggestion that the cranial base represents a phylogenetically stable area of the skull (Ford, 1958; Scott, 1967; Moss, et al., 1969). The anterior cranial base (sella-nasion) has been used as a plane of superimposition in lateral cephalometric studies by many investigators (Brodie, 1941; Bjork, 1941; Riedel, 1952; Bjern, 1957), however, it has been criticized due to variation in

the relative positions of the reference points (Baume, 1957; Scott, 1956). This study does not dispute the variation that occurs in the spatial arrangement of points sella and nasion, but it does suggest that in spite of this variation, the anterior cranial base remains one of the most reliable planes of orientation. The basion-nasion plane, or basicranial axis, (Broadbent, 1937; Ricketts, 1952, 1957) and the ethmoidale-sella line (Koski, 1957; Wei, 1968) were also found to demonstrate low variability thus supporting the use of these planes for superimposition in cephalometric studies.

The Frankfort Horizontal, with anatomic porion as the posterior landmark (Blair, 1954; Craig, 1951; Williams, 1955) was also found to demonstrate minimal change. Significantly increased variation ($P < 0.01$) found in Frankfort Horizontal, with machine porion as the posterior landmark, demonstrated the necessity for standardizing the cephalometric technique and for complete patient cooperation when this non-anatomic landmark was used.

For each of the eleven planes being considered, variation was significantly greater in the trisomy 21 group than in the control group ($P < 0.01$). These findings can be

explained, if one considers the cranial base as a type of "hafting zone" between the neural and facial elements and in view of the recent evidence of disturbed endochondral bone growth in trisomy 21 individuals (Sommer and Eaton, 1970; Alimchandani, 1973; Nevile, 1973).

The present study would suggest that there is no reference line completely void of changes in shape and position during growth and this is indicative of the multidirectional connections within a holistic system (Vinkka, et al., 1975). For each component of the craniofacial skeleton the possibility exists that there may be several "governors" which may exercise their influence singly or jointly, depending on the prevailing circumstances. Koski (1957) found that cross sectional studies resulted in an apparent stability of the growth pattern, while individual growth patterns were quite flexible up to 17 years. Correlations between the various linear and angular dimensions within the craniofacial skeleton were generally low. Under these circumstances, the "ideal" plane of orientation or superimposition would be that which is intimately related to the area of interest and, at the same time, demonstrates low variability, regardless of the

parameters used to measure this variability.

The remaining seven reference lines exhibited a high degree of variation and much of this can be attributed to combinations of the following variables: difficulty in locating the defining landmarks, the geometric or spatial variation of the landmarks, and the biologic variation of the skeletal structures involved.

II. SKELETAL ANALYSIS

A. The Cranial Base

An overall shortening of the cranial base in Down's syndrome has been well documented in past investigations (Rezk, 1964; Kisling, 1966; Ghiz, 1969), and the results of the present study support these findings. Grouping of the trisomy 21 and control samples by skeletal rather than chronological age did not effectively alter the significant differences previously observed between the two groups and the anterior cranial base was found to be shortened more than the posterior cranial base. The length of the basicranial axis, or Ba-N plane, was also found to be smaller in the trisomy 21 group in spite of the more obtuse cranial base angle. This illustrates the significance of the linear differences of cranial base dimensions between the

the samples.

Elongation of the cranial base elements is dependent upon endochondral bone formation at the sphenoethmoidal and sphenoccipital synchondroses (Ford, 1958; Scott, 1958). Elongation of the anterior cranial base has been found to cease at about 7 years of age, when the sphenoethmoidal synchondrosis closes. Growth of the posterior cranial base has been found to continue into adolescence when the sphenoccipital synchondrosis closes at 13-16 years of age. Roche, et al. (1974) found elongation of all cranial base measurements to continue into adolescence. In the present study, a discrepancy in the length of the anterior cranial base was observed between the trisomy and control groups by the 3-5 year age range. Such findings would suggest that normal development and differentiation are being interfered with at an early age, possibly at the 8th to the 10th week of fetal life (Frostad, 1970). Subsequent development of this parameter occurred in a parallel manner to that of the control group with the initial discrepancy being maintained.

The horizontal linear measurements from nasion and sella to the vertical P.M. line also support these findings, with both parameters being significantly shorter ($P < 0.01$)

in the trisomy 21 group. This would suggest an initial growth disturbance, with subsequent development being "normal" or slightly retarded.

The posterior cranial base was found to have similar lengths for the trisomy 21 and control groups at ages 3-5 years. Subsequent increases in this parameter found in the control group, were delayed in the trisomy 21 group until ages 6-9 years, creating significant differences between the two samples. Such findings would suggest a disturbance in the endochondral bone formation of the sphenoccipital synchondrosis occurring in the trisomy 21 group at ages 6-9 years. As with the anterior cranial base, subsequent growth of the posterior cranial base occurred in a parallel manner for the two groups with the original discrepancy being maintained. Slight increases in this parameter for the control group during adulthood could be attributed to apposition at basion (Ford, 1958; Koski, 1960), repositioning of sella or latent apposition at the sphenoccipital synchondrosis (Roche, et al., 1974).

The basicranial axis (Ba-N plane) reflected the patterns of development found in the anterior and posterior portions of the cranial base. A similar discrepancy to

that found in the anterior cranial base at 3-5 years was also found in the Ba-N plane and this increased at ages 6-9 years coincident with previously mentioned growth disturbances in the posterior cranial base. The differences in the length of the Ba-N plane between the two groups was reduced somewhat with the clockwise flexure of the cranial base angle, but it remained significantly smaller than the control ($P < 0.01$).

The trisomy 21 group demonstrated a more obtuse cranial base angle in this study and this supports the findings of Rezk (1964), Kisling (1966), and Ghiz (1969). The analysis of variance indicated that the group X age interaction for this parameter was not signifianct, however, the extreme variation found in the two groups, represented by the standard deviations for each age range, could explain this phenomenon. Similarly, previous studies grouped the samples by chronological age and, with the developmental rates being different between the trisomy 21 and control groups (Nevile, 1973), this methodology would effectively produce more significant interactions for the various parameters. The present study, utilizing skeletal age groupings, would be expected to demonstrate less significant differences for

several of the parameters studied.

Although variation in the two groups was high for the cranial base angle, when mean values were used, a slight difference was present at 3-5 years ($P < 0.05$) and this increased with age. The explanation of the alternate directions of cranial base flexure between the two samples is uncertain. It has been suggested that it could be associated with a lowering of sella (Sassouni, et al., 1964; Kisling, 1966) or to a change in direction of growth at the sphenoccipital synchondrosis (Ghiz, 1969). The present study, suggesting a disturbance of fetal development of certain cranial base elements, could be interpreted to indicate differences in the configuration of the original cartilaginous anlage of the cranial base, possibly of genetic origin, which in turn produces changes in the direction of growth at the sphenoccipital synchondrosis, lowering of sella and flattening of the central and lateral parts of the cranial base (Kisling, 1966).

B. Nasomaxillary Complex

In contrast to earlier studies of Down's syndrome utilizing the anterior cranial base for superimposition (Sassouni, et al., 1964; Kisling, 1966; Ghiz, 1969), the

present investigation examined the relationship of the nasomaxillary complex to the basicranial axis (Ba-N plane).

The linear dimension representing maxillary length (point "A" to the vertical P.M. line) was found to be significantly shorter in the trisomy group at all ages ($P < 0.01$), thus supporting the findings of Benda (1956), Spitzer, et al., (1961), Rezk (1964), Kisling (1966), Ghiz (1969) and Frostad (1970). An initial size difference, with the trisomy 21 group consistently smaller in this parameter, was maintained with parallel growth trends in the two groups until the age range 10-14 years, at which time there was an early cessation of growth in the trisomy group. Nevile (1973) suggested that epiphyseal maturity was reached by the trisomy 21 sample approximately 2 years earlier than the control group, and this phenomenon was observed in the present study, in spite of grouping the sample by skeletal ages. This early stoppage of growth could be attributed to interferences with cartilaginous bone formation as evidenced by the shorter cranial base and reduced size of the nasal septal cartilage (Ghiz, 1969; Frostad, 1970; Alimchandani, 1973).

Parallel lowering of the palatal plane in control

populations, relative to the anterior cranial base, has been well documented by Broadbent (1937) and Brodie (1941, 1953). Kisling (1966) found the maxilla to be tipped downward anteriorly and he attributed this feature to abnormal tongue posture in Down's syndrome. This was supported by the findings of Queen (1975). Frostad (1970) observed a similar anterior tipping of the maxilla in the trisomy 21 males of his study. In the present investigation, the inclination of the maxilla, as measured to the basicranial axis, was found to be similar for the two groups until ages 10-14 years. Subsequently, the divergence of the palatal plane angle increased in the control group and decreased slightly in the trisomy 21 group. These changes in the spatial orientation of the maxilla relative to the Ba-N plane appear to be related to the direction and magnitude of cranial base flexure in each of the groups.

Although the midfacial area is underdeveloped in the trisomy 21 sample (Fink, et al., 1975), it is believed to be normally positioned relative to the anterior cranial base (Kisling, 1966; Ghiz, 1969; Frostad, 1970). In the present study, the antero-posterior position of the maxilla relative to the basicranial axis (angle Ba-N-A) was found

to be similar for the trisomy and control groups at all ages studied, with the exception of the 10-14 year age range. When the basicranial axis is used as the plane of orientation, the relative constancy of angle Ba-N-A in the two groups and the more obtuse cranial base angle in the trisomy 21 sample, effectively changes the spatial orientation of the maxilla to the rest of the craniofacial skeleton in the two groups. The result is a midfacial retrusion characteristic of the trisomy 21 phenotype. The within group variation in the cranial base angle for such a cross sectional study as well as the slightly divergent directions of cranial base flexure in the two samples appears to have eliminated the effect of the downward and forward translation of the maxilla in response to the nasal septal cartilage (Scott, 1954) and/or functional matrix (Moss, 1967).

Maxillary incisors were found to be more proclined relative to the Ba-N plane in the trisomy 21 group, which concurred with the findings of Frostad (1970) who suggested that increased proclination of maxillary incisors was related to openmouth posture and a protruding tongue. This etiology has also been supported by Queen (1975). Significant differences between the groups occurred at ages 6-9 years

($P < 0.01$), coinciding with the eruption of the permanent incisors. The linear measurement maxillary incisal tip to the vertical P.M. line was found to be larger in the control group at ages 6-9 and during adolescence and adulthood. These differences, significant at the 0.1 per cent confidence level, appear to be a reflection of greater maxillary length in the control group.

C. Mandible

In view of the recent evidence suggesting cartilaginous growth disturbances in Down's syndrome (Sommer and Eaton, 1970; Alimchandani, 1973, Nevile, 1973), the cause of the "apparent" mandibular prognathism in these individuals is uncertain. Previous investigations have reported the mandible in trisomy 21 samples to be smaller in size than normal (Spitzer, et al., 1955; Kisling, 1966; Ghiz, 1969; Fink, et al., 1975). Whether or not this prognathism is due to a severe midface deficiency (Brown, et al., 1961), to a mandibular prognathism relative to the cranial base (Kisling, 1966; Ghiz, 1969) or to a combination of the two is, as yet, unknown.

In the present study, linear dimensions representing the body of the mandible ("B" point, pogonion and gonion to

the vertical P.M. line) were found to be similar in the trisomy and control groups until ages 10-14 years. Continued incremental growth in the control sample created slight discrepancies ($P < 0.05$) at adult ages. These findings would suggest that mandibular growth in Down's syndrome closely parallels that of the control group until adolescence, with their respective antero-posterior dimensions being similar. Nevile (1973) demonstrated that skeletal maturity was reached at an earlier age in the trisomy sample and it appears that subsequent growth in the control group results in a larger mandible. These findings agree with several reports in the literature (Emmerich, 1969; Penrose, 1967) which showed no changes or an increase in mandibular size in Down's syndrome, but they disagree with the studies of Spitzer, et al. (1955), Thompson (1907), and Fink, et al. (1975). An explanation of this apparent contradiction could be the different maturation rates between the two samples (Nevile, 1973), with the present study, comparing groups by skeletal age, showing less significant or even non significant differences between the two groups for this parameter.

An explanation for disturbances in endochondral bone

formation in the cranial base and nasomaxillary complex and not in the mandible has been suggested in the investigations of Durkin (1968, 1971, 1973). He found striking similarities in the morphohistologic features of the embryonic cartilages of the rat, as well as, similar responses to changes in the relationships of their surrounding structures during development. In contrast, growth plate cartilages were found to be highly specialized and a unique type of cartilage. Sarnat (1968) further explained this "unique" quality of the mandibular condyle in that it has a fibrous covering under which the proliferating fibroblasts provide a reservoir of cells for the chondroblasts which, in turn, will become involved with endochondral bone formation. Petrovic and his associates (1968, 1973) have demonstrated conclusively that these fibroblasts approximating the fibrous covering of the condyle form a prechondroblastic layer that is responsive to extrinsic forces. The results of this study would suggest that the specialization of a prechondroblastic zone in the condyle provides this bone with a type of "auxillary growth potential" which, in turn, differentiates the effects of the genetic variation found in trisomy 21 on the endochondral growth of the condyle from that of the

cranial base and nasomaxillary complex. Fink, et al. (1975) suggested that it was unlikely that the overall differences in size of the Down's group subjects when compared to controls was due to environmental effects, however, the results of this study would, indeed, indicate that it is such environmental or extrinsic factors that play a significant role in the development of the mandible.

Nevile (1973) measured the "effective" mandibular length (condylion to gnathion) and found the trisomy 21 group consistently smaller at all age levels. This measurement, however, is dependent not only on the actual size of the mandible, but also on the shape of the mandible. Fink, et al. (1975) suggested that mandibular prognathism in trisomy 21 is related not to an increase in the midsagittal area of the mandible, but to its shape. Angular measurements used in this study to define mandibular shape would support this hypothesis; at ages 3-5 years, the gonial and mandibular plane angles in the trisomy 21 group were significantly smaller than in the control group ($P < 0.01$) and this contributed both to a greater "effective" mandibular length in the control group and to a prognathic skeletal pattern in the trisomy 21 group. Subsequent remodelling of the mandible in both groups

eliminated significant differences for these parameters, however, corresponding changes in the configuration of the respective cranial bases (previously mentioned) apparently contributed to the maintenance of the prognathic profile in the trisomy sample. Early cessation of growth in Down's syndrome (Nevile, 1973) resulted in increased differences in size between the two groups in older age ranges.

Kisling (1966) and Ghiz (1969) found the mandible to be prognathic relative to the anterior cranial base in the trisomy 21 sample. This study supports these findings with "B" point occupying a prognathic position relative to the Ba-N plane, when mean values were considered. When individual values for this parameter were considered, the extreme variation characteristic of the trisomy 21 group became obvious with smaller than normal mandibles as well as mandibles exhibiting extreme prognathism being evident. Such findings would appear to be related to the method of grouping the samples, by skeletal age, and coincide with the results of Frostad (1970) who suggested the variability could have a hereditary basis.

The spatial orientation of the mandible relative to the cranial base, as illustrated by angle Ba-N-B, did not

significantly change over the age ranges studied in the control group. It would appear that the downward and forward translation of the mandible in this cross sectional sample was offset by the slight reduction in the cranial base angle at 10-14 years and by the natural variation in this parameter. In the trisomy 21 group, a significant increase ($P < 0.05$) in the relative mandibular prognathism was observed with age and this can be attributed to a combination of downward and forward mandibular growth and a slight clockwise rotation of the posterior cranial base. In contrast to the naso-maxillary complex, the antero-posterior position of the mandible to the remainder of the craniofacial complex is not affected by the degree of cranial base flexure, as the sphenoid and occipital bones are midline structures while the occipital lobes are bilateral structures. Thus, when the Ba-N plane is used as the plane of orientation, the larger cranial base angle in the trisomy 21 group "effectively" produces a more prognathic mandible, while the opposite affect is observed in the control group. These phenomena, along with variations in the shape and size of the mandible, contribute to the prominent lower face in the Down's syndrome phenotype.

The relationship of the mandibular incisors to the apical bases is felt to be influenced by the soft tissues: the lips, cheeks, and tongue. The abnormally large, protruding tongue and the openmouth posture frequently observed in Down's syndrome is felt to result in the proclination of the mandibular incisors (Frostad, 1970; Queen, 1975). The findings of the present study would support these observations as the incisor inclination in the trisomy 21 group was significantly larger than in the control group until the 10-14 year age range ($P < 0.01$). A subsequent reduction in angulation during the adolescent and adult age ranges in the trisomy sample eliminated significant differences between the groups for this parameter. Bjork and Palling (1954) reported the decrease in angulation occurred shortly after the age of 12 years. Frostad (1970) suggested that uprighting of the mandibular incisors could be related to skeletal growth which eventually provided space to accommodate the large tongue. It also seems possible that involution of the tonsillar and adenoid tissue in the nasopharynx with age eliminated the necessity for the functional compensation of mouth breathing and, with it, the low, protruding tongue position which is believed to be

the etiologic factor responsible for lower incisor proclination (Queen, 1975).

The horizontal linear distance from the incisal tip of the mandibular incisor to the vertical P.M. line was greater in the trisomy 21 group at ages 3-5 years, however, progressive mandibular growth in the control group resulted in this sample demonstrating significantly greater values for this parameter at later ages ($P < 0.01$).

D. Interrelationships of Craniofacial Components

Recent lateral cephalometric radiographic studies of Down's syndrome have described a phenotype characterized by a hypoplastic midfacial area intimately related to an underdevelopment of the anterior cranial base (Kisling, 1966; Ghiz, 1969; Frostad, 1970). The effectiveness of this maxillary retrusion was felt to be magnified by an increased convexity of the frontal bone (Frostad, 1970) and an "apparent" mandibular prognathism (Kisling, 1966; Ghiz, 1969).

The present study supports the findings of these investigations and the use of the basicranial axis (Ba-N plane) as the plane of orientation assisted in clarifying the growth and developmental processes of the craniofacial complex, thus, providing information on the influence of genetic variation on craniofacial morphology and growth.

As was discussed earlier, shortening of the anterior and posterior elements of the cranial base is believed to be the result of disturbances in endochondral bone formation in the sphenoethmoidal and sphenoccipital synchondroses. The timing and magnitude of these disturbances appears to be variable, with earlier, more severe shortening of the anterior cranial base and later, less severe shortening of the posterior cranial base. This is supported by the knowledge that the sphenoethmoidal synchondrosis closes around 7 years of age (Decoster, 1952; Ford, 1958; Scott, 1954, 1958; Bjork, 1955), while the sphenoccipital synchondrosis closes around 13-16 years of age, or adolescence (Sassouni, 1958).

Sassouni (1958) suggested that angular and linear changes in the posterior cranial base could alter the relationship of the nasomaxillary complex and mandible, relative to one another, as well as to the rest of the craniofacial complex. The larger cranial base angle in the trisomy 21 group and the opposite directions of rotation of the clivus relative to the anterior cranial base appear to be factors partly responsible for the different phenotypes of the trisomy 21 and control samples.

The antero-posterior relationsthip of the maxilla to the cranial base, represented by angle Ba-N-A in this study, is similar for the trisomy 21 and control groups. When the basicranial axis is used as the plane of orientation, the more obtuse cranial base angle, the slight clockwise rotation of the clivus, and the early cessation of naso-maxillary growth (Frostad, 1970; Nevile, 1973) all contribute to a midface retrusion in the trisomy sample. The contrasting smaller cranial base angle, counterclockwise rotation of the posterior cranial base and continued downward and forward translation of the nasomaxillary complex contribute to a normal midfacial skeletal profile in the control sample. Thus, it is suggested that although the relationship of the nasomaxillary complex to the cranial base is similar for the two groups, orientation on the basicranial axis effectively changes the relationship of this midfacial area to the rest of the craniofacial skeleton. This is shown diagrammatically in Figure 58.

The various linear dimensions used in this study suggested that the absolute size of the mandible was similar for the two groups until ages 10-14 years. Direct linear measurements, from the cephalometric points pogonion, "B" point, gonion and articulare to the vertical P.M. line,

were not found to be statistically significant when comparing trisomy and control samples. On the other hand, variations in the shape of the mandible at early ages, as measured with gonial and mandibular plane angles, produced a prognathic skeletal profile for the trisomy 21 group.

Positional changes in the mandible coincident with cranial base flexure at 10-14 years, resulted in significant differences between the trisomy 21 and control groups and thus, assisted in explaining their respective phenotype differences.

This study would suggest that the "apparent" mandibular prognathism found in Down's syndrome is the result of a combination of developmental characteristics. The underdevelopment of the cranial base and nasomaxillary complex has been illustrated in many studies. Increased convexity of the frontal bone (Frostad, 1970) has the effect of accentuating this midface deficiency. In contrast to many studies (Spitzer, et al., 1955; Sassouni, et al., 1964; Kisling, 1966; Ghiz, 1969; Fink, et al., 1975), the absolute size of the mandible was found to be similar for the two groups until adolescence; this would be more

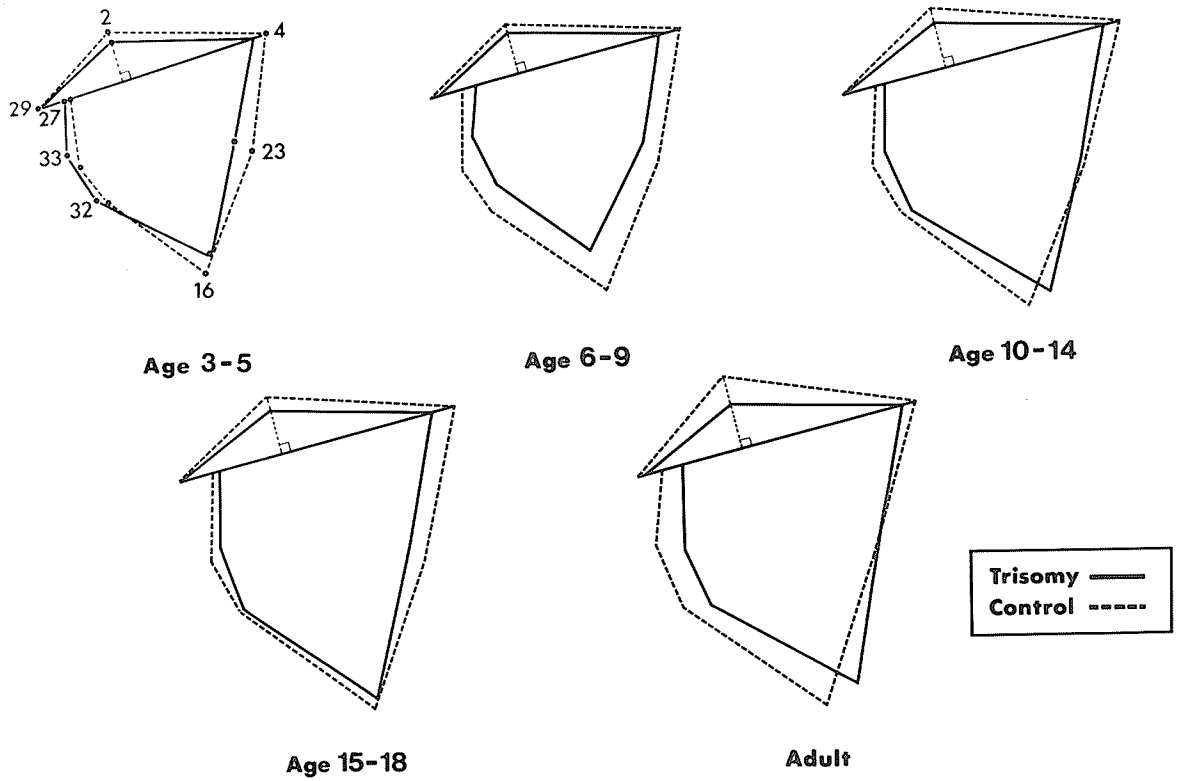


Figure 58. Craniofacial development based on the means of cephalometric measurements for the trisomy 21 and control groups, at each of the five age ranges studied. The plane of orientation is the basicranial axis (Ba-N line) with origin at the point of intersection of a perpendicular from sella to the Ba-N line (point 61) and with direction to nasion (point 4).

in agreement with Frostad (1970) and could be a result of grouping the two samples by skeletal age rather than chronological age. It appears that the shape of the mandible and of the cranial base (cranial base angle), coupled with a midface retrusion and increased convexity of the frontal bone, are among the more relevant developmental characteristics that define the trisomy 21 phenotype. This is shown diagrammatically for each of the 5 age ranges studied in Figure 58.

Functional compensations assisting respiration, such as extended head and neck posture (Queen, 1975) could also be significant in creating the "apparent" mandibular prognathism.

SUMMARY AND CONCLUSIONS

CHAPTER VI

SUMMARY AND CONCLUSIONS

This cross sectional lateral cephalometric study was undertaken to gain a better understanding of the phenotypic differences between a group of individuals confirmed by cytogenetic analysis as having a trisomy of chromosome number 21 and a control sample. An investigation into the variability of several craniofacial reference lines was carried out to determine the most suitable plane of orientation for a comparative study of the two groups. This was necessitated by recent evidence supporting endochondral growth disturbances in Down's syndrome which questioned the suitability of the anterior cranial base as a plane of orientation.

A cephalometric analysis, consisting of angular and linear measurements, was then used to evaluate and compare the trisomy 21 and control groups to determine if a distinct phenotype existed in the craniofacial area. The effect of grouping the two samples by skeletal age rather than chronological age, on the significant differences previously reported for various parameters, was investigated.

The sample consisted of 117 trisomy 21 individuals and 100 control individuals, both groups being divided into

five age ranges. The evaluation of the significant differences between the trisomy 21 sample and the control sample was determined by a multivariant factorial analysis. The findings were statistically evaluated and led to the following conclusions:

1. The angular variability between craniofacial reference lines was found to be significantly greater in the trisomy 21 than in the control groups.
2. No craniofacial reference lines were completely void of changes in shape and position during growth, and the most suitable plane of orientation is one which is intimately related to the area under investigation and which demonstrates low variability.
3. Angular variability between craniofacial reference lines was found to have a negative association between the standard deviation and variance of an angle and the mean of the distances between the reference points for each of its arms. Other factors affecting variability were found to be the reproducibility

of cephalometric landmarks and the biological variation of the skeletal structures involved. The spatial orientation of points defining an angle did not significantly affect angular variation.

4. In spite of recent reports of endochondral growth disturbances in trisomy 21 individuals, the cranial base was shown to be one of the most stable and dependable areas of the cranio-facial skeleton in both the trisomy 21 and control samples. Three reference lines defined by cranial base landmarks demonstrated minimal angular variation for the two groups: the anterior cranial base (sella-nasion), the basicranial axis (basion-nasion), and the ethmoidale-sella line.

5. The Frankfort Horizontal also demonstrated low variability for both the trisomy 21 and control groups, when anatomic porion was used as the posterior landmark. The utilization of machine porion resulted in significant increases in the variation of this line.

6. In the cephalometric analysis, grouping of the trisomy 21 and control samples by skeletal age rather than chronological age did not eliminate significant differences previously mentioned for most parameters, however, the significance of many of the higher order interactions of group, age and sex were reduced or eliminated altogether. Whether this diminished significance is the result of skeletal age grouping, the natural variability within the groups, or to a combination of the two, is undetermined.
7. Linear measurements involving the cranial base and nasomaxillary complex of the trisomy 21 sample were significantly smaller than the control sample, indicating an underdevelopment of the midfacial region from 3 years to adulthood. When compared to the basicranial axis, the maxilla of the trisomy 21 group was found to be in a normal antero-posterior position.
8. The anterior cranial base of the trisomy 21 group was proportionately shorter in relation to the

posterior cranial base, suggesting a greater retardation of growth at the sphenoethmoidal than sphenoccipital synchondroses.

9. Linear measurements of the mandible were similar for the trisomy 21 and control groups, until the 10-14 year age range, suggesting similar growth increments for the two groups. Subsequent mandibular growth in the control sample resulted in a larger absolute size for the mandible of this group.

10. The shape of the mandible at ages 3-5 years in the trisomy 21 group, as well as an underdevelopment of the midfacial region, are believed to be responsible for the prognathic skeletal pattern in young children with Down's syndrome. Postural implications related to mouth breathing also contribute to the trisomy 21 phenotype.

11. When the basicranial axis is used as the plane of orientation, the direction and magnitude of rotation of the cranial base angle are believed to be involved with the phenotypic appearance of trisomy 21 individuals.

12. The "apparent" mandibular prognathism characteristic of Down's syndrome appears to be the result of a combination of development characteristics, including the underdevelopment of the cranial base and nasomaxillary complex, increased convexity of the frontal bone, and the shape and size of the mandible and cranial base.
13. The maxillary incisors were slightly more proclined in the trisomy 21 group relative to the basicranial axis and the mandibular incisors were more proclined relative to the mandibular plane.

BIBLIOGRAPHY

BIBLIOGRAPHY

Acheson, R.M.: A method of assessing skeletal maturity from radiographs. J. Anat. 88:498-508, 1954a.

Acheson, R.M.: The Oxford Method of assessing skeletal maturity. Clinical Orthopedics. 10:19-39, 1954b.

Acheson, R.M.: Maturation of the Skeleton in Human Development. F. Falkner, Ed., Saunders, Philadelphia, 1966.

Alimchandani, S.: Craniofacial morphology in trisomy 21 (Down's Syndrome) individuals. A cephalometric cross section study. Master's Thesis, University of Manitoba, 1973.

Baume, L.J. and Derichweiler, H.: Is the condylar growth centre responsive to orthodontic therapy? An experimental study in Macaca mulatta. Oral Surg. 14:347-362, 1961.

Baumrind, S. and Frantz, R.C.: The reliability of head film measurements. Am. J. Orthod. 60:111-127, 1971.

Beltrami, G., Autissier, J. and Beauvieux, H.: The vertico-frontal plane of the head. Arch. Orthod. 1:58-65, 1951.

Benda, C.E.: Growth disorder of the skull in mongolism. Am. J. Path. 16:71-86, 1940.

Benda, C.E.: Mongolism. A comprehensive review. Arch. Pediatr. 73:391-407, 1956.

Benda, C.E.: The Child With Mongolism. New York: Grune and Stratton. 1960.

Benda, C.E.: Down's Syndrome. Mongolism and its Management. New York: Grune and Stratton, 1969.

Bergersen, E.O.: Comparative study of cephalometric superimposition. Angle Orthod. 31:216-229, 1961.

Bjern, R.: Comparison between the Frankfort Horizontal and the sella turcica-nasion as reference planes in cephalometric analysis. Acta Odontol. Scand. 15:1-12, 1957.

Bjork, A.: The Face in Profile. Svensk Tandlakare Tidskrift. 40: No. 56, 1947.

Bjork, A.: The cranial base development. Am. J. Orthod. 41:198-225, 1955.

Bjork, A.: Variation in the growth pattern of the human mandible - longitudinal radiographic study by the implant method. J. Dent. Res. 42:400-411, 1963.

Blair, E.S.: A cephalometric roentgenographic appraisal of the skeletal morphology of I, II (1), and II (2) (Angle) malocclusions. Angle Orthod. 24(2):106-119, 1954.

Book, J.A., Fraccaro, M., and Lindstrom, J.: Cytogenetical observations in mongolism. Acta Paediatr., (Uppsala) 48:453-468, 1959.

Breitner, C.: Bone changes resulting from experimental orthodontic treatment. Am. J. Orthod. and Oral Surg. 26:521-546. Disc. 54 -546. 1940.

Broadbent, B.H.: A new x-ray technique and its application to orthodontics. Angle Orthod. 1:45-66, 1931.

Broadbent, B.H.: The face of the growing child. Angle Orthod. 7:209-233, 1937.

Brodie, A.G.: On the growth pattern of the human head from the third month to the eighth year of life. Am. J. Anat. 68:209-262, 1941.

Brodie, A.G.: Facial pattern, a theme of variation. Angle Orthod. 14:75-87, 1946.

Brodie, A.G.: Late growth changes in the human face. Angle Orthod. 23:146-157, 1953.

Brousseau, K., and Brainerd, H.G.: Mongolism: A Study of the Physical and Mental Characteristics of Mongolian Imbeciles. London: Bailliere, Tindall, and Cox. 1928.

Brown, R.H., and Cunningham, W.M.: Some dental manifestations of mongolism. Oral Surg. 14:664-676, 1961.

Carter, C.D.: A life-table for mongols. J. Ment. Defic. Res. 2:64-67, 1958.

Charlier, J.P. and Petrovic, A.: Lack of independent growth potential of rat mandibular condylar cartilage, as revealed in organ culture. Abst. 18th Annual Meeting of the Tissue Culture Association, Philadelphia, U.S.A. n° 83, 1967.

Charlier, J.P., Petrovic, A., et Herrmann, J.: Déterminisme de la croissance mandibulaire: effets de l'hyperpropulsion et de l'hormone somatotrope sur la croissance condylienne de jeune rat. Orthod. Fr. 39:567-579, 1968.

Charlier, J.P., Petrovic, A., et Herrmann-Stutzmann, J.: Effects of mandibular hyperpropulsion on the prechondroblastic zone of young rat condyle. Am. J. Orthod. 55:71-74, 1969a.

Clarke, C.M., Edwards, J.H., and Smallpeice, V.: 21 trisomy/normal mosaicism in an intelligent child with mongoloid characters. Lancet. 1:1028-1030, 1961.

Cleall, J.F.: Deglutition: a study of form and function. Am. J. Orthod. 51:566-594, 1965.

Cleall, J.F., Alexander, W.J., and McIntyre, H.M.: Head posture and its relationship to deglutition. Angle Orthod. 36(4):335-350, 1966.

Cleall, J.F., Wilson, G.W., and Garnett, D.S.: Normal craniofacial skeletal growth of the rat. Am. J. Phys. Anthropol. 29:225-242, 1968.

Cleall, J.F. and Chebib, F.S.: Coordinate analysis as applied to orthodontic studies. Angle Orthod. 41:214-218, 1971.

Clift, M.W.: Roentgenological findings in mongolism. Am. J. Roentgenol. 9:420-422, 1922.

Collman, R.D. and Stoller, A.: A survey of mongoloid births in Victoria, Australia, Am. J. Public Health. 52:813, 1962.

Collman, R.D. and Stoller, A.: A life-table for mongols in Victoria, Australia. J. Ment. Defic. Res. 7:53-58, 1963.

Craig, C.E.: The skeletal patterns characteristic of Class I and Class II division I malocclusions in Norma lateralis. Angle Orthod. 21(1):44-56, 1951.

Craven, A.H.: Growth in width of the head of the Macaca rhesus monkey as revealed in vital staining. Am. J. Orthod. 42(5):341-362, 1956.

DeCoster, L.: A new line of reference for the study of lateral facial teleradiographs. Am. J. Orthod. 39:304-306 (Abstract), 1951.

DeCoster, L.: The familial line studied by a new line of reference. Trans. Eur. Orthod. Soc.: 50-56, 1952.

DeCoster, L.: L'Orthopedie dento-faciale, facteur de morphogenese. Rev. Stomatol. 50(1)15-38, 1953.

Delattre, A. and Fenart, R.: Le development du crâne du gorille et due chimpanze comparé au development du crâne humain. Bull. et men. de la Soc. d'Anth. de Paris. 6(4/5):159-173, 1955.

Down, J. Langdon: Observations on ethnic classification of idiots. London Hospital Reports, III:259-262, 1866.

Durkin, J.F.: A study of the mandibular condylar cartilage: a comparison of circulatory and calcification changes induced in the mandibular condyle and tibial epiphyseal cartilage by the onset and healing of scurvy. M.S. degree thesis, University of Rochester, 1968.

Durkin, J.F., Heeley, J.D., and Irving, J.T.: Changes in the mandibular condylar and tibial articular cartilages during maturation. I.A.D.R. 49th General Meeting, Abstract 516, 1971.

Durkin, J.F.: Secondary cartilage: a misnomer? Am. J. Orthod. 62:15-41, 1972.

Elgoyhen, J.C., Riolo, M.G., Graber, L.W., et al.: Craniofacial growth in juvenile Macaca mulatta: a cephalometric study. Am. J. Phys. Anthropol. 36:369-376, 1972.

Elmajian, K.E.: A serial study of facial growth as related to cranial base morphology. Master's Thesis. University of Washington, 1959.

Engler, M.: Mongolism. John Wright & Sons, Ltd., Bristol. 1949.

Enlow, D.H.: The Human Face. New York: Hoeber Med. Div. of Harper and Row. 1968.

Enlow, D.H. et al.: A procedure for the analysis of intrinsic facial form and growth. Am. J. Orthod. 56:6-24, 1969.

Enlow, D.H. and McNamara, J.A.: The neurocranial basis for facial form and pattern. Angle Orthod. 43:256-270, 1973.

Esquirol, J.E.D.: Des Maladies Mentales Considerees sous les Rapports Medical, Hygienique, et Medico-Legal (Mental Disorders Considered from the Medical, Hygienic, and Medico-Legal Points of View), Paris, 1838.

Feuer, D.D.: The value of the P.M. reference line for estimating natural head position. Angle Orthod. 44:189-193, 1974.

Fink, G.B., Madaus, W.K., and Walker, G.F.: A quantitative study of the face in Down's syndrome. Am. J. Orthod. 67:540-553, 1975.

Ford, C.E.; and Hamerton, J.L.: The chromosomes of man. Nature, Lond. 168:1020-1023, 1956.

Ford, C.E., Jones, K.W., Miller, O.J., Mittwock, U., Penrose, L.S., Ridler, M., Shapiro, A.: The chromosomes in a patient showing both mongolism and Klinefelter's syndrome. Lancet. 1:709-710, 1959.

Ford, C.E.: Mosaics and Chimaeras. Br. Med. Bull. 25:104-109, 1969.

Ford, E.H.R.: Growth of the human cranial base. Am. J. Orthod. 44:498-509, 1958.

Fraccaro, M., Kaiser, K., and Lindsten, J.: Chromosomal abnormalities in father and mongol child. Lancet. 1:724-727, 1960.

Fraser, J. and Mitchell, A.: Kalmuck idiocy: report of a case with autopsy, with notes on 62 cases by A. Mitchell. J. Ment. Sci. 22:169-179, 1876.

Frostad, W.A.: Cephalometric analysis of the craniofacial area in trisomy 21 syndrome (Down's Syndrome). Master's Thesis, University of Manitoba, 1969.

Frostad, W.A., Cleall, J.F., and Melosky, L.C.: Craniofacial complex in the trisomy 21 syndrome (Down's Syndrome). Arch. Oral Biol. 16:707-722, 1971.

Garn, S.M. and Rohmann, C.G.: Communalities of the ossification centres of the hand and wrist. Am. J. Phys. Anthropol. N.S. 17:319-323, 1959.

Garn, S.M. and McCreery, L.D.: Variability of post-natal ossification timing and evidence for a dosage effect. Am. J. Phys. Anthropol. 32:139-144, 1970.

Garrod, A.E.: Cases illustrating the association of congenital heart disease with mongolian form of idiocy. Trans. Clin. Soc. Lond. 31:316, 1899.

Gasson, Mlle. N. and Petrovic, A.: Mécanismes et regulation de la croissance antéro-postérieure du maxillaire supérieur. Recherches expérimentales, chez le jeune rat, sur le rôle de l'hormone somatotrope et du cartilage de la cloison nasale. Orthod. Fr. 43:255-270, 1972.

Ghiz, F.A.: A cephalometric analysis of the trisomy 21 syndrome (Down's Syndrome). Master's Thesis, University of Manitoba, 1968.

Green, L.J.: Interrelationships among height, weight and chronological, dental and skeletal ages. Angle Orthod. 31:189-193, 1961.

Greulich, W.W. and Pyle, S.I.: Radiographic Atlas of Skeletal Development of the Hand and Wrist, Stanford, Cal., Stanford Univ. Press, 1950.

Gustavson, K.H.: Down's Syndrome: A Clinical and Cytogenetical Investigation. Uppsala: Almquist and Wiksell. 1964.

Hall, B.: Mongolism in Newborns. Acta Pediatr. Suppl. 154:1-95, 1964.

Hamerton, J.L., Giannelli, F., and Polani, P.E.: Cytogenetics of Down's Syndrome (mongolism). I Data on a consecutive series of patients referred for genetic councilling and diagnosis. Cytogenetics Basel. 4:171-185, 1965.

Hamerton, J.L.: Human Cytogenetics. Vol. 2. New York: Academic Press, 1971.

Haupl, K. and Psansky, R.: Experimental investigation of the changes in the mandibular joint caused by applying functional orthopedics. Prog. Deutsche Zahn-Mund-und-Kufer-Leilkunde. 6:439, 1939.

Hefke, H.W.: Roentgenologic study of anomalies of the hands in 100 cases of mongolism. Am. J. Dis. Child. 60:1319-1323, 1940.

Henry, H.L. and Cleall, J.F.: Radiographic cephalometric method of assessment of craniofacial growth in monkeys. J. Dent. Res. 53:369-374, 1974.

Higley, L.B.: Cephalometric standards for children 4 to 8 years of age. Am. J. Orthod. 40:51-59, 1954.

Himwich, H.E. and Fazekas, J.F.: Cerebral metabolism in mongolian idiocy and phenylpyruvic oligophrenia. Arch. Neurol Psychiat. 44:1213-1218, 1940.

His, W. and Rütimeyer, L.: Crania Helvetica. Basel U Denf. 1864.

Hofrath, B.: "Die Beteutung der Rontgenfernund Abstandsaufnahme fur die Diagnostik der Kieferanomalien". Portschritte der Orthontik. 1:232; 1931.

Hsu, T.C.: Mammalian chromosomes in vitro. The Karyotype of Man. J. Hered. 43:167-172, 1952.

Jacobs, P.A., Baikie, A.G., Court Brown, W.M., and Strong, J.A.: The somatic chromosomes in mongolism. Lancet. 1:710, 1959.

Jacobs, P.A.: Chromosome Abnormalities and Population Studies, F. Clarke Fraser and V.A. Mckusick (Eds.), Congenital Malformation, Proceedings of the Third International Conference, The Hague, 7-13 September, pp. 284-290. Amsterdam, New York, Excerpta Medica. 1970.

Jarabak, J.R. and Thompson, J.R.: Growth of the mandible of the rat following bilateral resection of the mandibular condyles. Am. J. Orthod. 39(1):58 (Abstract), 1953.

Jenkins, R.L.: Etiology of mongolism. Am. J. Dis. Child. 45:506-519, 1933.

Jensen, G.M.: A study of the dentoalveolar morphology and developmental changes in Down's Syndrome (Trisomy 21). Master's Thesis, University of Manitoba, 1972.

Jones. R.: The mouth in backward children of the mongolian type. J. Ment. Sci. 36:187-190, 1890.

Kanar, H.L.: The morphology of the mandible in Down's Syndrome. Master's Thesis, University of Michigan, 1971.

Keith, A. and Campion, G.G.: A contribution to the mechanism of growth of the human face. Int. J. Orthod. 8:607-633, 1922.

Kisling, E.: Cranial Morphology in Down's Syndrome. Copenhagen: Munksgaard, 1966.

Klaauw, C.J. van der: Size and position of the functional components of the skull. Arch. Neerl. Zool. 9:1-559, 1948-1952.

Koski, K.: Analysis of profile roentgenograms by means of a new "circle" method. DR. pp: 704-713, 1953.

Koski, K. et al.: Relation of His' Line to the nasal floor. Dent. Rec. 75:45-50, 1955.

Koski, K. et al.: On the relationship between roentgenographic cephalometric lines of reference. Acta Odontol. Scand. 14:23-32, 1956.

Koski, K.: Growth changes in the relationship between some basicranial planes and the palatal plane. Suomen Hammaslääk Toim. 57:15-26, 1961.

Koski, K. et al.: Growth potential of subcutaneously transplanted cranial base synchondroses of the rat. Acta Odontol. Scand. 27:343-357, 1969.

Koski, N. et al.: Growth potential of intracerebrally transplanted cranial base synchondroses in the rat. Arch. Oral Biol. 15:1107-1108, 1970.

Koski, K.: Variability of the craniofacial skeleton. Am. J. Orthod. 64:188-196, 1973.

Krogman, W.M.: The problem of timing in facial growth, with special reference to the period of the changing dentition. Am. J. Orthod. 37:253-276, 1951.

Krogman, W.M. and Sassouni, V.: Syllabus in Roentgenographic Cephalometry. College Offset, Philadelphia, 1957.

Lande, M.J.: Growth behavior of human profile as revealed by serial cephalometric roentgenology. Angle Orthod. 22(2):78-90, 1952.

Lejeune, J.: The 21 trisomy - current stage of chromosomal research. Medical Genetics. Vol. 3. Ed. by A.G. Steinberg and A.G. Bearn. New York: Grune and Stratton. 1964.

Lejeune, J., Gauthier, M., Turpin, R.: Etudes des chromosomes somatiques de neuf enfants mongoliene. C.R. Acad. Sci. (Paris), 248-1721-1722, 1959b, quoted in: Penrose and Smith, 1966; Hamerton, 1971.

Levinson, A., Friedman, A., and Stamps, F.: Variability of mongolism. Pediatrics. 16:43-54, 1955.

Lilienfeld, A.M., and Benesch, C.H.: Epidemiology of Mongolism, Baltimore, John Hopkins Press, 1969.

Lindegard, B.: Intra-racial variations in the profile pattern of the human facial skeleton. Acta Odontol. Scand. 9(3,4):215-246, 1951.

Luke, M.J., Mehrizi, A., Folger, G.M. Jr., Rowe, R.D.: Chronic nasopharyngeal obstruction as a cause of cardiomegily cor pulmonale and pulmonary edema. Pediatrics. 37:762, 1966.

Luscher, E.: Die Alkahreserve des Blutes ber behinderter nasenatmung und bie Tonsillenhyperplasie. Acta Otolaryngol. 14:90, 1930.

Mackay, D.H.: Skeletal maturation in the hand: a study of development in East African children. Trans. R. Soc. Trop. Med. Hyg. 46:135-150, 1952.

Massler, M. et al.: The growth pattern of the cranium. Anat. Rec. 79(3):92, 1941.

Massler, M. et al.: Post-natal growth pattern of the facial skeleton as measured by vital injections of alizarine red. J. Dent. Res. 23(3):Abst., 1944.

Massumi, R.A.; Sarin, R.K.; Pooya, M. et al.: Tonsillar hypertrophy, airway obstruction, alveolar hypo-ventilation and cor pulmonale in twin brothers. Dis. Chest. 55:110, 1969.

McDowell, R.M.: The use of lateral head radiographs for evaluating orthodontic results as distinguished from growth changes. Am. J. Orthod. and Oral Surg. 27:59-74, 1941.

Meikle, M.C.: The role of the condyle in the post-natal growth of the mandible. Am. J. Orthod. 64:50-62 1973a.

Meikle, M.C.: In vivo transplantation of the mandibular joint of the rat; an autoradiographic investigation into cellular changes at the condyle. Arch. Oral Biol. 18:1011-1020, 1973b.

Menashe, V.D.; Farrehi, C.; Miller, M.: Hypoventilation and cor pulmonale due to chronic upper airway obstruction. J. Pediatr. 67:198, 1965.

Mikkelsen, M.: Down's Syndrome; Current stage of cytogenetic research. Humangenetik. 12:1-28, 1971.

Midtgärd, J.; Bjork, G.; Sten-Linder-Aronson: Reproducibility of cephalometric landmarks and errors of measurements of cephalometric cranial distances. Angle Orthod. 44:56-61, 1974.

Moore, A.W.: A method of studying the cranio-facial growth sites in the Macaque Monkey as these are exhibited by vital staining with alizarine red. J. Dent. Res. 25:157, 1946.

Moore, A.W.: Head growth of the Macaque monkey as revealed by vital staining, embedding and undecalcified sectioning. Am. J. Orthod. 35(9):654-671, 1949.

Moorrees, F.C.: Normal variation and its bearing on the use of the cephalometric radiographs in orthodontic diagnosis. Am. J. Orthod. 39(12):942-950, 1953.

Moss, M.L. and Greenberg, S.N.: Postnatal growth of the human skull base. Angle Orthod. 25:77-84, 1955.

Moss, M.L.: The functional matrix. In: Kraus, B.S. and Riedel, R. (Ed.), Vistas in Orthodontics. Philadelphia: Lea and Febiger, 1962.

Moss, M.L.: Ontogenic aspects of craniofacial growth. In: Moyers, R.E., and Krogman, W.H. (Ed.), Craniofacial Growth in Man. New York: Pergamon Press, 1967.

Moss, M.L. and Salentijn, L.: The primary role of functional matrices in facial growth. Am. J. Orthod. 55:566-577, 1969.

Moss, M.L., Salentijn, L. and Ostreicher, H.: The logarithmic properties of active and passive mandibular growth. Am. J. Orthod. 66:645-664, 1974.

Nelson, T.O.: Analysis of facial growth utilizing elements of the cranial base as registration. Am. J. Orthod. 46:379, 1960.

Nevile, M.D.: Dental and skeletal maturation in trisomy 21 (Down's Syndrome). Master's Thesis, University of Manitoba, 1973.

Noonan, J.A.: Reversible cor pulmonale due to hypertrophied tonsils and adenoids; studies in two cases. Circulation 32. 1965.

Oliver, C.A.: A clinical study of the ocular symptoms found in the so-called mongolian type of idiocy. Trans. Am. Ophthalmol. Soc. 6:140-148, 1891.

Oster, J. Mongolism: A Clinicogenealogical Investigation Comprising 526 Mongols Living on Seeland and Neighboring Islands in Denmark. Copenhagen: Danish Science Press Ltd., 1953.

Oster, J.: The causes of mongolism. Dan. Med. Bull. 3:158-164, 1956.

Penrose, L.S.: The relative effects of paternal and maternal age in mongolism. J. Genet. 27:219-224, 1933a.

Penrose, L.S.: Observations on the aetiology of mongolism. Lancet. 2:502-509, 1954.

Penrose, L.S. Mongolism. Br. Med. Bull. 17:184-189, 1961.

Penrose, L.S.: Biology of Mental Defect. London. Sidgwick and Jackson, 1963.

Penrose, L.S. and Smith G.F.: Down's Anomaly. London: J. and A. Churchill Ltd., 1966.

Petrovic, A.: Recherches sur les mécanisms histophysiologiques de la croissance osseuse cranio-faciale. Annee Biol. 9:303-311, 1970.

Petrovic A.: Mechanisms and regulation of mandibular condylar growth. Acta. Morphol. Neerl. Scand. 10:25-34, 1972.

Petrovic, A. and Stutzmann, J.: Le muscle ptérygoidien externe et la croissance du condyle mandibulaire. Recherches expérimentales chez le jeune rat. Orthod. Fr. 43:271-285, 1972.

Petrovic, A.; Oudet, M.C.; and Gasson, Mlle. N.: Effets des appareils de propulsion de la rétropulsion mandibulaire sur le nombre des sarcomères en série du muscle ptérygoidien externe et sur la croissance du cartilage condylien du jeune rat. Orthod. Fr. 44:191-210, 1973.

Polani, P.E., Briggs, J.H., Ford, C.E., Clarke, C.M., and Berg, J.M.: A mongol girl with 46 chromosomes. Lancet. 1:721-724, 1960.

Poszonyi, J., Gibson, D., and Zarfas, D.E.: Skeletal Maturation in Mongolism (Down's Syndrome). J. Pediatr. 64:75-78, 1964.

Pritchard, J.J., Scott, J.H., and Girgis, F.G.: The structure and development of cranial and facial sutures. J. Anat. 90:73-86, 1956.

Pryor, J.W.: Development of the bones of the hand as shown by the x-ray method. Bull. State Coll. Kentucky, Series 2, No. 5, 1905.

Pryor, J.W.: Differences in the time of development of centers of ossification in the male and female skeleton. Anat. Rec. 25:257-273, 1923.

Pryor, J.W.: Time of ossification of the bones of the hand of the male and female, and union of the epiphyses with the diaphyses. Am. J. Phys. Anthropol. 8:401-410, 1925.

Pyle, I. and Sontag, L.W.: Variability in onset of ossification in epiphyses and short bones of the extremities. Am. J. Roentgenol. 49:795-798, 1943.

Queen, L.R.: A morphological cineflourographic study of (trisomy 21) mongolism. Master's Thesis, University of Manitoba, 1975.

Rezk, Enrique, R.: A comparative cephalometric study of mongoloid and non-mongoloid children. Master's Thesis, University of Michigan, 1964.

Richards, B.W., Stewart, A., Sylvester, P.E., and Jasiewicz, V.: Cytogenetic survey of 225 patients diagnosed clinically as mongols. J. Ment. Defic. Res. 8:245-259, 1966.

Richardson, A.: An investigation into the reproducibility of some points, planes and lines used in cephalometric analysis. Am. J. Orthod. 52:637-651, 1966.

Ricketts, R.M.: A study of changes in temporomandibular relations associated with the treatment of Class II malocclusion. Am. J. Orthod. 38(12):918-933, 1952.

Riedel, R.A.: The relation of maxillary structures to cranium in malocclusion and in normal occlusion. Am. J. Orthod. 22(3):142-145, 1952.

Robinow, M.: Appearance of ossification centers: groupings obtained from factor analysis. Am. J. Dis. Child. 64:229-236, 1942.

Robinson, I.B. and Sarnat, B.G.: The growth patterns of the pig mandible. A serial roentgenographic study using metallic implants. Am. J. Anat. 96(1):37-64, 1955.

Roche, A.F. and Barkla, D.H.: Eruption of deciduous teeth in mongols. J. Ment. Defic. Res. 8:54-64, 1964.

Roche, A.F. and Lewis, A.B.: Sex differences in the elongation of the cranial base during pubescence. Angle Orthod. (Oct.):279-291, 1974.

Rotch, T.M.: A study of the development of bones in childhood with a view to establishing a developmental index. Trans. Assoc. Am. Phycns. 24:603-621, 1909.

Sassouni, V.: The Face in Five Dimensions. Morgantown: West Virginia University, School of Dentistry Publication, 1962.

Sassouni, V., Little, R., Romig, R., Panchura, F., and Toye, J.: The Face and Teeth in Mongolism. Pittsburg: University of Pittsburg, School of Dentistry, Orthodont. Dept. Publication, 1964.

Sassouni, V., Little, R., Romig, R., Panchura, F., and Toye, J.: The Face and Teeth in Mongolism. Pittsburg: Orthodont. Dept. of the School of Dentistry, 1964.

Schmidt, E.: Die horizontal above des men children schadils. Arch. Anthropol. 9:25-60, 1876.

Schour, I. and Massler, M.: Studies in tooth development the growth pattern of human teeth. J. Am. Dent. Assoc. 28:1153-1160, 1941.

Schuller, A.: Roentgen. Diagnosis of Disease of the Head. St. Louis, C.V. Mosby, 1918.

Scott, J.H.: The growth of the human face. Proc. Roy. Soc. Med. 47:91-100, 1954a.

Scott, J.H.: Growth of the facial sutures. Am. J. Orthod. 42(5):381-387, 1956.

Scott, J.H.: The analysis of facial growth. II. The horizontal and vertical dimensions. Am. J. Orthod. 44:585-589, 1958.

Scott, J.H.: The cranial base. Am. J. Orthod. 16:319-348, 1958.

Scott, J.H.: Dento-facial Development and Growth. New York: Pergamon Press, 1967.

Selman, A.J. and Sarnat, B.G.: Growth of the rabbit snout after extirpation of the frontonasal suture: a gross and serial roentgenographic study by means of metallic implants. Am. J. Anat. 101:273-293, 1957.

Seguin, E.: Le traitement moral, L'hygiene et l'education des idiots. Paris: J.B. Bailliere. 1846. Quoted in Lejeune, 1964; Penrose and Smith, 1966.

Seguin, E.: Idiocy and its Treatment by the Physiological Method. New York: William Wood and Co. 1866. Quoted in: Benda, 1969; Penrose and Smith, 1966.

Shuttleworth, G.E.: Clinical lecture on idiocy and imbecility. Br. Med. J. 1:183-186, 1886.

Sicher, H. and Du Brul, L.E.: Oral Anatomy. Saint Louis The C.V. Mosby Company, 1970.

Silversten, R. and Hasund, A.: The His Line and opisthion-nasion line in relation to the general pattern of craniofacial association. Angle Orthod. 39-40:11-19, 1970.

Smith, T.: A peculiarity in the shape of the hand in idiots of the mongol type. Pediatrics. 2:315-320, 1896.

Solow, B.: The pattern of craniofacial association. Acta Odontol. Scand. Vol.24, Supple. 46, 1966.

Sommer, A. and Eaton, A.P.: Achondroplasia and Down's syndrome. J. Med. Genetics. 7:63-66, 1970.

Spitzer, R. and Robinson, M.I.: Radiological changes in teeth and skull in mental defectives. Br. J. Radiol. 28:117-127, 1955.

Spitzer, R., Rabinowitch, J.Y., and Wybar, K.C.: A study of the abnormalities of the skull, teeth and lenses in mongolism. Can. Med. Assoc. 84:567-572, 1961.

Steiner, C.: Cephalometrics for you and me. Am. J. Orthod. 39:729-755, 1953.

Stutzmann, J. and Petrovic, A.: Particularités de croissance de la suture palatine sagittale de jeune rat. C.R. Assoc. Anat. 148:552-562, 1970.

Tanner, J.M. and Whitehouse, R.H.: Standards for Skeletal Maturity. Paris, International Children's Centre, 1959.

Tanner, J.M., Whitehouse, R.H., and Healy, M.J.R.: A New System for Estimating Skeletal Maturity From the Hand and Wrist, With Standards Derived from a Study of 2,600 Healthy British Children. Part II, The Scoring System, Paris, International Children's Centre, 1962.

Tanner, J.M.: Growth at Adolescence, 2nd Ed., Blackwell, Oxford, 1962.

Therman, E.M., Patau, K., Smith, D.W., and DeMars, R.I.: The D Trisomy Syndrome and XO Gonadal Dysgenesis in Two Sisters. Am. J. Hum. Genet. 13:193-204, 1961.

Tjio, J.H. and Levan, A.: The chromosome number of man. Hereditas. 42:1-6, 1956.

Uchida, I.A.: Epidemiology of Mongolism: The Manitoba Study. Ann. N.Y. Acad. Sci. 171:361-369, 1970.

Unno, T., Nelson, J.R., Ogura, J.H.: The effect of nasal obstruction on pulmonary airway and tissue resistance. Laryngoscope. 78:1119, 1968.

Van der Linden, F.P.G.: A study of roentgenocephalometric bony landmarks. Am. J. Orthod. 59:111-125, 1971.

Vinkka, H. and Koski, K.: Variability of the craniofacial skeleton. Am. J. Orthod. 67:34-43, 1975.

Waardenburg, P.J.: Das menschliche Auge and seine Enbanlangen. Haag: Martinus Nijhoff, 1932, as quoted in Penrose and Smith, 1966; and Gustavson, 1964.

Wahrman, J. and Fried, K.: The Jerusalem prospective newborn survey of mongolism. Annals New York Academy of Science 171:341-360, 1970.

Watson, E.H. and Lowrey, G.H.: Growth and Development of Children, 5th ed. Year Book Medical Publishers Inc. Chicago, 1967.

Wei, S.H.Y.: The variability of roentgenographic cephalometric lines of reference. Angle Orthod. 38:74-78, 1968.

Welcker, H.: Kraniologische Mittheilungen. Arch. J. Anthropol. 1:89-160, 1868.

Weinmann, J.P. and Sicher, H.: Bone and Bones. St. Louis: C.V. Mosby, 1947.

Wieslander, L.: The effect of orthodontic treatment on the concurrent development of the craniofacial complex. Am. J. Orthod. 49:15-27, 1963.

Wilkinson, L.: Factors contributing to facial growth and development. Am. J. Orthod. and Oral Surg. 26:1019-1026, 1940.

Wilms, : Die Entwicklung des Knochen der Oberen Extremitat Dargestellt in Rontgentbilden, Fortschr. Rontgenstr. (Erg. Bd.), 9, 1902.

Wylie, W.L.: The assessment of antero-posterior dysplasia. Am. J. Orthod. 17:97-109, 1947.

Yen, P.K.J.: Identification of landmarks in cephalometric radiographs. Angle Orthod. 30:35-41, 1960.

Yunis, J.J., Hook, E.B., and Mayer, M.: Identification of the mongolism chromosome by DNA replication analysis. Am. J. Hum. Genet. 17:191-201, 1965.

APPENDIX

APPENDIX

TABLE III

TABLE OF POOLED STANDARD DEVIATIONS FOR ANGLES BETWEEN REFERENCE LINES FOR TRISOMY

	2-4	29-2	29-4	6-1	4-39	59-38	54-26	2-54	54-56	40-2	6-60
2-4	0.0	5.04	2.18	4.45	3.33	2.79	6.89	5.39	5.44	3.67	3.30
29-2	5.04	0.0	3.15	6.13	4.89	4.02	6.94	7.04	7.37	5.81	4.81
29-4	2.18	3.15	0.0	4.46	3.15	2.20	6.37	5.76	5.69	4.05	3.24
6-1	4.45	6.13	4.46	0.0	4.78	0.0	7.54	6.74	6.88	0.0	4.42
4-39	3.33	4.89	3.15	4.78	0.0	3.12	6.67	6.47	5.80	5.00	3.85
59-38	2.79	4.02	2.20	0.0	3.12	0.0	6.12	6.19	5.33	4.63	0.0
54-26	6.89	6.94	6.37	7.54	6.67	6.12	0.0	8.15	8.60	7.70	6.80
2-54	5.39	7.04	5.76	6.74	6.47	6.19	8.15	0.0	9.09	3.60	5.81
54-56	5.44	7.37	5.69	6.88	5.80	5.33	8.60	9.09	0.0	6.85	5.85
40-2	3.67	5.81	4.05	0.0	5.06	4.63	7.70	3.60	6.85	0.0	4.35
6-60	3.30	4.81	3.24	4.42	3.85	0.0	6.80	5.81	5.85	4.35	0.0
SUMS	42.48	55.21	40.25	45.40	47.13	34.41	71.77	64.23	66.01	45.74	42.44
MEANS	4.25	5.52	4.03	5.67	4.71	4.30	7.18	6.42	6.60	5.08	4.72
N	10	10	10	8	10	8	10	10	10	9	9

TABLE IV

TABLE OF POOLED VARIANCES FOR ANGLES BETWEEN REFERENCE LINES FOR TRISOMY

	2-4	29-2	29-4	6-1	4-39	59-38	54-26	2-54	54-56	40-2	6-60
2-4	0.0	25.41	4.75	19.85	11.06	7.78	47.42	29.01	29.64	13.48	10.90
29-2	25.41	0.0	9.95	37.54	23.92	16.17	48.16	49.52	54.35	33.79	23.17
29-4	4.75	9.95	0.0	19.86	9.93	4.83	40.59	33.15	32.36	16.43	10.51
6-1	19.85	37.54	19.86	0.0	22.89	0.0	56.82	45.39	47.28	0.0	19.56
4-39	11.06	23.92	9.93	22.89	0.0	9.73	44.52	41.85	33.69	25.65	14.81
59-38	7.78	16.17	4.83	0.0	9.73	0.0	37.47	38.35	28.46	21.45	0.0
54-26	47.42	48.16	40.59	56.82	44.52	37.47	0.0	66.37	73.94	59.31	46.21
2-54	29.01	49.52	33.15	45.39	41.85	38.35	66.37	0.0	82.68	13.00	33.74
54-56	29.64	54.35	32.36	47.28	33.69	28.46	73.94	82.68	0.0	46.92	34.23
40-2	13.48	33.79	16.43	0.0	25.65	21.45	59.31	13.00	46.92	0.0	18.91
6-60	10.90	23.17	10.51	19.56	14.81	0.0	46.21	33.74	34.23	18.91	0.0
SUMS	199.31	321.99	182.36	269.18	238.05	164.24	520.81	433.07	463.56	248.94	212.07
MEANS	19.93	32.20	18.24	33.65	23.80	20.53	52.08	43.31	46.36	27.66	23.56
N	10	10	10	8	10	8	10	10	10	9	9

TABLE V

POOLED RESULTS READY FOR REGRESSION ANALYSIS - TRISOMY

ANGLE	STDEV	VARIANCE	ARM LENGTH 1	ARM LENGTH 2	ARM LENGTH 3	
1	5.040	25.3996	5.874	3.816	4.845	*
2	2.180	4.7521	5.874	9.150	7.512	*
3	3.326	11.0641	5.874	14.898	10.386	*
4	5.386	29.0135	5.874	2.287	4.080	*
5	4.455	19.8495	5.874	6.331	6.103	
6	2.790	7.7827	5.874	10.408	8.141	
7	6.886	47.4174	5.874	2.699	4.286	
8	5.445	29.6521	2.335	5.874	4.104	
9	3.672	13.4835	5.874	3.437	4.656	*
10	3.302	10.9001	5.874	6.679	6.277	
11	3.155	9.9561	3.816	9.150	6.483	*
12	7.036	49.5033	3.816	2.287	3.052	*
13	5.812	33.7804	3.816	3.437	3.627	*
14	6.127	37.5425	3.816	6.331	5.074	
15	4.891	23.9241	3.816	14.898	9.357	
16	4.020	16.1635	3.816	10.408	7.112	
17	6.940	48.1667	2.699	3.816	3.257	
18	7.373	54.3584	3.816	2.335	3.075	
19	4.814	23.1757	3.816	6.679	5.248	
20	3.151	9.9316	9.150	14.898	12.024	*
21	4.456	19.8571	9.150	6.331	7.741	
22	2.197	4.8251	9.150	10.408	9.779	
23	6.371	40.5861	9.150	2.699	5.925	
24	5.758	33.1553	9.150	2.287	5.719	
25	5.689	32.3653	9.150	2.335	5.743	
26	4.053	16.4308	9.150	3.437	6.294	
27	3.242	10.5124	9.150	6.679	7.915	
28	4.423	19.5655	6.331	6.679	6.505	*
29	4.784	22.8819	6.331	14.898	10.615	
30	4.797	23.0113	6.331	10.408	8.370	
31	7.538	56.8177	6.331	2.699	4.515	
32	6.737	45.3893	6.331	2.287	4.309	
33	6.876	47.2814	6.331	2.335	4.333	
34	5.309	28.1810	6.331	3.437	4.884	
35	3.119	9.7285	14.898	10.408	12.653	
36	6.672	44.5140	14.898	2.699	8.799	
37	6.469	41.8449	14.898	2.287	8.593	
38	5.804	33.6817	14.898	2.335	8.616	
39	5.065	25.6529	14.898	3.437	9.168	
40	3.849	14.8153	14.898	6.679	10.789	
41	6.121	37.4701	10.408	2.699	6.554	
42	6.193	38.3521	10.408	2.287	6.348	
43	5.335	28.4665	10.408	2.335	6.371	
44	4.628	21.4211	10.408	3.437	6.923	
45	3.225	10.3992	10.408	6.679	8.544	
46	8.146	66.3607	2.699	2.287	2.493	*
47	8.599	73.9384	2.699	2.335	2.517	*
48	7.701	59.3113	2.699	3.437	3.068	
49	6.798	46.2165	2.699	6.679	4.689	
50	9.093	82.6843	2.287	2.335	2.311	*
51	3.605	12.9995	2.287	3.437	2.862	*
52	5.809	33.7488	2.287	6.679	4.483	
53	6.850	46.9256	2.335	3.437	2.886	
54	5.851	34.2320	2.335	6.679	4.507	
55	4.351	18.9273	3.437	6.679	5.058	

* 3 point angles

TABLE VI

TABLE OF POOLED STANDARD DEVIATIONS* FOR THE ANGLES BETWEEN THE REFERENCE LINES FOR TRISOMY

	2-4	29-2	29-4	6-1	4-39	59-38	54-26	2-54	54-56	40-2	6-60
2-4	0.0	4.83	3.38	4.30	6.05	3.44	6.02	4.77	4.50	3.36	3.22
29-2	4.83	0.0	3.81	5.57	6.02	4.26	5.66	5.88	6.03	4.96	4.32
29-4	3.38	3.81	0.0	4.95	6.74	3.49	6.15	5.45	5.39	3.97	3.80
6-1	4.30	5.57	4.95	0.0	6.41	5.54	6.76	5.88	6.02	4.67	5.09
4-39	6.05	6.02	6.74	6.41	0.0	5.55	7.58	7.30	6.64	6.12	5.54
59-38	3.44	4.26	3.49	5.54	5.55	0.0	6.14	6.14	5.29	4.80	4.03
54-26	6.02	5.66	6.15	6.76	7.58	6.14	0.0	6.69	7.16	6.35	6.09
2-54	4.77	5.88	5.45	5.88	7.30	6.14	6.69	0.0	7.54	2.35	5.02
54-56	4.50	6.03	5.39	6.02	6.64	5.29	7.16	7.54	0.0	5.43	5.07
40-2	3.36	4.96	3.97	4.67	6.12	4.80	6.35	2.35	5.43	0.0	3.79
6-60	3.22	4.32	3.80	5.09	5.54	4.03	6.09	5.02	5.07	3.79	0.0
SUMS	43.88	51.34	47.15	55.19	63.95	48.68	64.60	57.01	59.07	45.80	45.97
MEANS	4.39	5.13	4.72	5.52	6.40	4.87	6.46	5.70	5.91	4.58	4.60
N	10	10	10	10	10	10	10	10	10	10	10

* Adjusted for angle arm length of 3 and 4 point angles

TABLE VII

TABLE OF POOLED VARIANCES* FOR THE ANGLES BETWEEN THE REFERENCE LINES FOR TRISOMY

	2-4	29-2	29-4	6-1	4-39	59-38	54-26	2-54	54-56	40-2	6-60
2-4	0.0	23.34	11.45	18.50	36.62	11.83	36.19	22.77	20.28	11.31	10.35
29-2	23.34	0.0	14.54	31.00	36.24	18.18	32.08	34.54	36.31	24.58	18.69
29-4	11.45	14.54	0.0	24.48	45.49	12.20	37.79	29.73	29.09	15.80	14.46
6-1	18.50	31.00	24.48	0.0	41.07	30.66	45.67	34.53	36.29	21.85	25.94
4-39	36.62	36.24	45.49	41.07	0.0	30.77	57.47	53.24	44.10	37.45	30.72
59-38	11.83	18.18	12.20	30.66	30.77	0.0	37.76	37.65	27.95	23.02	16.27
54-26	36.19	32.08	37.79	45.67	57.47	37.76	0.0	44.77	51.22	40.33	37.05
2-54	22.77	34.54	29.73	34.53	53.24	37.65	44.77	0.0	56.88	5.50	25.17
54-56	20.28	36.31	29.09	36.29	44.10	27.95	51.22	56.88	0.0	29.46	25.68
40-2	11.31	24.58	15.80	21.85	37.45	23.02	40.33	5.50	29.46	0.0	14.33
6-60	10.35	18.69	14.46	25.94	30.72	16.27	37.05	25.17	25.68	14.33	0.0
SUMS	202.64	269.02	235.02	309.99	413.18	246.28	420.34	344.78	357.26	223.62	218.65
MEANS	20.26	26.95	23.50	31.00	41.32	24.63	42.03	34.48	35.73	22.36	21.86
N	10	10	10	10	10	10	10	10	10	10	10

* Adjusted for angle arm length of 3 and 4 point angles

TABLE VIII

TABLE OF POOLED STANDARD DEVIATIONS FOR ANGLES BETWEEN REFERENCE LINES FOR CONTROL

	2-4	29-2	29-4	6-1	4-39	59-38	54-26	2-54	54-56	40-2	6-60
2-4	0.0	4.91	2.14	3.98	3.01	2.83	6.34	4.13	3.82	2.96	2.78
29-2	4.91	0.0	3.13	4.29	3.52	3.53	6.52	5.42	6.01	5.02	3.57
29-4	2.14	3.13	0.0	3.11	2.32	2.04	5.94	4.05	4.33	3.25	2.01
6-1	3.98	4.29	3.11	0.0	3.74	0.0	6.63	5.42	5.22	0.0	3.14
4-39	3.01	3.52	2.32	3.74	0.0	2.40	5.88	4.17	5.03	3.65	2.65
59-38	2.83	3.53	2.04	0.0	2.40	0.0	6.01	4.63	4.43	3.79	0.0
54-26	6.34	6.52	5.94	6.63	5.88	6.01	0.0	5.82	8.27	6.30	5.47
2-54	4.13	5.42	4.05	5.42	4.17	4.63	5.82	0.0	6.63	2.76	4.03
54-56	3.82	6.01	4.33	5.22	5.03	4.43	8.27	6.63	0.0	5.11	4.76
40-2	2.96	5.02	3.25	0.0	3.65	3.79	6.30	2.76	5.11	0.0	3.61
6-60	2.78	3.57	2.01	3.14	2.65	0.0	5.47	4.03	4.76	3.61	0.0
SUMS	36.89	45.91	32.32	35.53	36.39	29.67	63.18	47.05	53.62	36.46	32.03
MEANS	3.69	4.59	3.23	4.44	3.64	3.71	6.32	4.71	5.36	4.05	3.56
N	10	10	10	8	10	8	10	10	10	9	9

TABLE IX

TABLE OF POOLED VARIANCES FOR ANGLES BETWEEN REFERENCE LINES FOR CONTROL

	2-4	29-2	29-4	6-1	4-39	59-38	54-26	2-54	54-56	40-2
2-4	0.0	24.08	4.58	15.81	9.08	8.01	40.25	17.05	14.58	8.75
29-2	24.08	0.0	9.78	18.38	12.38	12.43	42.46	29.33	36.17	25.24
29-4	4.58	9.78	0.0	9.70	5.38	4.18	35.26	16.40	18.71	10.60
6-1	15.81	18.38	9.70	0.0	14.00	0.0	43.96	29.34	27.24	0.0
4-39	9.08	12.38	5.38	14.00	0.0	5.78	34.57	17.40	25.31	13.36
59-38	8.01	12.43	4.18	0.0	5.78	0.0	36.17	21.41	19.65	14.36
54-26	40.25	42.46	35.26	43.96	34.57	36.17	0.0	33.85	68.43	39.64
2-54	17.05	29.33	16.40	29.34	17.40	21.41	33.85	0.0	43.90	7.64
54-56	14.58	36.17	18.71	27.24	25.31	19.65	68.43	43.90	0.0	26.14
40-2	8.75	25.24	10.60	0.0	13.36	14.36	39.64	7.64	26.14	0.0
6-60	7.72	12.76	4.03	9.89	7.03	0.0	29.95	16.27	22.71	13.02
SUMS	149.91	223.01	118.61	168.32	144.30	122.00	404.53	232.59	302.85	158.70
MEANS	14.99	22.30	11.86	21.04	14.43	15.25	40.45	23.26	30.28	17.64
N	10	10	10	8	10	8	10	10	10	9

TABLE X

POOLED RESULTS READY FOR REGRESSION ANALYSIS - CONTROL

ANGLE	STDEV	VARIANCE	ARM LENGTH 1	ARM LENGTH 2	ARM LENGTH 3
1	4.907	24.0762	6.466	4.072	5.269 *
2	2.139	4.5740	6.466	9.607	8.037 *
3	3.008	9.0492	6.466	15.757	11.111 *
4	4.131	17.0687	6.466	2.370	4.418 *
5	3.976	15.8054	6.466	6.834	6.650
6	2.831	8.0138	6.466	12.497	9.482
7	6.344	40.2513	6.466	2.753	4.610
8	3.819	14.5881	2.741	6.466	4.604
9	2.958	8.7527	6.466	3.587	5.026 *
10	2.778	7.7167	6.466	7.191	6.829
11	3.127	9.7794	4.072	9.607	6.840 *
12	5.416	29.3280	4.072	2.370	3.221 *
13	5.025	25.2504	4.072	3.587	3.829 *
14	4.287	18.3820	4.072	6.834	5.453
15	3.519	12.3858	4.072	15.757	9.914
16	3.526	12.4348	4.072	12.497	8.285
17	6.516	42.4563	2.753	4.072	3.413
18	6.014	36.1662	4.072	2.741	3.407
19	3.573	12.7632	4.072	7.191	5.631
20	2.319	5.3772	9.607	15.757	12.682 *
21	3.114	9.6990	9.607	6.834	8.220
22	2.044	4.1781	9.607	12.497	11.052
23	5.938	35.2566	9.607	2.753	6.180
24	4.050	16.4011	9.607	2.370	5.988
25	4.326	18.7154	9.607	2.741	6.174
26	3.255	10.5978	9.607	3.587	6.597
27	2.007	4.0284	9.607	7.191	8.399
28	3.143	9.8773	6.834	7.191	7.012 *
29	3.742	14.0002	6.834	15.757	11.295
30	3.628	13.1635	6.834	12.497	9.666
31	6.630	43.9511	6.834	2.753	4.794
32	5.417	29.3475	6.834	2.370	4.602
33	5.219	27.2421	6.834	2.741	4.788
34	4.885	23.8592	6.834	3.587	5.210
35	2.404	5.7786	15.757	12.497	14.127
36	5.880	34.5691	15.757	2.753	9.255
37	4.171	17.3953	15.757	2.370	9.063
38	5.032	25.3200	15.757	2.741	9.249
39	3.655	13.3591	15.757	3.587	9.672
40	2.652	7.0338	15.757	7.191	11.474
41	6.014	36.1641	12.497	2.753	7.625
42	4.627	21.4061	12.497	2.370	7.434
43	4.433	19.6508	12.497	2.741	7.619
44	3.788	14.3525	12.497	3.587	8.042
45	2.167	4.6977	12.497	7.191	9.844
46	5.817	33.8385	2.753	2.370	2.562 *
47	8.272	68.4238	2.753	2.741	2.747 *
48	6.296	39.6364	2.753	3.587	3.170
49	5.473	29.9519	2.753	7.191	4.972
50	6.626	43.8989	2.370	2.741	2.556 *
51	2.764	7.6406	2.370	3.587	2.978 *
52	4.033	16.2637	2.370	7.191	4.780
53	5.113	26.1445	2.741	3.587	3.164
54	4.765	22.7022	2.741	7.191	4.966
55	3.609	13.0252	3.587	7.191	5.389

* 3 point angles

TABLE XI

TABLE OF POOLED STANDARD DEVIATIONS* FOR THE ANGLES BETWEEN THE REFERENCE LINES FOR CONTROL

	2-4	29-2	29-4	6-1	4-39	59-38	54-26	2-54	54-56	40-2	6-60
2-4	0.0	4.78	3.08	3.83	5.13	3.60	5.54	3.68	3.01	2.74	2.69
29-2	4.78	0.0	3.61	3.75	4.43	3.91	5.32	4.50	4.82	4.35	3.10
29-4	3.08	3.61	0.0	3.48	5.05	3.33	5.64	3.69	4.03	3.09	2.43
6-1	3.83	3.75	3.48	0.0	5.10	4.46	5.88	4.61	4.47	4.27	3.69
4-39	5.13	4.43	5.05	5.10	0.0	4.68	6.58	4.81	5.73	4.49	4.07
59-38	3.60	3.91	3.33	4.46	4.68	0.0	6.18	4.74	4.60	4.09	3.06
54-26	5.54	5.32	5.64	5.88	6.58	6.18	0.0	4.65	7.18	5.02	4.78
2-54	3.68	4.50	3.69	4.61	4.81	4.74	4.65	0.0	5.46	1.76	3.28
54-56	3.01	4.82	4.03	4.47	5.73	4.60	7.18	5.46	0.0	3.84	4.07
40-2	2.74	4.35	3.09	4.27	4.49	4.09	5.02	1.76	3.84	0.0	3.05
6-60	2.69	3.10	2.43	3.69	4.07	3.06	4.78	3.28	4.07	3.05	0.0
SUMS	38.09	42.57	37.42	43.54	50.08	42.66	56.77	41.16	47.19	36.70	34.22
MEANS	3.81	4.26	3.74	4.35	5.01	4.27	5.68	4.12	4.72	3.67	3.42
N	10	10	10	10	10	10	10	10	10	10	10

* Adjusted for angle arm length of 3 and 4 point angles

TABLE XII

TABLE OF POOLED VARIANCES* FOR THE ANGLES BETWEEN THE REFERENCE LINES FOR CONTROL

	2-4	29-2	29-4	6-1	4-39	59-38	54-26	2-54	54-56	40-2	6-60
2-4	0.0	22.87	9.49	14.67	26.36	12.99	30.65	13.53	9.05	7.51	7.24
29-2	22.87	0.0	13.02	14.08	19.64	15.29	28.30	20.27	23.19	18.89	9.59
29-4	9.49	13.02	0.0	12.09	25.50	11.07	31.81	13.61	16.21	9.56	5.90
6-1	14.67	14.08	12.09	0.0	26.04	19.90	34.60	21.22	19.97	18.25	13.62
4-39	26.36	19.64	25.50	26.04	0.0	21.94	43.29	23.12	32.83	20.16	16.58
59-38	12.99	15.29	11.07	19.90	21.94	0.0	38.25	22.42	21.17	16.76	9.35
54-26	30.65	28.30	31.81	34.60	43.29	38.25	0.0	21.62	51.49	25.21	22.87
2-54	13.53	20.27	13.61	21.22	23.12	22.42	21.62	0.0	29.77	3.09	10.76
54-56	9.05	23.19	16.21	19.97	32.83	21.17	51.49	29.77	0.0	14.71	16.59
40-2	7.51	18.89	9.56	18.25	20.16	16.76	25.21	3.09	14.71	0.0	9.33
6-60	7.24	9.59	5.90	13.62	16.58	9.35	22.87	10.76	16.59	9.33	0.0
SUMS	154.36	185.15	148.25	194.44	255.46	189.14	328.08	179.42	234.99	143.45	121.81
MEANS	15.44	18.51	14.83	19.44	25.55	18.91	32.81	17.94	23.50	14.35	12.18
N	10	10	10	10	10	10	10	10	10	10	10

* Adjusted for angle arm length of 3 and 4 point angles

TABLE XIII

TABLE OF POOLED LOG (VARIANCES)* FOR ANGLES BETWEEN THE REFERENCE LINES FOR TRISOMY

	2-4	29-2	29-4	6-1	4-39	59-38	54-26	2-54	54-56	40-2	6-60
2-4	0.0	1.37	1.06	1.27	1.56	1.07	1.56	1.36	1.31	1.05	1.01
29-2	1.37	0.0	1.16	1.49	1.56	1.26	1.51	1.54	1.56	1.39	1.27
29-4	1.06	1.16	0.0	1.39	1.66	1.09	1.58	1.47	1.46	1.20	1.16
6-1	1.27	1.49	1.39	0.0	1.61	1.49	1.66	1.54	1.56	1.34	1.41
4-39	1.56	1.56	1.66	1.61	0.0	1.49	1.76	1.73	1.64	1.57	1.49
59-38	1.07	1.26	1.09	1.49	1.49	0.0	1.58	1.58	1.45	1.36	1.21
54-26	1.56	1.51	1.58	1.66	1.76	1.58	0.0	1.65	1.71	1.61	1.57
2-54	1.36	1.54	1.47	1.54	1.73	1.58	1.65	0.0	1.75	0.74	1.40
54-56	1.31	1.56	1.46	1.56	1.64	1.45	1.71	1.75	0.0	1.47	1.41
40-2	1.05	1.39	1.20	1.34	1.57	1.36	1.61	0.74	1.47	0.0	1.16
6-60	1.01	1.27	1.16	1.41	1.49	1.21	1.57	1.40	1.41	1.16	0.0
SUMS	12.62	14.11	13.23	14.76	16.07	13.57	16.17	14.76	15.32	12.89	13.09
MEANS	1.26	1.41	1.32	1.48	1.61	1.36	1.62	1.48	1.53	1.29	1.31
N	10	10	10	10	10	10	10	10	10	10	10

* Adjusted for angle arm length of 3 + 4 point angles

TABLE XIV

TABLE OF POOLED LOG (VARIANCES)* FOR ANGLES BETWEEN THE REFERENCE LINES FOR CONTROL

	2-4	29-2	29-4	6-1	4-39	59-38	54-26	2-54	54-56	40-2	6-60
2-4	0.0	1.36	0.98	1.17	1.42	1.11	1.49	1.13	0.96	0.88	0.86
29-2	1.36	0.0	1.11	1.15	1.29	1.18	1.45	1.31	1.37	1.28	0.98
29-4	0.98	1.11	0.0	1.08	1.41	1.04	1.50	1.13	1.21	0.98	0.77
6-1	1.17	1.15	1.08	0.0	1.42	1.30	1.54	1.33	1.30	1.26	1.13
4-39	1.42	1.29	1.41	1.42	0.0	1.34	1.64	1.36	1.52	1.30	1.22
59-38	1.11	1.18	1.04	1.30	1.34	0.0	1.58	1.35	1.33	1.22	0.97
54-26	1.49	1.45	1.50	1.54	1.64	1.58	0.0	1.33	1.71	1.40	1.36
2-54	1.13	1.31	1.13	1.33	1.36	1.35	1.33	0.0	1.47	0.49	1.03
54-56	0.96	1.37	1.21	1.30	1.52	1.33	1.71	1.47	0.0	1.17	1.22
40-2	0.88	1.28	0.98	1.26	1.30	1.22	1.40	0.49	1.17	0.0	0.97
6-60	0.86	0.98	0.77	1.13	1.22	0.97	1.36	1.03	1.22	0.97	0.0
SUMS	11.35	12.48	11.22	12.67	13.92	12.44	15.01	11.94	13.25	10.95	10.52
MEANS	1.13	1.25	1.12	1.27	1.39	1.24	1.50	1.19	1.32	1.10	1.05
N	10	10	10	10	10	10	10	10	10	10	10

* Adjusted for angle arm length of 3 + 4 point angles

TABLE XV

TEST FOR SIGNIFICANT DIFFERENCES BETWEEN REFERENCE LINE STABILITY WITHIN TRISOMY 21 SAMPLE - ANALYSIS OF VARIANCE

	02-04	29-02	29-04	06-01	04-39	59-38	54-26	02-54	54-56	40-02	06-60
02-04	1.260	1.370	1.060	1.270	1.560	1.070	1.560	1.360	1.310	1.050	1.010
29-02	1.370	1.410	1.160	1.490	1.560	1.260	1.510	1.540	1.560	1.390	1.270
29-04	1.060	1.160	1.320	1.390	1.660	1.090	1.580	1.470	1.460	1.200	1.160
06-01	1.270	1.490	1.390	1.480	1.610	1.490	1.660	1.540	1.560	1.340	1.410
04-39	1.560	1.560	1.660	1.610	1.610	1.490	1.760	1.730	1.640	1.570	1.490
59-38	1.070	1.260	1.090	1.490	1.490	1.360	1.580	1.580	1.450	1.360	1.210
54-26	1.560	1.510	1.580	1.660	1.760	1.580	1.620	1.650	1.710	1.610	1.570
02-54	1.360	1.540	1.470	1.540	1.730	1.580	1.650	1.480	1.750	0.740	1.400
54-56	1.310	1.560	1.460	1.560	1.640	1.450	1.710	1.750	1.530	1.470	1.410
40-02	1.050	1.390	1.200	1.340	1.570	1.360	1.610	0.740	1.470	1.290	1.160
06-60	1.010	1.270	1.160	1.410	1.490	1.210	1.570	1.400	1.410	1.160	1.310

ANALYSIS OF VARIANCE

Source of Variation	Degrees of Freedom	Sums of Squares	Means Squares	F Value
Replications	10	1.77554	0.17755	
Treatments	10	1.77554	0.17755	10.984
Exp. Error	100	1.61655	0.01617	
Total	120	5.16763		

TABLE XVI

COMPARISON OF TREATMENTS - TRISOMY

54-26	IS BETTER THAN 02-54	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 06-01	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 29-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 59-38	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 29-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 06-60	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 40-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 02-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 02-54	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 06-01	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 29-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 59-38	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 29-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 06-60	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 40-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 02-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-56	IS BETTER THAN 29-02	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
54-56	IS BETTER THAN 59-38	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-56	IS BETTER THAN 29-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-56	IS BETTER THAN 06-60	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-56	IS BETTER THAN 40-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-56	IS BETTER THAN 02-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
02-54	IS BETTER THAN 59-38	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
02-54	IS BETTER THAN 29-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
02-54	IS BETTER THAN 06-60	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
02-54	IS BETTER THAN 40-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
02-54	IS BETTER THAN 02-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
06-01	IS BETTER THAN 59-38	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
06-01	IS BETTER THAN 29-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
06-01	IS BETTER THAN 06-60	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
06-01	IS BETTER THAN 40-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
06-01	IS BETTER THAN 02-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
29-02	IS BETTER THAN 40-02	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
29-02	IS BETTER THAN 02-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE

TABLE XVII

TEST FOR SIGNIFICANT DIFFERENCES BETWEEN REFERENCE LINE STABILITY WITHIN CONTROL SAMPLE - ANALYSIS OF VARIANCE

	02-04	29-02	29-04	06-01	04-39	59-38	54-26	02-54	54-56	40-02	06-60
02-04	1.130	1.360	0.980	1.170	1.420	1.110	1.490	1.130	0.960	0.880	0.860
29-02	1.360	1.250	1.110	1.150	1.290	1.180	1.450	1.310	1.370	1.280	0.980
29-04	0.980	1.110	1.120	1.080	1.410	1.040	1.500	1.130	1.210	0.980	0.770
06-01	1.170	1.150	1.080	1.270	1.420	1.300	1.540	1.330	1.300	1.260	1.130
04-39	1.420	1.290	1.410	1.420	1.390	1.340	1.640	1.360	1.520	1.300	1.220
59-38	1.110	1.180	1.040	1.300	1.340	1.240	1.580	1.350	1.330	1.220	0.970
54-26	1.490	1.450	1.500	1.540	1.640	1.580	1.500	1.330	1.710	1.400	1.360
02-54	1.130	1.310	1.130	1.330	1.360	1.350	1.330	1.190	1.470	0.490	1.030
54-56	0.960	1.370	1.210	1.300	1.520	1.330	1.710	1.470	1.320	1.170	1.220
40-02	0.880	1.280	0.980	1.260	1.300	1.220	1.400	0.490	1.170	1.100	0.970
06-60	0.860	0.980	0.770	1.130	1.220	0.970	1.360	1.030	1.220	0.970	1.050

ANALYSIS OF VARIANCE

Source of Variation	Degrees of Freedom	Sums of Squares	Means of Squares	F Value
Replications	10	2.00816	0.20082	
Treatments	10	2.00816	0.20082	11.070
Exp. Error	100	1.81410	0.01814	
Total	120	5.83043		

TABLE XVIII

COMPARISON OF TREATMENTS - CONTROL

54-26	IS BETTER THAN 54-56	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 06-01	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 29-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 59-38	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 02-54	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 02-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 29-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 40-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-26	IS BETTER THAN 06-60	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 06-01	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 29-02	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 59-38	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 02-54	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 02-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 29-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 40-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
04-39	IS BETTER THAN 06-60	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-56	IS BETTER THAN 02-54	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
54-56	IS BETTER THAN 02-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-56	IS BETTER THAN 29-04	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-56	IS BETTER THAN 40-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
54-56	IS BETTER THAN 06-60	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
06-01	IS BETTER THAN 02-04	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
06-01	IS BETTER THAN 29-04	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
06-01	IS BETTER THAN 40-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
06-01	IS BETTER THAN 06-60	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
29-02	IS BETTER THAN 29-04	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
29-02	IS BETTER THAN 40-02	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
29-02	IS BETTER THAN 06-60	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
59-38	IS BETTER THAN 29-04	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
59-38	IS BETTER THAN 40-02	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE
59-38	IS BETTER THAN 06-60	AT THE 1 PERCENT LEVEL OF SIGNIFICANCE
02-54	IS BETTER THAN 06-60	AT THE 5 PERCENT LEVEL OF SIGNIFICANCE

TABLE XIX

Linear Dimension Sella-Nasion (in Centimeters) Means, Standard Error and the Significance of the Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	5.15	0.11	5.92	0.09	7.42 ***
6-9 yrs.	5.38	0.11	6.17	0.08	8.33 ***
10-14 yrs.	5.97	0.09	6.57	0.10	6.36 ***
15-18 yrs.	5.83	0.08	6.65	0.09	9.32 ***
18+ yrs.	6.05	0.04	6.82	0.06	15.67 ***

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XX

Linear Dimension Basion-Sella (in Centimeters)
Means, Standard Error and the Significance of the
Differences Between Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	3.38	0.10	3.40	0.08	0.28
6-9 yrs.	3.23	0.09	3.63	0.07	5.06 ***
10-14 yrs.	3.98	0.07	4.17	0.08	2.44
15-18 yrs.	3.90	0.07	4.18	0.08	3.80 **
18+ yrs.	3.93	0.04	4.43	0.05	11.63

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXI

Linear Dimension Basion-Nasion (in Centimeters)
Means, Standard Error and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	8.02	0.16	8.59	0.13	4.00 ***
6-9 yrs.	8.07	0.15	9.08	0.11	7.77 ***
10-14 yrs.	9.38	0.12	9.88	0.14	3.84 *
15-18 yrs.	9.15	0.12	9.98	0.13	6.88 ***
18 + yrs.	9.44	0.06	10.25	0.08	11.54 ***

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXII

Linear Dimension Sella to the P.M. Vertical Line (in Centimeters)
Means, Standard Error and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	1.98	0.06	2.07	0.05	1.59
6-9 yrs.	2.00	0.06	2.17	0.04	3.39 *
10-14 yrs.	2.24	0.05	2.23	0.05	0.16
15-18 yrs.	2.07	0.05	2.22	0.05	3.09 *
18+ yrs.	2.18	0.02	2.34	0.03	5.90 ***

* Significant at the 5% level of confidence
** Significant at the 1% level of confidence
*** Significant at the 0.1% level of confidence

TABLE XXIII

Linear Dimension Nasion to the P.M. Vertical Line (in Centimeters)
Means, Standard Error and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	2.50	0.13	3.58	0.11	8.83 ***
6-9 yrs.	3.01	0.13	3.59	0.09	5.23 ***
10-14 yrs.	3.34	0.10	4.04	0.12	6.38 ***
15-18 yrs.	3.46	0.10	4.03	0.11	5.58 ***
18+ yrs.	3.49	0.05	4.16	0.07	11.63 ***

* Significant at the 5% confidence limit
** Significant at the 1% confidence limit
*** Significant at the 0.1% confidence limit

TABLE XXIV

Linear Dimension Basion to the P.M. Vertical Line (in Centimeters)
Means, Standard Error and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	3.27	0.14	3.57	0.11	2.38
6-9 yrs.	3.52	0.13	3.69	0.09	0.39
10-14 yrs.	4.24	0.11	4.03	0.12	1.85
15-18 yrs.	4.15	0.10	3.96	0.11	1.78
18+ yrs.	4.23	0.05	4.07	0.07	2.78

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXV

Angular Dimension Basion-Sella-Nasion (in Degrees) Means, Standard Error and the Significance of the Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	139.53	1.67	132.65	1.34	4.55 ***
6-9 yrs.	138.17	1.58	134.39	1.12	2.75
10-14 yrs.	140.38	1.29	132.65	1.45	5.63 ***
15-18 yrs.	139.61	1.22	133.24	1.34	4.98 ***
18+ yrs.	141.36	0.62	130.18	2.85	15.08 ***

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXVI

inear Dimension "A" Point to the P.M. Vertical Line (in Centimeters)
Means, Standard Error and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	3.48	0.10	4.14	0.08	7.03 ***
6-9 yrs.	3.75	0.10	4.48	0.07	8.48 ***
10-14 yrs.	4.27	0.08	4.65	0.09	4.45 **
15-18 yrs.	4.15	0.08	5.01	0.08	10.87 ***
18 + yrs.	4.32	0.04	5.05	0.05	16.45 ***

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXVII

Angular Dimension Basion-Nasion - "A" Point (in Degrees)
Means, Standard Error and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	63.67	1.19	64.54	0.95	0.81
6-9 yrs.	65.67	1.13	65.01	0.80	0.68
10-14 yrs.	65.59	0.92	61.70	1.03	3.99 ***
15-18 yrs.	65.24	0.87	64.36	0.95	0.96
18 + yrs.	64.94	0.44	63.40	0.60	2.92 *

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXVIII

ngular Dimension Palatal Plane to the Basion-Nasion Plane (in Degrees)
Means, Standard Errors and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	22.82	1.15	22.51	0.92	0.29
6-9 yrs.	25.43	1.09	22.95	0.77	2.62 *
10-14 yrs.	24.44	0.89	25.44	1.00	1.06
15-18 yrs.	24.17	0.84	27.34	0.92	3.61 **
18+ yrs.	23.52	0.43	25.43	0.58	3.73 **

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXIX

Linear Dimension Upper Incisor to the P.M. Vertical Line (in Centimeters)
Means, Standard Error and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	4.02	0.15	4.32	0.12	2.16
6-9 yrs.	4.15	0.14	4.80	0.10	5.19 **
10-14 yrs.	4.97	0.12	5.20	0.13	1.83
15-18 yrs.	4.83	0.11	5.74	0.12	7.82 ***
18+ yrs.	5.08	0.06	5.73	0.07	9.66 ***

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXX

Angular Dimension Upper Incisor to the Basion-Nasion Plane (in Degrees)
Means, Standard Error and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	84.52	2.84	77.03	2.27	2.91 *
6-9 yrs.	81.37	2.84	83.37	1.90	0.83
10-14 yrs.	93.28	2.20	83.25	2.46	4.30 ***
15-18 yrs.	91.64	2.06	85.13	2.27	3.00
18+ yrs.	92.78	1.16	83.82	1.44	7.25

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXXI

Mandibular Plane Angle (in Degrees)
Means, Standard Error and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	46.41	3.39	54.76	1.63	3.14 **
6-9 yrs.	51.77	2.40	51.80	1.35	0.01
10-14 yrs.	48.23	1.70	52.66	1.70	2.61 *
15-18 yrs.	50.95	1.63	52.42	1.57	0.92
18 + yrs.	45.71	0.92	48.00	0.99	2.40

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXXII

Gonial Angle (in Degrees)
Means, Standard Error and the Significance of the Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	122.10	4.11	135.66	1.97	4.21 ***
6-9 yrs.	123.87	2.90	129.04	1.63	2.19
10-14 yrs.	122.81	2.05	125.59	2.05	1.35
15-18 yrs.	126.29	1.97	127.34	1.90	0.54
18+ yrs.	122.64	1.13	121.70	1.15	0.82

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXXIII

Angular Dimension Basion-Nasion - "B" Point (in Degrees)
Means, Standard Errors and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	61.28	2.18	59.87	1.05	0.82
6-9 yrs.	60.41	1.54	60.34	0.84	0.06
10-14 yrs.	64.69	1.09	58.73	1.09	5.48 ***
15-18 yrs.	63.72	1.05	60.64	1.01	3.01 *
18+ yrs.	65.97	0.58	60.60	0.64	8.85 ***

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXIV

Linear Dimension "B" Point to the P.M. Vertical Line (in Centimeters)
Means, Standard Errors and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	4.52	0.34	3.92	0.16	2.25
6-9 yrs.	3.81	0.24	4.49	0.13	3.52 *
10-14 yrs.	4.78	0.17	4.60	0.17	1.03
15-18 yrs.	4.58	0.16	5.11	0.16	3.28 *
18 + yrs.	4.98	0.09	5.19	0.10	2.30

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXV

Linear Dimension Pogonion to the P.M. Vertical Line (in Centimeters)
Means, Standard Errors and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	4.77	0.42	3.87	0.20	2.75 *
6-9 yrs.	3.85	0.29	4.66	0.16	3.43 *
10-14 yrs.	5.09	0.21	4.81	0.21	1.35
15-18 yrs.	4.92	0.20	5.41	0.19	2.47 *
18+ yrs.	5.38	0.11	5.70	0.12	2.84 *

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXXVI

Linear Dimension Articulare to the P.M. Vertical Line (in Centimeters)
Means, Standard Errors and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	2.43	0.12	2.69	0.09	2.39
6-9 yrs.	2.40	0.11	2.83	0.07	4.46 **
10-14 yrs.	2.98	0.09	3.17	0.09	2.07
15-18 yrs.	3.08	0.09	3.10	0.09	0.26
18+ yrs.	3.03	0.05	3.28	0.05	4.84 **

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXXVII

Linear Dimension Gonion to the P.M. Vertical Line (in Centimeters)
Means, Standard Errors and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	1.35	0.32	1.65	0.15	1.23
6-9 yrs.	1.67	0.22	1.71	0.12	0.19
10-14 yrs.	2.12	0.16	2.22	0.16	0.62
15-18 yrs.	2.24	0.15	1.93	0.15	2.06
18+ yrs.	1.96	0.08	2.18	0.09	2.54

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXXVIII

near Dimension Lower Incisor to the P.M. Vertical Line (in Centimeters)
Means, Standard Errors and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	4.55	0.27	4.09	0.13	2.16
6-9 yrs.	4.14	0.19	4.63	0.11	3.13 *
10-14 yrs.	4.93	0.14	4.86	0.14	0.55
15-18 yrs.	4.92	0.13	5.36	0.13	3.41 *
18+ yrs.	5.06	0.07	5.39	0.08	4.46 **

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XXXIX

Angular Dimension Lower Incisor to Mandibular Plane (in Degrees)
Means, Standard Errors and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	99.11	3.91	90.52	1.88	2.80 **
6-9 yrs.	98.44	2.77	91.85	1.56	2.94 **
10-14 yrs.	94.80	1.96	95.48	1.96	0.35
15-18 yrs.	94.29	1.88	93.86	1.81	0.24
18+ yrs.	92.94	1.06	94.75	1.10	1.68

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XL

Angular Dimension "A" Point - Nasion - "B" Point (in Degrees)
Means, Standard Error and the Significance of the
Differences Between the Trisomy and Control Groups

	TRISOMY		CONTROL		
Group Age	Mean	Standard Error	Mean	Standard Error	Duncan Test Difference
3-5 yrs.	5.50	1.52	4.69	0.73	0.68
6-9 yrs.	4.68	1.07	4.67	0.59	0.01
10-14 yrs.	0.29	0.76	2.97	0.76	3.54 **
15-18 yrs.	0.86	0.73	3.73	0.70	4.00 **
18+ yrs.	0.99	0.40	2.75	0.43	4.25 *

* Significant at the 5% confidence level
** Significant at the 1% confidence level
*** Significant at the 0.1% confidence level

TABLE XLI

Linear Measurement Basion to the P.M. Vertical Line
Mean and Standard Error (in Centimeters)

Age Range	TRISOMY 21				CONTROL			
	MALE		FEMALE		MALE		FEMALE	
	Mean	S.E.	Mean	S.E.	Mean	S.E.	Mean	S.E.
3-5 yrs.	3.68	0.10	2.45	0.35	3.66	0.88	3.39	0.14
6-9 yrs.	3.26	0.22	3.70	0.08	3.73	0.10	3.67	0.12
10-14 yrs.	4.29	0.11	4.16	0.20	3.97	0.13	4.09	0.10
15-18 yrs.	4.34	0.08	3.87	0.18	4.21	0.13	3.78	0.13
18 + yrs.	4.39	0.09	4.07	0.06	4.26	0.11	3.88	0.13

TABLE XLII

Linear Measurement Pogonion to the P.M. Vertical Line

Mean and Standard Error (in Centimeters)

Age Range	TRISOMY 21				CONTROL			
	MALE		FEMALE		MALE		FEMALE	
	Mean	S.E.	Mean	S.E.	Mean	S.E.	Mean	S.E.
3-5 yrs.	3.96	0.42	6.39	0.10	3.72	0.15	4.12	0.22
6-9 yrs.	4.02	0.34	3.68	0.18	5.04	0.19	4.41	0.16
10-14 yrs.	5.00	0.27	5.21	0.25	4.96	0.20	4.66	0.10
15-18 yrs.	5.04	0.30	4.54	0.81	5.04	0.29	5.68	0.23
18 + yrs.	5.52	0.15	5.21	0.14	6.00	0.20	5.39	0.22

TABLE XLIII

Linear Measurement Articulare to the P.M. Vertical Line
Mean and Standard Error (in Centimeters)

Age Range	TRISOMY 21				CONTROL			
	MALE		FEMALE		MALE		FEMALE	
	Mean	S.E.	Mean	S.E.	Mean	S.E.	Mean	S.E.
3-5 yrs.	2.86	0.20	1.88	0.25	2.73	0.10	2.62	0.09
6-9 yrs.	2.14	0.24	2.56	0.08	2.91	0.09	2.77	0.08
10-14 yrs.	3.10	0.10	2.81	0.11	3.17	0.09	3.17	0.10
15-18 yrs.	3.20	0.07	2.67	0.06	3.24	0.14	2.99	0.15
18 + yrs.	3.10	0.08	2.95	0.06	3.50	0.09	3.06	0.08

GLOSSARY

GLOSSARY

LANDMARKS:

1. Machine Porion

   The most superior point on the ear rods of the cephalostat and believed to represent the mid-point on the upper edge of the external auditory meatus.

2. Sella (S)

   The centre of the sella turcica (pituitary fossa).

3. Frontale

   The most anterior point on the frontal bone determined by a perpendicular line from the SN line.

4. Nasion

   The mid-point of the fronto-nasal suture at its most anterior margin.

5. Nasal Tip

   The most anterior inferior point on the nasal bones.

6. Orbitale

   The deepest point on the infraorbital margin of the bony orbit.

7. Soft Tissue Nasion

The most anterior point on the soft tissue nose parallel to nasion.

8. Pronasale

The most anterior point on the contour of the soft tissue nose as measured from the N-Pog line.

9. Soft Tissue "A" Point

The most posterior point of the philtrum of the upper lip.

10. Labrale Superius

The most prominent point on the upper lip measured perpendicular to the N-Pog line.

11. Stomion

The lowest point on the upper lip and the highest point on the lower lip (Burstone, 1952).

12. Labrale Inferius

The most prominent point on the lower lip measured perpendicular to the N-Pog line.

13. Soft Tissue "B" Point

The most posterior point on the contour between the labrale inferius and the soft tissue pogonion.

14. Soft Tissue Pogonion

The most prominent point on the contour of the soft tissue covering of the chin.

15. Menton

The most inferior point on the symphysis menti of the mandible.

16. Gnathion

The most anterior and inferior point on the contour of the chin.

17. Pogonion

The most anterior point on the contour of the chin.

18. "B" Point

The deepest point on the midline contour of the mandible between infradentale and pogonion.

19. The apex of the mandibular central incisor.

20. The incisal edge of the maxillary central incisor.

21. The incisal edge of the mandibular central incisor.

22. The apex of the maxillary central incisor.

23. "A" Point

The deepest point on the midline contour at the alveolar process between the anterior nasal spine and the alveolar crest of the maxillary central incisor.

24. Anterior Nasal Spine (ANS)

The median, sharp bony process of the maxilla at the lower margin of the anterior nasal opening.

25. Posterior Nasal Spine (PNS)

The process formed by the united projecting ends of the posterior borders of the palatal processes of the palatal bones.

26. Pterygomaxillary Fissure (PTM)

The projected contour of the fissure formed by the anterior curvature of the pterygoid process and the posterior wall of the tuberosity of the maxilla. The cephalometric radiographic point is the most posterior point on the posterior wall of the maxillary tuberosity.

27. Articulare (Ar)

The point of intersection of the external dorsal contour of the mandibular condyle and the temporal bone. The midpoint is used when the profile radiograph shows double projections of the rami.

28. Condylion

The most superior and posterior point on the mandibular condyle.

29. Basion (Ba)

The most forward and lowest point on the anterior margin of the foramen magnum.

30. Distobuccal cusp tip of the maxillary left first molar.

31. Distobuccal cusp tip of the mandibular left first molar.

32. The most inferior point on the posterior one-third of the lower border of the mandible.

33. Gonion (Go)

The lowest most posterior, and the most outward point on the angle of the mandibular base line and the line tangent to the posterior border of the ramus.

34-37. Anterior and posterior extensions of the palatal plane used as registration points for maxillary and mandibular superimposition techniques and permitting an assessment of changes in the relationships of the dental units (Chebib, Cleall and Carpenter, in press).

38. Opisthion

The mid point of the lower border of the foramen magnum.

39. Inion

The most prominent point on the external occipital protuberance.

40. Ethmoidale

The point of intersection of a tangent to the inferior border of the cribiform plate.

41. The point of intersection of a tangent to the superior border of the odontoid process of Cervical 2.

42. The most posterior inferior point on the odontoid process of Cervical 2.

43. The most anterior point on the anterior tubercle of the atlas.

44. The height of the concavity of the anterior surface of the second cervical vertebrae.

45. The most anterior inferior point on the second cervical vertebrae.

46. The height of the concavity of the anterior surface of the third cervical vertebrae.

47. The most anterior inferior point on the third cervical vertebrae.

48. The height of the concavity of the anterior surface of the fourth cervical vertebrae.

49. The most anterior inferior point on the fourth cervical vertebrae.

50-53. The most posterior points on the fourth, third, second and first cervical vertebrae, respectively.

54. S.E. Point

The point of intersection of the shadows of the greater wings of the sphenoid with the floor of the anterior cranial fossa (representing the boundary between the anterior and posterior portions of the anterior cranial base as well as the boundary between the anterior and middle endocranial fossae - Enlow, 1971).

55. The posterior edge of the olfactory fossa identified by the change in contour of the anterior cranial floor at this point (Enlow, 1973).

56. The anterior limit of the olfactory fossa located at the point where the cribiform plate joins the frontal bone. The roof of the nasal chamber also leads directly into this point (Enlow, 1973).

57. The most anterior superior point on the endocranial surface of the frontal bone (Enlow, 1973).

58. Superior Prosthion

The most anterior inferior point on the premaxilla.

59. That point on the palatal plane formed by the vertical extension from point "A" (point 23) perpendicular to the palatal plane (Queen, 1974).

60. Anatomic Porion

The mid point on the upper edge of the external auditory meatus.

61. That point on the basion-nasion plane formed by the vertical extension from sella (point 2) perpendicular to the basion-nasion plane and used as the origin for superimposition techniques.

CRANIOFACIAL REFERENCE LINES:

1. Anterior Cranial Base

   As defined by cephalometric points sella nasion (2-4).

2. Posterior Cranial Base

   As defined by cephalometric points basion and sella (29-2).

3. Huxley's Basi-cranial Axis

   As defined by cephalometric points basion and nasion (29-4).

4. Ethmoidale-Sella Line

   As defined by the tangent from the cephalometric point sella to the lowermost point on the cribiform plate (2-40).

5. Sella-Sphenoethmoidale Junction

   As defined by the cephalometric point sella and the point of intersection of the shadows of the greater wings of the sphenoid with the floor of the anterior cranial fossa (2-54).

6. Cribiform Plane

   As defined by the anterior and posterior limits of the olfactory fossa (55-56).

7. Martin's Plane

As defined by cephalometric points nasion and inion (4-39).

8. His' Plane

As defined by cephalometric points anterior nasal spine and opisthion (24-38).

9. Frankfort Horizontal (machine porion)

As defined by the cephalometric point orbitale and the most superior point of the ear rods (6-1).

10. Frankfort Horizontal (anatomic porion)

As defined by the cephalometric point orbitale and the upper perifery of the external auricular canal (6-60).

11. P.M. Vertical Line

As defined by the point of intersection of the shadows of the greater wings of the sphenoid with the floor of the anterior cranial fossa and the most inferior point of the pterygomaxillary fissure (54-26).

GENERAL COORDINATE ANALYSIS

PURPOSE: To standardize sets of coordinate points and to calculate angular and distance relationships within them.

METHOD:

a) For each of a group of N subjects, a set of M coordinate (x,y) points is read in. New points may first be generated and added to the original ones. Each subject's points are then "standardized" by having them transformed to a common x-y axis, possibly magnified to bring them to "life size", and/or converted from inches to centimeters. The N subject's original and standardized points are optionally listed and the standardized points are optionally punched. Also an "average" subject is calculated, having as points, the mean values of the group.

b) Then a series of selection cards is read, each requesting a certain operation to be performed on selected points in the N subject group and "average" subject. These operations can be data point checking, calculation of given angles or

distances or rotation centers, etc. All this may be listed and/or punched.

The mean and standard deviation for each selection operation are listed also (and may be punched if desired).