CRANIOFACIAL MORPHOLOGY IN DOWN'S ANOMALY (TRISOMY 21) - A - CROSS SECTIONAL STUDY USING POSTERO-ANTERIOR RADIOGRAPHS

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by

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ABSTRACT

Previous investigations have indicated that there are marked differences in the craniofacial complex of individuals with Down's syndrome as compared with normal subjects.

The purpose of this investigation was to determine if individuals having a Trisomy 21 karyotype show a distinct phenotype and to observe on a cross sectional basis the changes occurring with growth.

The sample consisted of 127 Trisomy 21 and 137 Control subjects, who ranged in age from three to fifty-six years. Linear measurements were obtained from postero-anterior radiographs and by direct measurement on the subject's face. These measurements were statistically analyzed to assess the significant differences between the Trisomy 21 and Control groups through six age ranges.

The significant findings were as follows:

The overall size of the Trisomy 21 individual was

smaller at the age of three years and this smallness persisted into adulthood. In most of the areas studied, growth occurred at a comparable rate and direction to that found in the Controls. However, there were some areas in the Trisomy 21 group, such as the nasal cavity height, maxillary width, and the inter-orbital width which were affected more than other areas of the craniofacial complex. Growth retardation in these areas was present at the age of three years and increases in these measurements occurred at a comparatively decreasing rate as compared to that of the Control group, suggesting that the retardation in the growth of cartilage may be responsible for the characteristic craniofacial morphology of the Trisomy 21 subjects.

The females were smaller than the males in both groups. The differences in growth rates that were found between the sexes in the Trisomy 21 group were also found to occur in the Control group.

Changes in the orbital region of the Trisomy 21 group indicated that at younger age ranges, the most superior points on the orbital outlines were located laterally in relation with the most inferior points on the orbital outlines, giving a lateral slant to the orbits. However, as their ages advanced, the most superior points on the orbital outlines were located medial to the most inferior points on the orbital outlines so that the orbits appeared to have a medial slant similar to that seen in the Control group at all age ranges. This change in the slant of the orbits

of the Trisomy 21 group was due to a diminished increase in the supraorbital width accompanied by the compensatory and normal changes occurring at the inferior and lateral orbital margins respectively.

Asymmetries were found to be present in the craniofacial complex of both the Trisomy 21 and Control groups with a tendency for the left side to be larger. The largest asymmetries occurred in the temporal region of the Trisomy 21 group.

The metopic suture was patent in a high percentage of the Trisomy 21 individuals, similar findings were observed for the presence of sutural bones in the craniofacial complex of the Trisomy 21 group.

The bony orbits in the Trisomy 21 group showed the presence of orbital hypotelorism associated with pupillary hypotelorism. In contrast, the separation between the endocanthions or the eyes showed the presence of occular hypertelorism at all ages.

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CHAPTER I

INTRODUCTION

Over a hundred years ago, the congenital anomaly known as Down's syndrome was described. Since then, not only have several names been used to describe this condition, but several craniofacial abnormalities of these individuals have been reported in the literature. In the light of present day cytogenetic knowledge, it is now realized that Down's syndrome individuals show an extra chromosome, number 21, in the "G" group. Cytogenetic investigations also tell us that these twenty-first chromosome abnormalities may be of the type known as the primary trisomy, the translocation Down's syndrome or the mosaic Down's syndrome. Superficially, the phenotypic manifestations of all these karyotypes seen in Down's syndrome resemble each other to some degree.

It is conceivable that these chromosomal abnormalities represent alterations of gross amounts of chromosomal material, possibly involving hundreds of genes. How this imbalance in the karyotype affects the biochemical mechanisms, which in turn may modify the phenotype, is not yet known. However, it is still necessary to be able to identify the phenotype of these individuals more precisely, so that they may be associated more accurately with their genotype.

With the exception of a few studies, most of the past

roentgenographic investigations have utilized Down's syndrome samples whose karyotype was not identified cytogenetically. Furthermore, several investigators such as Benda (1941), Hall (1964) and Oster (1951) have mentioned that the phenotype of these individuals is more abnormal at a younger age than at older age levels.

This investigation was undertaken to characterize the phenotype of Trisomy 21 individuals in the coronal plane by the use of postero-anterior radiographs. All the Trisomy 21 individuals used in this study were karyotyped, and were found to have 47 chromosomes, with the extra one being number 21 in the "G" group.

The specific purposes of this study were as follows:

1. To measure various craniofacial widths in the Trisomy 21 individuals within six age ranges, and compare them with the widths in a Control sample.

2. To study the horizontal asymmetry of selected bilateral structures in the craniofacial skeleton of the Trisomy 21 individuals, and compare these values with the asymmetry presented by the Control sample.

3. To objectively assess the changes in the orbital outlines as seen on the postero-anterior radiographs of the individuals in the Trisomy 21 and Control groups.

4. To measure the distance between the bony orbits, the pupils and the endocanthions in the Trisomy 21 group relative to the width of the face, and to compare these measurements to that of the Control group.

5. To note the percentage of individuals showing patent metopic sutures in both groups.

6. To note the percentage of individuals showing the presence of sutural bones (wormian) in the cranial sutures in both groups.

CHAPTER II

REVIEW OF THE LITERATURE

I. DOWN'S ANOMALY

History and Terminology

Seguin (1846) described a particular type of mental retardation which he called furfuraceous idiocy. Seguin believed these individuals to be similar to cretins, and in 1866, he gave a detailed description of the furfuraceous cretins. He describes them as having a milky white, rosy, and peeling skin, with a shortcoming of all integuments, giving an unfinished aspect to the truncated fingers and nose, and having cracked lips and tongue, with red ectopic conjunctiva coming out to supply the curtailed skin at the margin of the lids.

James Langdon Down (1866) has been credited by several authors to have recognized this group of individuals as a separate entity. He gave a very precise description of the physical characteristics exhibited by these individuals and suggested that this group of mental defectives was related to the resurgence of traits of the great mongolian race. Hence the term "Mongolism" or "Mongoloid" came into being.

Over the years, since Down wrote his description of the "Mongol", various terms like Kalmuc Idiocy (Fraser and Mitchell, 1876), Unfinished children (Shuttleworth, 1886),

and Congenital Acromicria (Clift, 1922; Benda, 1941) have been used to describe the condition. Allen et al. (1961) proposed avoiding the term "Mongolism" and suggested the names "Langdon Down Anomaly", "Down's Syndrome", or "21 Trisomy". Of these terms, "Down's Syndrome" has come to be preferred, although some investigators still tend to use the term "Mongolism".

Recently, Lejeune (1964) prefers to use the term "21 Trisomy" and avoid the term "Langdon Down Syndrome" on the basis of etiology. He states that the latter term would represent a perpectuation of both an historical error, since Seguin was the first to describe the condition, and an etiological error, since the additional chromosome which causes the disease has no relation to the "Mongolian races".

One must keep in mind, however, that it was Lejeune Gauthier and Turpin (1959b) who were the first to demonstrate that patients having Down's syndrome had 47 chromosomes. The extra chromosome is generally accepted as being an autosomal acrocentric chromosome number 21 located in the "G" group, according to the Paris Conference (1971) report. In this report it is also mentioned that the extra chromosome associated with Down's syndrome is smaller than No. 22 on the basis of their fluorescent banding patterns. This type of Down's syndrome is usually referred to as "Trisomy 21". Hamerton (1971) prefers to refer to these individuals as "Primary Trisomics".

Shortly after the discovery of Trisomy 21, it was evident that not all cases of Down's syndrome were characterized by Trisomy. Polani, Briggs, Ford, Clarke and Berg (1960) reported on an individual showing similar physical characteristics to Trisomy 21 but having only 46 chromosomes. This type of Down's syndrome is due to the fertilized ovum containing an extra chromosome number 21 which becomes attached to a chromosome of the "D" or "G" group or due to isochromosome formation. This type of Down's syndrome is known as the translocation Down's syndrome. Hamerton (1971) refers to these individuals as "secondary trisomics".

A third cytological type of Down's syndrome is the mixoploid or mosaic Down's syndrome. Clarke, Edwards, and Smallpiece (1961) showed that in this condition a certain proportion of the cells in the affected individuals contain the extra chromosome, but the remaining cells have a normal number of chromosomes.

The term "Down's syndrome", therefore, describes a group of mentally defective individuals whose physical characteristics bear some resemblance to each other. However, at a cytogenetic level various types of karyotypes may be exhibited by these individuals.

Etiology

Down's concept of reversion to an earlier phylogenetic type was short lived (Down, 1866). Since that time, several

theories have been advanced to explain the etiology of Down's syndrome.

Warkany, in 1960, presented a list of 39 theories that had been proposed until 1959 to explain the etiology of Down's syndrome. These were divided into four main groups.

> (1) reversion to a primitive ancestral type, (2) a genetic origin involving one or more genes, mutations, injury to germ cells, or interaction of the embryonic genetic constitution with the uterine condition, (3) disturbances in the uterine environment, including accidents during gestation, disease states, ageing of the mother, or ageing of the ovum, and (4) changes within the child, especially endocrine deficiencies.

The area where there is general agreement is that the frequency of Down's syndrome births increase with maternal age. As long ago as 1909, Shuttleworth had suggested that the condition was related to the advanced age of the mother but he also felt that the affected individual was the last born in a large family. Thus, he did not differentiate whether Down's syndrome was related to maternal age or birth order.

Jenkins (1933) and Penrose (1933a), from the examination of the maternal and paternal ages of Down's syndrome individuals, independently showed that the age of the father by itself was of no significance. Penrose (1954) has shown that the incidence of Down's syndrome is related to the increased age of the mother and is not dependent on paternal age or birth order.

The fact that a chromosomal aberration might be implicated in Down's syndrome was suggested by Waardenburg (1932). He believed that it occurred due to non-disjunction. This theory was not accepted, because as yet, the normal number of chromosomes in man was not firmly established. Furthermore, there was no evidence to suggest that non-disjunction could be influenced by maternal age.

Tjio and Levan (1956) found that the normal diploid chromosomal number in man was 46. Shortly thereafter, this was confirmed by Ford and Hamerton (1956), who found that the haploid number of chromosomes in man was 23.

To Lejeune, Gauthier and Turpin (1959b) goes the credit for being able to demonstrate an extra autosomal chromosome number 21 in the "G" group of Down's syndrome individuals. This was believed to occur due to non-disjunction, occurring in the early meiotic division. The karyotype of a Trisomy 21 individual showing an extra chromosome in the "G" group is shown in Figure 1.

The finding of the translocation or secondary Trisomy type of Down's syndrome was important, as it could explain one of the major reasons for the familial occurrence of Down's syndrome. The translocated chromosome can be carried by a normal person and be transmitted through several generations. Several ways in which a translocation can occur in Down's syndrome have been postulated by various authors.

In the mosaic Down's syndrome, certain cells contain the extra chromosome, but the remaining cells have the normal

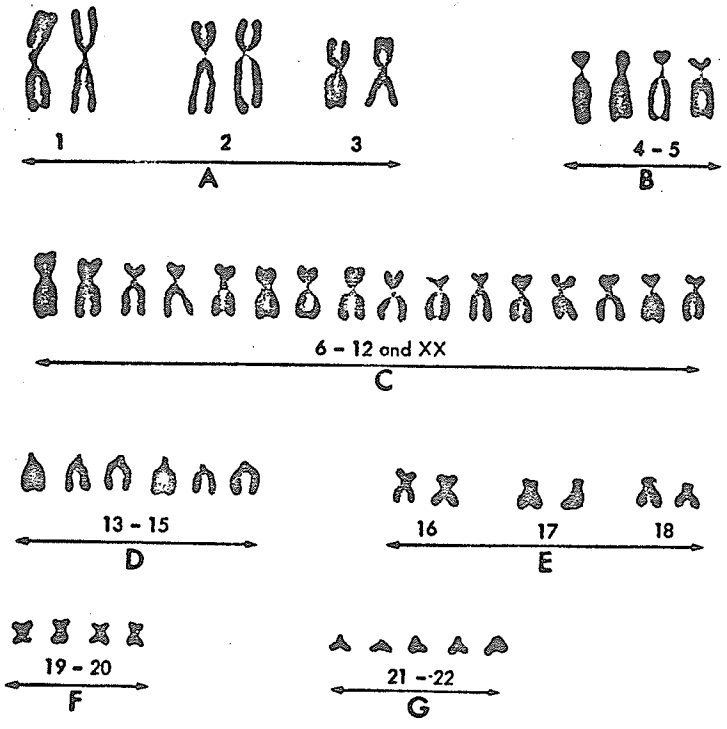

Figure 1. Karyotype of a Trisomy 21 female. Three chromosomes instead of two are noted in group G, site number 21.

number of chromosomes. 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.

Penrose and Smith (1966) have reviewed the reports on the finding of Down's syndrome individuals with other chromosomal anomalies, such as Klinefelters, Triple X, and Turner's syndromes. In some cases, the karyotype of individuals with Trisomy of the 21st chromosome also showed a Trisomy of chromosome 18, and in another case the individual was trisomic for a chromosome in the 13-15 group. Recently, Sommer and Eaton (1970) reported the finding of an extra chromosome number 21 in an Achondroplastic dwarf.

It is interesting to note that in the case of achondroplasia with Trisomy 21, described by Sommer and Eaton (1970), the diagnosis of Trisomy 21 was initially missed, because achondroplasia is a condition where the growth of bone derived from cartilage is reflected in the dramatic shortening of the limbs, and the chondrocranium shows a shortened cranial base. This malformation of the cranial base gives the achondroplastic dwarf an appearance of having a depression of the root of the nose with a large cranium and an overhanging brow. This appearance is similar in some ways to the midfacial deformity seen in Down's syndrome.

Clinical Diagnosis

Attempts to make a clinical diagnosis of this syndrome does not depend upon one single factor being present in these individuals but rather on a number of cardinal signs that these individuals may exhibit. Identification of these cardinal signs in an individual may be difficult because of individual variability, and the possibility that some of these signs may be present at one age but may not be at another. Some of the physical characteristics seen in Down's syndrome are shown in Figure 2.

Since Down's syndrome is a chromosomal disorder, characterized by a general growth deficiency which affects every organ system in the body, several clinical features of this syndrome have been described.

The presence of a high incidence of cardiac malformations in Down's syndrome individuals has been shown by several investigators such as Berg, Crome and France (1960), Rowe and Uchida (1961), and Rowe (1962). These authors, along with Esen (1957), have commented on the high infant mortality rate within the first year or two of life due to these cardiac malformations.

Lowe (1949) has mentioned the various abnormalities in the eyes. Penrose and Smith (1966), among others, have noted that the skin appears to be too large for the skeleton in these individuals. Caffey and Ross (1956, 1958)

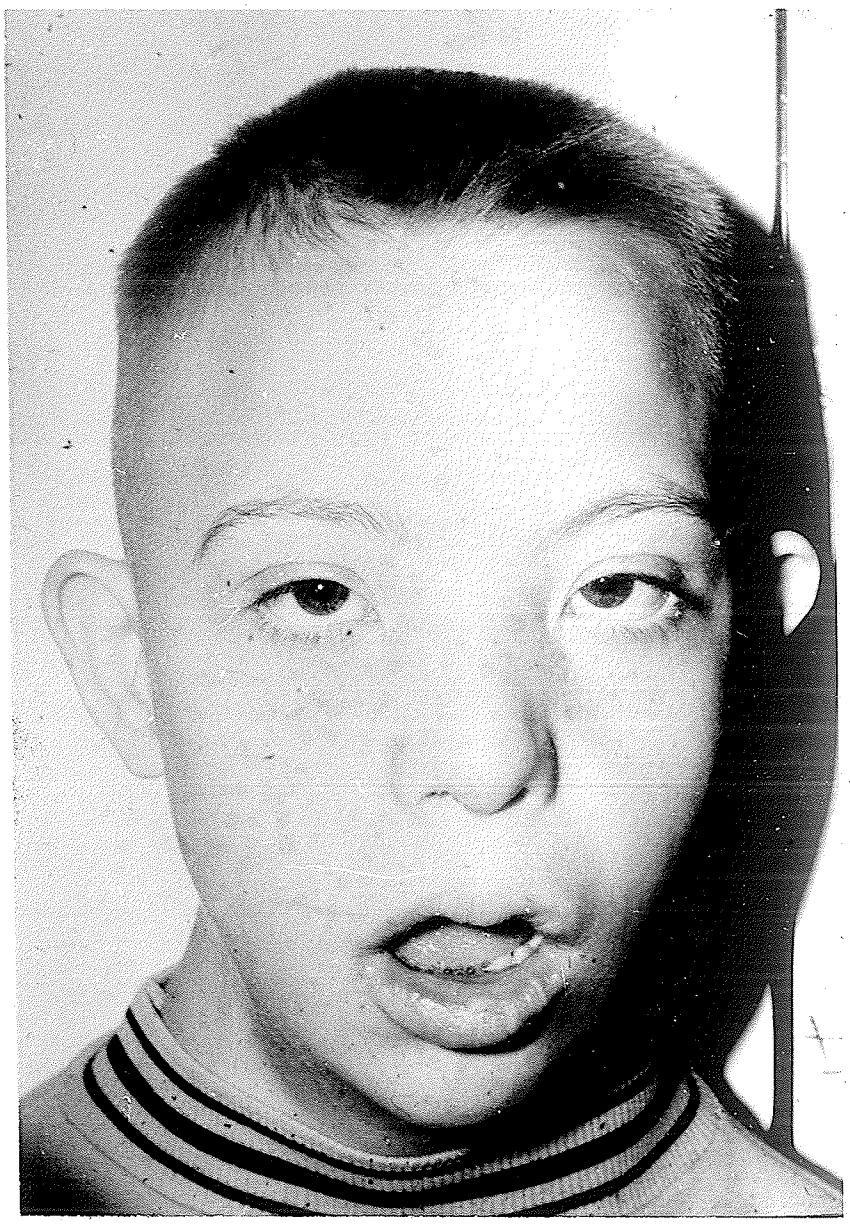

Figure 2. Some physical characteristics seen in a Down's syndrome male. Note: Epicanthic folds, slanting palpebral fissures, convergent strabismus, depressed nasal bridge, open mouth posture and fissured lips.

showed that the morphological characters of the pelvis deviated from normal, as the iliac and acetabular angles were decreased in Down's syndrome. McIntire, Menolascino, and Wiley (1965) have reported on the generalized hypotonia and other abnormalities in these individuals.

Characteristic dermatoglyphic patterns in Down's syndrome were first mentioned by Cummins (1936, 1939). It is known that in Down's syndrome there is a strong tendency for every finger to possess a loop rather than a whorl or arch. The distal triradius is high, giving a maximal Atd angle. Hypothenar patterns are common and usually a single palmar flexion crease and a single fifth finger crease is present.

Oster (1953) selected ten cardinal signs and felt that individuals showing four or more of these signs could be classed as having Down's syndrome. His ten signs were: (1) a four finger line, (2) a short, crooked fifth finger, (3) short broad hands, (4) hyperflexibility, (5) oblique, palpebral fissures, (6) epicanthus, (7) a furrowed tongue, (8) irregular, abnormal sets of teeth, (9) a narrow, high palate, and (10) a flat occiput (brachycephaly). Gustavson (1964) selected his sample on the basis of four of Oster's signs and listed an additional 21 signs.

Hall (1964, 1966) felt that in many newborn Down's syndrome individuals a clear cut picture was not evident at birth but became more evident at the age of one

year. He cites ten cardinal signs in the order of frequency of occurrence in the newborn: (1) a flat facial profile 90%, (2) an absent moro-reflex 85%, (3) muscle hypotonia 80%, (4) oblique palpebral fissues 80%, (5) an excess of skin in the back of the neck 80%, (6) hyperflexibility of the joints 80%, (7) a dysplastic pelvis (x-ray) 70%, (8) a dysplastic ear 60%, (9) a dysplastic middle phalanx of the fifth finger 60%, and (10) a simian crease of the palm 45%.

Gustavson (1964) has come to the conclusion that the diagnostic value of the chromosomal analysis in suspected cases of Down's syndrome, where a clinical diagnosis cannot be made, is invaluable. Present day methods of diagnosis of Down's syndrome in individuals tend to rely on cytological confirmation of the condition, even though it may have been diagnosed clinically.

Attempts have also been made to distinguish the phenotype of the three basic types of Down's syndrome, that is, Primary Trisomy 21, Translocation Down's syndrome, and Mosaic Down's syndrome. It is generally agreed that in Mosaics, a wide range of physical signs of Down's syndrome to an apparently normal phenotype may be seen (Gustavson, 1964; Hamerton, 1971). This variability in phenotype is presumably related to the proportion of cells in the body which are trisomic for chromosome number 21. Phenotypic differentiations between translocation and primary trisomics are, however, difficult to find. Hall (1964) could not demonstrate any significant differences between these two

groups. Gibson and Pozsonyi (1965) have noted some differences on the basis of morphological and dermatoglyphic patterns and psychological behavior in the translocations and primary trisomics. However, since there were only 20 individuals in their sample, further evaluation with larger groups would be required to reach some definite conclusions.

The craniofacial area in Down's syndrome

The craniofacial area in the Down's syndrome individual is believed to have a distinct phenotype. These phenotypic traits are believed to be of considerable diagnostic significance. Roentgenographic studies by Sassouni et al. (1964), Ghiz (1968), and Frostad, Cleall and Melosky (1971) indicate that these phenotypic traits may be recognized quite early in the life of the Down's syndrome individual.

Cranium. Several investigators have stated that in Down's syndrome, the growth of the cranium in length is more severely affected than the growth of the cranium in width (Benda, 1940; Gosman and Vineland, 1951; Roche, Seward and Sunderland, 1961a; Thelander and Pryor, 1966; Spitzer, Rabinowitch and Wybar, 1961; Kisling, 1966; Roche, 1966). These authors note that this great deficit in the length of the skull results in extreme brachycephaly. Kisling, in 1966, from his measurements of the cranial index of 69 Down's syndrome adults, showed that 52% of Down's syndrome individuals were brachycephalic, 18% showed hyperbrachycephaly, 21% were mesocephalic, and 3% were dolichocephalic. In

contrast, his normal sample showed 55% of the individuals were mesocephalic, 22% were dolichocephalic, and 21% were brachycephalic. Very low percentages were found in the hyperdolichocephalic or hyperbrachycephalic range in the normal sample.

Benda, in 1940, has mentioned that in the newborn Down's syndrome individual, there is an increase in cranial breadth, due to increase in the size of the brain. This, he felt, resulted in the protrusion of the parietal and temporal bones, which gave a rounded appearance to the skull, so that the length and the width of the skull were equal in some cases. Hall (1970), in a follow-up study of Down's syndrome individuals, noted that the round head shape of the newborn was changed with age and was characterized in the adult by a flat occiput in 16 out of his 22 cases. Gosman and Vineland (1951) also felt that in Trisomy 21 individuals, the greatest deficiency was in the occipital region. However, Moss (1967), using Kisling's templates, felt that the microcephaly in Down's syndrome was uniform if the posterior cranial base was used as a plane for the superimposition of the radiographs.

Thelander and Pryor (1966) suspected brain damage to be a possible cause for the greater deficit in cephalic length than in cephalic breadth. Benda (1940), however, felt that the cranial length was affected, due to insufficient growth at both the synchondrosis, lack of frontal sinus development, and failure of the flat bones to

develop.

Studies of the Trisomy 21 individuals by the use of lateral cephalometric radiographs by Ghiz (1968), indicate that in the Trisomy 21 individuals, the cranial base angle is obtuse at four years and continues to become more obtuse with increasing age, resulting in the flexion of the posterior cranial base. Kisling (1966) noted that in adult mongoloids, the anterior cranial base was shorter than the posterior cranial base, as measured from Sella to Nasion, and Sella to Basion, respectively. The findings of Ghiz and Kisling as regards flexion of the cranial base are in agreement with each other. Kisling also notes that on the postero-anterior radiograph, the width of the anterior cranial base is smaller than normal in the Down's syndrome individuals.

Upper face. Spitzer and Quilliam (1958), when comparing the morphological characteristics of Down's syndrome individuals and another group of mental defectives, came to the conclusion that mainly the visceral part of the skull, that is, the facial skeleton and the dentition, were affected in Down's syndrome individuals.

Thelander and Pryor (1966), in a cross-sectional study of Down's syndrome individuals from six months to 15 years of age, found by anthropometric measurements that the width of the face was reduced in Down's syndrome individuals. Kisling (1966), in his study, also found that

the biauricular and bizygomatic widths were reduced in adult Down's syndrome subjects.

Spitzer, Rabinowitch and Wybar (1961) reported that 50% of the individuals with Down's syndrome had abnormally low cribriform plates, shortened nasal septa and high arched palates which resulted in a considerable narrowing of the nasal cavities. Jensen (1972), however, reported that the individuals with the Trisomy 21 had significantly narrow but low palates.

Kisling (1966) stated that all three dimensions of the maxilla were considerably reduced, in adult Down's syndrome individuals. Spitzer et al. (1961) also reported on the hypoplasia of the maxilla, and commented that the retracted position of the maxilla under the protruding forehead is due to a lack of antero-inferior thrust of the maxilla during growth periods.

Frostad, Cleall and Melosky (1971),with lateral cephalometric radiographs, made from the individuals with Trisomy 21, observed that the maxilla appeared to be less retrusive because of the more sloping forehead due to its growth changes, although the maxilla was definitely underdeveloped. They also reported the agenesis of the nasal bones in 8.25% of the Trisomy 21 group, and stated that the nasal bones, when present, were reclined at a more acute

angle with the Sella Nasion plane. Changes in the frontal bone were also observed, despite the fact that bilateral absence of frontal sinuses was recorded in over 85% of the Trisomy 21 individuals. Similar observations on the diminutive size or missing air sinuses and sclerotic mastoid air cells have been reported by Benda (1940), Spitzer and Quilliam (1958), and Spitzer et al. (1961).

The eyes in Down's syndrome reveal several abnormal findings. These findings are usually slanting, palpebral fissures, epicanthic folds, blepharitis, estropia, cataracts, nystagmus, and Brushfield spots (Lowe, 1949; Penrose and Smith, 1966).

Clemens (1949), and Penrose and Smith (1966), state that there are differences in the epicanthic folds seen in Down's syndrome, Oriental and in normal Caucasian individuals (Figure 3A, B and C). Clemens discusses the epicanthic fold in detail and states that the epicanthic fold in Oriental races (Figure 3B) hides a large part of the pars tarsalis or the upper eyelid, while the epicanthic fold in Down's syndrome (Figure 3A) arises from the pars orbitalis as a skin fold, which is called the plica marginalis. This skin fold covers the more medial part of the eyelids or only the caruncle, without stretching across a major portion of the pars tarsalis. Penrose and Smith (1966) state that, the

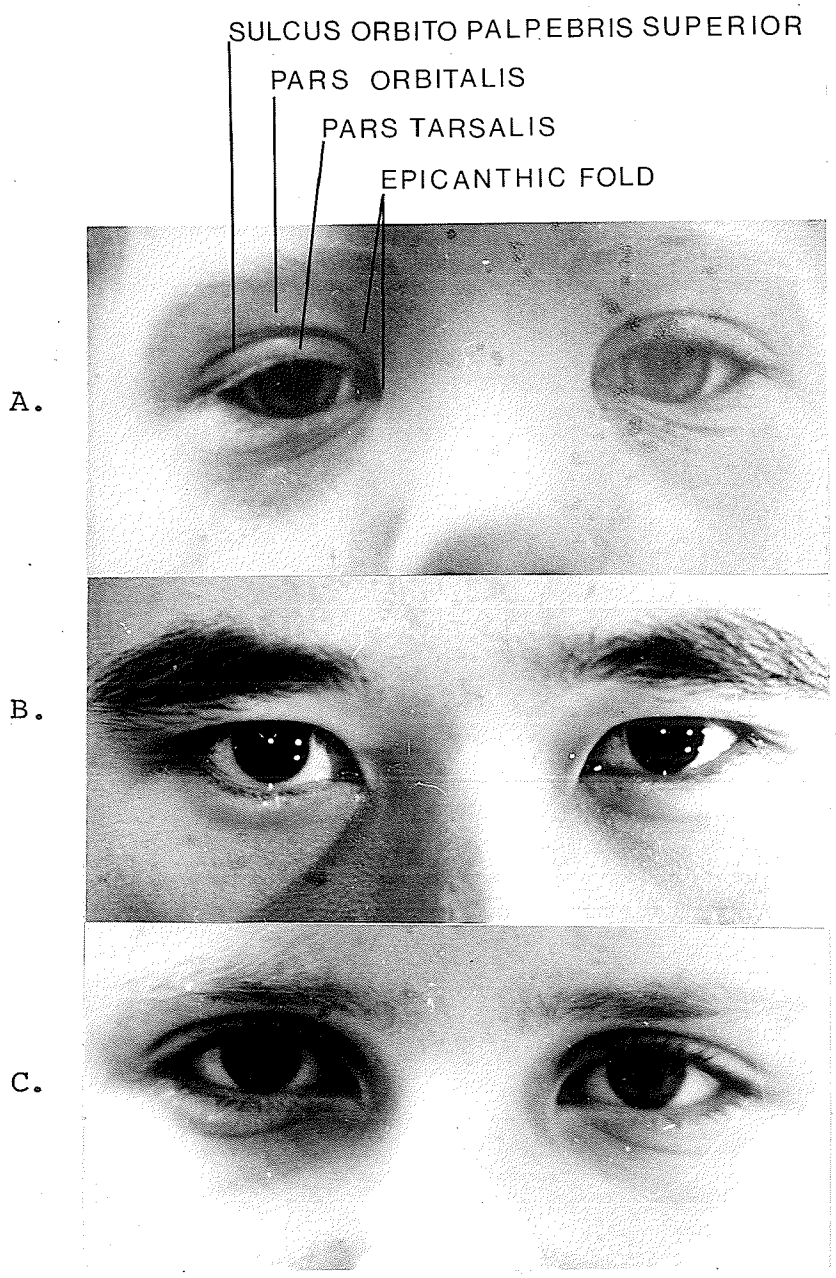

Figure 3. The eyes in A. Trisomy 21, B. Oriental, and C. Normal Caucasian. See text for differences in epicanthic folds in Trisomy 21 and Oriental.

type of epicanthic fold seen in Down's syndrome is also believed to be present in normal children at very young ages but is found to be usually absent in normal Caucasian children (Figure 3C) after the age of four years.

Clemens (1949), reports that the epicanthic fold in Down's syndrome, is usually present before five years of age. Benda (1969) believes that this epicanthic fold tends to disappear by 12 years of age. Eissler and Longenecker (1962), in their study on the presence of the epicanthic fold, showed a higher incidence in younger individuals than in older ones, and some Down's syndrome individuals in their sample showed the presence of epicanthic folds, even in the age range of 51-55 years. Cohen and Winer (1965) found the epicanthic fold to be present in 79.7% of his subjects, ranging in age from 3-30 years. Solomons, Zellweger, Jahnke and Opitz (1965) found that 68% of Down's syndrome individuals below the age of 10 years showed epicanthic folds, and these folds were only present in 9% of individuals above the age of 10 years. In comparison, they found epicanthic folds to be present in 20% of normal children below 10 years of age and 3.3% of normal children above the tenth year of life. Benda (1940) listed this characteristic as one of the pathognomonic signs for the recognition of Down's syndrome in the age group from 2-15 years. In 1956, Benda does not consider it as a reliable symptom, as he believes their frequency is less than what one would expect them to be. Benda attributes the epicanthic folds to the presence of a flat bridge of the

nose, especially in the newborn.

Conflicting reports exist on the presence of occular telorism. Thelander and Pryor (1966) found the inter-pupillary distance to be close to the mean of the normals at each age and sex level in Down's syndrome. Kisling (1966) found the inter-pupillary distance to be smaller than the Controls in adult Down's syndrome individuals. He also noted that the distance between the endocanthions of the eyes was the same for the Control and Down's syndrome groups. Kisling quotes Weygandt (1927), who holds that the distance between the eyes was greater in Down's syndrome than in normal children. Kanner, in 1935, felt that the eyes were very near to each other, although the flat bridge of the nose may give the impression that they are more widely spaced. Wilson (1940) notes that the eyes were set wide apart. Spitzer, Rabinowitch and Wybar (1961) held the distance between the eyes to be greater than normal for Down's syndrome children. Draper, Dupertuis and Caughey (1944) also believed the eyes were wide apart in Down's syndrome. Lowe (1949) reported that the mean inter-pupillary distance in adult cases with Down's syndrome was 5 mm. less than in normal individuals, and Kerwood, Lang-Brown and Penrose (1954) found that in comparison with the head breadth, the inter-pupillary distance in Down's syndrome adults was reduced.

Gerald and Silverman (1965), indicated from their study of Down's syndrome individuals that a narrowing of the inter-orbital distance was a pathognomonic sign in Down's

syndrome, although no correlation was made of the inter-orbital distance in relation to the individuals facial or cranial measurements. Contrary to these findings, Spitzer, Rabinowitch and Wybar (1961) report a widening of the inter-orbital distance in 51% of their sample.

Frostad, Cleall and Melosky (1971) showed, in a study using lateral cephalometric radiographs of Trisomy 21 individuals, that the height of convexity of the roof of the orbit was higher than that found in the Control group. As regards the anterior opening of the orbit, which was represented by the angle formed by superior orbitale to inferior orbitale to sella, they note that this angle was larger in the Trisomy 21 group than in the Control, however, it tended to decrease with age. Similar findings were reported by Kisling (1966) in his adult group of Down's syndrome individuals. In addition, Kisling could not show any differences in the orbital height of his Control or Down's syndrome group. Benda (1941) wrote that the orbits seemed to be extremely large in proportion to the face in the newborn, while, in 1956, Benda wrote that they were smaller in Down's syndrome than in normal children of comparable ages. Lowe (1949) described the orbits as shorter.

Lowe, in 1949, from the measurements of four adult Down's syndrome skulls, found that the antero-posterior axis of the orbits in Down's syndrome is about 75 degrees, as compared to 45 degrees in the normal. He notes that the

apices of the orbits were very close to their medial walls, and the anterior opening faced downwards and outwards.

Benda (1946, 1969) reported the presence of "Egg shaped" orbits in Down's syndrome. He indicated that the shape of the superior orbital outline sloped upwards and outwards. Spitzer, Rabinowitch and Wybar (1961) do not accept the contention of Benda (1946) that the superior orbital border follows an upward curve towards its external border, even though subjective assessments in their sample showed 50% of Down's syndrome individuals to have the egg-shaped orbital margins as mentioned by Benda. However, Frostad, Cleall and Melosky (1971)*, from subjective observations on P.A. radiographs, felt that the orbits were obliquely situated in Trisomy 21 individuals.

Lower face. In contrast to the facial abnormalities seen in the upper face, the lower face in the Down's syndrome individual has a prognathic appearance. Ghiz (1968) showed that this characteristic prognathic appearance in Trisomy 21 individuals appears to be due to a mandibular basilar prognathism in conjunction with a normal positioning of the maxilla. Korkhaus (1957) believed that Down's syndrome individuals had macroglossia, and he states that the extra-ordinary antero-posterior growth of the mandible in Down's

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* It may be noted that in the paper by Frostad et al. (1971) Figure 7a may be read as Trisomy 21 and Figure 7b should read as normal, as there is a typographical error in the article.

syndrome could be explained by the presence of a large tongue. Jensen (1972), in his study of maxillary and mandibular arch widths in Trisomy 21 individuals, found that mean values for arch width in the Trisomy 21 were smaller at younger ages but approached that of the Control individuals at older ages. Jensen (1972) states that this finding may be the result of abnormal tongue size and function.

Spitzer et al. (1961) noted that both the body and ascending ramus were small. They attributed these findings to deficient condylar and appositional growth of the mandible. Similar findings have been reported by Ghiz (1968) and Kisling (1966) for the length of the body and ramus. In addition, Kisling (1966) found the bigonial width to be smaller than that of the normal in adult Down's syndrome individuals. Gosman and Vineland (1951) found the bigonial distances slightly reduced, the body of the mandible was short, but the height of the ramus was normal.

II. NORMAL GROWTH OF THE CRANIOFACIAL COMPLEX

General Considerations

Krogman (1951) reports on useful approximations of prenatal and postnatal facial growth. He indicates that prenatally facial growth in width is already 55 to 60% complete, while height is 40 to 45% complete and depth (antero-posterior) is 30 to 35% complete. Therefore, he states that postnatally, one could expect the largest

increases would occur with depth, followed by height and least in width.

A few years after the advent of roentgenographic cephalometry, Broadbent (1937) published an article where he mentions that the face grew downwards and forwards from the cranial base. Brodie (1941), from his longitudinal lateral cephalometric study of growth in individuals from three months to eight years, concluded that the morphological pattern of the head was established by the third month of postnatal life, and thereafter, remained constant. This conclusion by Brodie was brought about by his using the mean values of his sample, although he had recognized that individual variations did exist. Brodie, again, in 1953, working on an older group of individuals from eight to seventeen years, came to the same conclusion, i.e., the morphological pattern of the face remains constant.

Contrary to the idea of constancy in craniofacial growth, as suggested by Brodie (1941, 1943), and Broadbent (1937); Bjork (1955) established that individual variation in the growth of the craniofacial complex did exist. He states that the "individual age changes in form vary in magnitude irrespective of whether or not the average form for a given feature changes with age".

Salzmann (1966) notes that postnatally there are three principle sites of skull growth which are as follows: (1) The cartilagenous growth areas of the craniofacial complex represented by the spheno-ethmoidal synchondrosis,

the spheno-occipital synchondrosis, the mandibular condyles, and the nasal septum; (2) growth may occur by proliferation from the growth centers towards the sutures. Salzmann indicates that this method of skull growth is most active in the early years of life; and (3) finally, he mentions that surface apposition and resorption is an important method of face growth, especially during late childhood and adolescence.

There is no doubt that all these three methods contribute to growth of the craniofacial area. However, controversy still exists as to whether the cartilage or sutural connective tissue plays a leading role. Sicher and Du Brul (1970) state that the suture is an active growth site and that the cranial vault expands by proliferation of the sutural connective tissue and not by a mere apposition of new bone at the suture.

Scott (1953a, 1954a) suggests that cartilage or an organ such as the brain is the main component of growth which acts to separate different bones, while sutures serve a secondary function, by acting as adjustment sites. According to this view, the bones grow by separating mechanisms which may be situated at some distance from the sutures.

Moss (1962) believes in the theory of growth called the functional matrix theory. According to this theory, each function is carried out by a group of soft tissues which are supported and/or protected by related skeletal elements. This group of soft tissues and skeletal elements is called

a functional cranial component. The soft tissue related to the function is termed the functional matrix while the skeletal element related to the same function is called the skeletal unit. It is considered that the origin, growth, and maintenance of the skeletal unit depends almost exclusively upon its related functional matrix. In short, it is implied that the shape and size of any given skeletal unit is related to the form and function of its soft tissue contents.

As regards the relationship of growth between the individual parts of the facial skeleton, Scott (1953a) states that there is a low correlation between the growth of the facial skeleton with the growth of the cranium. He considers the facial skeleton as a unit that is built up of semi-independent regions, each with its own pattern of growth and development. He states that certain regions, such as the orbital cavities, the upper parts of the nasal cavities, and the lower border of the mandible are largely under genetic control and show a high degree of independence of functional activity in their development, while other regions, such as the alveolar process, the zygomatic arches, and the lower parts of the nasal capsule may probably show a greater response to functional variations.

In the same vein, Meredith and Higley (1951) studied the relations of dental arch width to cranial width, bizygomatic width, and the width of the mandible. No significant correlations were found by these investigators.

Growth of the human craniofacial complex is essentially a three dimensional process. Several articles have been written of the growth of the craniofacial complex in the vertical and antero-posterior dimensions. The literature, however, is lacking on the growth in the width of the craniofacial complex. Since this study is based on finding the differences in width of the craniofacial complex in the Trisomy 21 and Normal individuals, the literature explaining growth mechanisms involved in the growth of the craniofacial complex in the horizontal and vertical dimensions will be reviewed.

Cranium

The cranium consists of the cranial vault and the cranial base. The cranial vault is made up of bones which are membranous in origin and consist of the frontal, the parietals, the squamous portion of the occipital, the temporals, and a part of the greater wings of the sphenoid. The cranial base mainly is made up of bones derived from cartilage, except for the frontal and the greater wings of the sphenoid which ossify in membrane. According to Scott (1957), growth of the cranial vault is closely correlated to the growth of the brain. Growth of the cranial vault also takes place by surface deposition and partly at the coronal, lambdoidal, and sagittal suture systems. Sicher (1970) states that the growth of the external surfaces of the cranial vault is associated with

its superstructures.

Scott (1957) notes that the growth in width of the cranial base takes place at the suture between the body and greater wings of the sphenoid. He believes this area plays an active role in regulating the width between the eyes during the first year of life, after which the greater wings are united to the sphenoid body.

Ford (1958) studied the width of the cartilagenous cribriform plate of the ethmoid in skulls ranging from birth to adulthood. He found that the cribriform plate was united with the orbital part of the frontal bone prior to completion of the eruption of the deciduous dentition, which occurs at the age of approximately two years. His findings also indicate that the cribriform plate increased in width by 1.6 mm. from birth to two years, although his adult group showed a 1 mm. shorter cribiriform plate than that found in the newborn skull, he believes that this was due to encroachment of the orbital plates of the frontal bone upon its intracranial surface.

Upper face

Face width. The width of the face is represented by the width between the zygomatic arches, as measured on postero-anterior radiographs. Scott (1967) states that this measurement is taken approximately in the region of the zygomatico-temporal suture which is an important growth

site. Growth at this suture continues for a longer time than at any other facial suture. Scott believes that this growth is concerned with the growth of the brain and may also be correlated in its growth with the cartilage of the spheno-occipital synchondroses.

Enlow (1968) presents a very interesting concept of the deposition and resorption changes that take place in the zygomatic arch area. He divides the zygomatic arch into an anterior part, which is related to the growth of the lateral wall of the orbit and the cheek bone, while the posterior portion of the zygomatic arch is related with the temporal fossa and represents the width of the face, as measured on the postero-anterior radiographs. He notes that in the anterior part of the zygomatic arch, the lateral orbital wall moves laterally and posteriorly. The posterior part of the zygomatic arch is depository in nature on its lateral surface, while the medial surface of the arch is resorptive in nature. He states that it is these combined processes of apposition and resorption that allow a lateral movement of the entire arch.

Woods (1950), from his data on serial postero-anterior radiographs corrected for magnification on a group of children from three to fifteen years, found that the bizygomatic width increases at a slowly decreasing rate. The females in his group increased in the same fashion as the males. Most of the females were smaller than the males, although exceptions were found. His findings also

tend to indicate that the female increases slightly in the tenth and eleventh year so that her measurements approach that of the male until the thirteenth year, and then the males goes ahead once again. This, he believes is probably due to the onset of adolescence.

Meredith (1954) determined the soft tissue bizygomatic width of children from the age of four to ten years, and he provides norms for North American children for each age within that age range. His findings indicate that the increase in bizygomatic width is somewhat rapid up to six years, but the increments are reduced for the ensuing four year period.

Nasal cavity. The nasal cavity can be divided into an upper nasal part and a lower inferior maxillary part. Scott (1957) believes that the height of the nasal cavity is determined by the cartilagenous nasal septum, and at birth the upper part of the nasal cavity is twice as high as the lower part, while the lower part continues to grow until adult life is reached. He also states that the width dimensions of the upper nasal cavity are about 75% of their adult dimensions by one year of age, and their adult dimensions are reached by about the tenth year of life. The width of the lower part of the nasal cavity continues to increase beyond the first decade of life, due to apposition and resorption changes at the partition between the lateral nasal wall and the lower part of the antrum.

Keith and Campion (1922), commenting on the deviation of the nasal septum, felt that the bending of this structure occurred partly due to a lack of harmony in the growth of the septal cartilage and the maxillary sutural sites, inclusive of the vomer.

Sassouni and Forrest (1971) felt that rarely before the age of seven is the septal cartilage deviated, and from this age onwards, increased deviations are seen. They attribute these deviations to the fact that, until the age of seven, the nasal septum promotes downward growth of the palate and the sutures adjust to this force. Later on, the nasal septum may no longer be the prime force, or the sutures tend to loose their growth potential, which may lead to a disproportional co-ordinated activity, creating a deviated septum.

Maxilla. Scott (1959) observed that the relationship between the pterygoid plates and the maxillary tuberosity was interesting, because the growth between the greater wings of the sphenoid during fetal life is correlated with the growth at the midpalatal suture. However, soon after birth, when the greater wings of the sphenoid unite with the sphenoid body, the pterygoid processes no longer undergo a bodily separation, and this, Scott feels, would greatly limit the amount of growth in width of the palatine bones at the midpalatal suture.

Scott, in 1957, had stated that lateral separation

of the maxillary bones was still possible after the third year, due to the growth at the suture between the maxilla and the zygomatic bone, as the growth of the orbital contents involved some outward growth of the zygomatic bone, which forms part of the lateral wall of the orbital cavity. Scott also felt that the growth of the lower jaw, by acting through the articulation of the teeth, may influence the separation of the maxillary bones at the midpalatal suture. He also believes that in the latter part of childhood, any growth in width of the maxilla, or the facial skeleton for that matter, took place by surface apposition with internal resorption.

Sicher and Du Brul (1970) indicated that the lower parts of the pterygoid processes of the sphenoid were divergent, and appositional changes took place in this region to allow for changes in the width of the maxilla. They also felt that transverse growth at the median palatine suture was simultaneous with, and correlated to, the widening and downward shifting of the antero-posteriorly growing maxilla. They, however, have associated the downward and forward shift of the maxilla to active growth at the fronto-maxillary, zygomatico-maxillary, zygomatico-temporal, and the ptergo-palatine sutures. This is in contrast to Scott's belief that the septal cartilage of the nose is the main component concerned with the downward and forward growth of the maxilla. Supporting Scott's belief are the animal experiments of Wexler and Sarnat (1961), who showed that

the growth of the maxilla was affected when the growth of the nasal septum was interfered with.

Keith and Campion (1922), from their simplistic superimpositions of a five year old and adult skull, felt that the most important suture contributing to the width of the maxilla was the midpalatal suture. Sassouni and Forrest (1971) comment that the role of the midpalatal suture is not well understood and feel that it is an area of adjustment rather than an area which causes the two halves of the maxilla to expand. They believe that increases in dental arch width are associated with alveolar remodelling, mesial drift of the molar, and anterior relocation of the maxilla.

Bjork (1964), with the aid of metallic implants on either side of the midpalatal suture, showed that there was activity in the midpalatal suture until early adulthood. He found that there was a 1 mm. per year separation of the implants till five years of age, with decreased growth activity prior to puberty, followed by a 1.5 mm. per year separation of the implants thereafter. No growth activity was seen in the sagittal suture after the age of 17 years in boys.

Orbits. The growth of the orbits is probably the most complex, as its walls are composed of the separate frontal, maxillary, sphenoidal, ethmoidal, lacrimal, and zygomatic bones. Enlow (1968) indicates that growth of the orbit is not only associated with its own soft tissue

contents but also with the nasal chambers on the medial side, the dental arch below, the brain above, and the muscles of mastication on its lateral sides. Enlow also states that the orbits grow and move in a forward, descending, and slightly lateral direction. This is brought about by the differential rates of growth between the different walls of each orbit. The medial wall is largely depository, while the lateral wall is resorptive in nature. The lateral wall shows resorptive activity while the roof grows in a forward direction.

Sassouni and Forrest (1971) indicate that in the orbits, rapid growth takes place during the first two years of life, and they reach 90% of their adult size by the third year. Subsequent growth is believed to take place by periostial apposition on the external orbital contours.

Moss and Greenberg (1955) indicate that the volume and dimensions of the eyeballs and its extrinsic musculature increase until the fifth year and remain constant thereafter until puberty. They believe that the growth of the eyeballs contribute to the vertical growth of the orbital roofs, relative to the cribriform plate in the early years of life.

Scott (1967) indicates that the size of the orbital cavities is largely determined by the growth of the eyeballs, although the shape of the orbital cavity is much less under the influence of its contents, and he feels that it is probably determined by independent genetic factors. He

indicates that growth in height and width is partly the result of growth at sutures of the bones bounding them, and this sutural growth ceases to be of importance after the seventh year of life. He does indicate that the antero-posterior depth of the orbital cavities may increase due to the surface apposition of bone on the facial aspect of the orbital orifices.

Ford (1958) measured the inter-orbital widths of skulls from birth to adulthood. He indicates that the increase in inter-orbital width exceeded 10 millimeters from the age of two years to adulthood. He had also found that the cribriform plate ceased to grow in width after two years, therefore, he associates the increase in inter-orbital width to an increase in thickness of the ethmoidal labyrinth, associated with pneumatization of the ethmoidal air sinuses.

Lower face

The skeletal component of the lower face is the mandible. The mandible at birth may be present as two halves, with a suture being present at the midline. Union between the two halves occurs soon after birth. Since the two halves of the mandible diverge posteriorly, any growth of the mandible in its antero-posterior direction is necessarily associated with an increase in its transverse diameter.

Enlow (1968) indicates that mandibular elongation

not only involves continued additions of bone at each condyle, but also, bone is added at the posterior border of the ramus. Due to the interstitial and appositional growth at the condyle, there is a linear movement of the condyle in an obliquely upward and backward course towards the temporal bone. This oblique backward and upward direction of growth would lead to an overall increase in the bicondylar width. The bigonial width would also be increased due to the backward facing margins, receiving additions of bone as they are keeping pace with the backward moving condyle. Enlow also notes that the buccal surface of the ramus of the mandible in the gonial region is depository in nature, which would contribute to the increase in bigonial width.

Woods (1950) obtained data for several facial widths on a group of children from three years to fifteen years. His measurements were made on serial postero-anterior radiographs, corrected for distortion. He noted that the female remained proportional to the male until the age of twelve years, after which the male values rose. The female, however, was smaller at all ages as compared to the male.

III. CEPHALOMETRIC ROENTGENOGRAPHY

Cephalometric roentgenography provides a method of examination of the craniofacial skeleton in the living and growing craniofacial complex of human beings.

The technique of radiographic cephalometrics was

first introduced by Broadbent (1931) in the United States. Since then, several modifications have been made to this technique by workers such as Higley (1936), Margolis (1940), and Weingart (1948), but the original technique, as designed by Broadbent, is still used today.

According to Salzmann (1966), cephalometrics provides a method of appraisal of the growth changes in the skull by ascertaining the dimensions of lines, angles, and planes between selected landmarks in the craniofacial skeleton, which have been established by physical anthropologists and orthodontists. Consequently, various cephalometric analyses have been devised for understanding craniofacial growth and the relationship of different craniofacial structures to each other (Downs, 1948; Steiner, 1953; Margolis, 1947; Wylie, 1947; Sassouni, 1962; Scott, 1958). These analyses have either used the lateral cephalometric radiograph or the postero-anterior cephalometric radiograph for understanding craniofacial growth in two dimensions, while a three-dimensional analysis of craniofacial growth has been obtained by the use of both the lateral and postero-anterior radiographs.

Errors

Several investigators have reported on various errors associated with making measurements on cephalometric films (Adams, 1940; Thurow, 1951). These errors pertain to the precise identification of anatomical landmarks, magnification and positioning of the patient in the cephalostat.

The identification of landmarks on the postero-anterior cephalometric radiograph have been studied by Yen (1960) and Marshall (1969). Adams (1940) pointed out the importance of a precise technique of selection of landmarks in order to reduce the errors of measurement. McGonagle (1960) and Broadway et al. (1962) have suggested that these errors could be reduced if the same individual was making the tracing.

Hatton and Grainger (1958), in a study of reproducibility of tracings from radiographs, concluded that the greatest source of variation was due to variation of subjects. They believed that this error could be reduced by using a sufficient number of subjects, rather than reducing the technical error.

In both the lateral and postero-anterior films, there is an inherent enlargement of the projected craniofacial structures because x-rays diverge from a point source. Methods to reduce and calculate this error on lateral cephalograms have been suggested by Broadbent (1931), Adams (1940), and Thurow (1951).

In the postero-anterior radiographs, the craniofacial structures show varying degrees of enlargement, depending upon how far these structures are located from the anode. Wylie and Elsasser (1948) suggested the use of a compensator for the correction of this enlargement by proper orientation of lateral and postero-anterior films. Mulick (1965), Savara (1965), and Wei (1970) utilized cartesian co-ordinates

and complex mathematical computations to obtain a three-dimensional correction of landmarks located on frontal and lateral cephalograms. These three-dimensional studies, however, are only applicable to studies for which landmarks can be located with significant reliability on both the frontal and lateral films.

That the position of the subject in the cephalostat is critical, when making vertical measurements on postero-anterior radiographs, was pointed out by Enlow in 1968. However, he indicates that width dimensions do not appear to be greatly affected by a tipping of the head in the postero-anterior projection. He estimates the error in width measurements to be less than 1% of the distance being measured when the tipping of the head is within 10 degrees either way from the Frankfort horizontal plane.

IV. ASYMMETRIES IN THE CRANIOFACIAL COMPLEX

The term symmetry implies correspondence in size, form, and arrangement of parts on opposite sides of a plane, line, or point. In other words, symmetry of the craniofacial skeleton would imply perfect balance in size, form, and shape between selected bilateral structures in the craniofacial complex from a selected midline or point in the skull. Conversely, the term asymmetry would imply imbalance. Furthermore, these asymmetries could occur antero-posteriorly, supero-inferiorly, or medio-laterally in relation with the selected point or line.

Peck and Peck (1970) studied soft tissue facial asymmetry using facial photographs of esthetically pleasing individuals. They have shown that asymmetries in facial width become more noticeable in the composite photograph and conclude that the disposition of the facial musculature is chiefly responsible for this soft tissue imbalance. Furthermore, they also point out that in our concept of good facial esthetics, a detectable degree of soft tissue asymmetry can be tolerated and that this degree of asymmetry serves to characterize the esthetically pleasing face rather than disfigure it.

Salzmann (1966) points out that structural asymmetry of the human body is manifested in the component parts as well as in over-all morphology. He indicates that at birth the head is almost always asymmetric, with the left side being larger usually in the frontal region.

Fisher (1954) found that facial asymmetries may exist in individuals with correct occlusions, while dental asymmetries may exist by themselves with adequate symmetry of facial structures, or there may be facial and dental asymmetries in the same individual.

Classifications of the causes of asymmetries have appeared in the literature. Campbell (1950) presented the causes of asymmetry and has presented a means of recognizing them. Thompson (1943) gives a comprehensive list of the probable causes of craniofacial asymmetry.

Studies on twins have been utilized as a means of

determining the effect of heredity versus environment on asymmetry. Goldberg (1929) found that monozygotic twins have a striking resemblance to even such a variable feature as occlusion. He felt, therefore, that growth is influenced to a greater degree by heredity than by environment.

In a recent roentgenographic three-dimensional study by Mulick (1965), no significant differences in craniofacial asymmetry were found between pairs of monozygotic and fraternal twin groups, and he is of the opinion that barring hereditary syndromes, heredity is not the controlling agent in the production of craniofacial asymmetry. Mulick was also able to demonstrate on a cross-sectional basis that there were decided differences in the amount of asymmetry in different parts of the craniofacial skeleton, but these differences were not intensified with an increase in age.

Tildesley (1932), from her work on measurements of a series of approximately 900 late dynastic Egyptian male crania, noted that the assumption of symmetry of the skull is a fallacy, as the human skull is definitely and markedly asymmetrical.

Harvold (1954), in his work on the asymmetries exhibited by cleft palate children, has pointed out the detail and accuracy required for selecting a midline on postero-anterior radiographs. In his study are mentioned the ranges for asymmetry of the upper-facial skeleton in normal as well as cleft palate children.

Subtelney (1955), using laminography for a study

of asymmetries on unoperated cleft palate children, noted a larger asymmetry in the angulation of right and left pterygoid plates in cleft palate children, as compared to the normal individuals.

The knowledge that several hereditary syndromes show asymmetries is well known. Generalized statements, as regards the asymmetries present in Down's syndrome individuals, have been made by several authors, such as Gorlin and Pindborg (1964) and Aita (1969). However, no specific structure has been mentioned or measured except for a recent study by Jensen (1972), dealing with the asymmetry of the teeth and the dental arches in Trisomy 21 individuals. He could not demonstrate any significant differences between the sides of the mesiodistal widths of the deciduous and permanent teeth in Trisomy 21 or Control groups, however, his findings indicate that the arch width was larger on the left side at all ages, in both the Control and the Trisomy 21 individuals.

V. CLOSURE OF THE METOPIC SUTURE

Davies and Davies (1962) indicate that the two halves of the frontal bone are separated by the frontal or metopic suture at birth. They mention that these two halves of the frontal bones develop in membrane from two ossification centers at the superciliary arch. Union between the two halves is believed to begin by the second year, and the suture is usually obliterated by the eighth year.

Bolk (1917) reports the incidence of metopism in

Dutch crania to be 9.5%. He found the forehead wider in metopic skulls as compared to the non-metopic ones, and he explains this on the basis that the growth center is probably active for a longer time. He puts forward the theory that, from a phylogenetic point of view, the smaller attachment and the more posterior location of the temporalis muscle on the frontal bone in man would tend to favor the presence of a patent metopic suture.

An histological differentiation has been made between the sutures of the cranial vault as compared to those found in the facial skeleton (Pritchard, Scott and Girgis, 1956).

As regards the presence of metopism in Down's syndrome individuals, Benda (1969) notes that normally the frontal suture, which is not present at birth, may be palpated down to the nasion several months after birth in these individuals. He is of the belief that delay of closure of the fontanelles and the open metopic sutures are due to insufficient growth activity at the margins of the flat bones. Roche, Seward and Sunderland (1961b), in their study of Australian children with Down's syndrome noted that the metopic suture was present in 42% of the females and in 67% of the males after the age of ten years.

Varying reports exist as regards the age of closure of the anterior fontanelle in Down's syndrome individuals. Levinson, Friedman, and Stamps (1955), who reviewed 50 cases of mongolism under the age of five years, stated

that the anterior fontanelle was open in all of these children up to the age of 2.5 years, and in 20% of those between the ages of 2.5 to 5 years. Roche and Sunderland (1960), on postmortem observations of 21 mongoloid crania, varying in age from one month to 55 years, have noted that the anterior fontanelle was open in 9 of the 11 autopsy specimens ranging in age from 2 to 3.5 years. The only two individuals above the age of 3.5 years in their sample, however, showed the anterior fontanelles to be closed. Roche and Sunderland have also shown that the cranial bones are thinner, and the anterior fontanelle is larger in mongolism, and they suggest that these two characteristics may be related.

VI. SUTURAL BONES

The presence of sutural bones in the normal human craniofacial skeleton has been reported by Davies and Davies (1962). These sutural bones are believed to occur most commonly in the course of the lambdoid suture but may occasionally be seen at the fontanelles, especially the posterior fontanelle. These irregular, isolated islands of bone, found in the course of the cranial sutures, occur in different sizes and have a tendency to be symmetrical on both sides of the skull. Usually they may be two or three in number, but in certain diseased conditions, e.g. hydrocephalic subjects, over a hundred may be found. Aita (1969) reports the frequent presence of wormian bones in

autosomal dominant disorders, such as cleidocranial dysostosis and osteogenesis imperfecta.

According to Grant (1965) and Last (1966), in some cases, the portion of the occipital bone above the superior nuchal line, which develops in membrane, may not fuse with the basillar part of the occipital bone, which develops in cartilage. In these cases, it is called an interparietal bone. The interparietal bone, itself, develops from several centers of ossification and failure of fusion of one of these centers may simulate a large sutural bone, although in actual fact it is part of the occipital bone.

Pritchard, Scott, and Girgis (1956) have noted the presence of cartilage in the sagittal and midpalatal sutures. They indicate that it is usually one of two types; the first type occurs as irregular islands of large celled cartilage with a scanty matrix interspersed with the trabeculae of woven bone at or near the sutural edges, and the second type was associated with the cambial layers of the suture, which were temporarily transformed into expanded epiphysis-like masses covering the margins of bones. Pritchard et al. note that Symons (1952) believed that this cartilage found in the sutures between two membrane bones may function as a growth cartilage for long periods. They also indicate that it may rapidly disappear, either by resorption, with or without endochondral replacement, or by direct conversion to bone.

Pritchard et al. have mentioned that Sisten (1933)

found the presence of cartilage in the lambdoid suture in infants under six months of age and regarded it to be present as a result of particularly strong pressure and shearing stresses between the bones associated with recumbency at this stage of life. Pritchard et al. also state that it is well known that an alteration of fibrous tissues to cartilage may take place when it is subject to such stresses.

There are relatively very few reports concerning the presence of sutural bones in Down's syndrome. Roche et al. (1961b) report that several sutural bones were present in the cases described by Fraser and Mitchell (1876) and Greig (1927). Roche et al. note that in one of the skulls reported by Greig, the inferior end of the metopic suture showed the presence of sutural bones, where their occurrence is unusual in normal individuals. In their study pertaining to the presence of sutural bones in Down's syndrome individuals, they were not able to demonstrate any difference in the incidence of sutural bones between normal and Down's syndrome individuals. They, however, report that most of the sutural bones that were present, were found in the lambdoid suture.

CHAPTER III

METHODS AND MATERIALS

Sample

The sample under investigation consisted of 127 Trisomy 21 individuals, which included 71 males and 56 females. All the Trisomy 21 individuals were residents of the Province of Manitoba. Some of these individuals were residing at home and others were in an institution for the mentally retarded. It is realized that differences may exist in the persons residing in institutions and at home, however, as complete residence histories of each individual were not available, no attempt has been made to analyze the data on the basis of institutionalized or non-institutionalized subjects.

The subjects in the Trisomy 21 group were karyotyped by Dr. Irene Uchida and the staff of the Department of Medical Genetics, Winnipeg Children's Hospital, Winnipeg, Manitoba, Canada. Each individual in this group was found to have an extra chromosome number 21, and hence, a cytogenetically confirmed Trisomy 21 sample was obtained.

The Trisomy 21 sample ranged in age from 3 to 56 years and was divided by sex and subgrouped into the following 6 age ranges: (1) pre-permanent dentition,

3-5 years, (2) early mixed dentition, 6-8 years, (3) late mixed dentition, 9-11 years, (4) early adolescence, 12-15 years, (5) late adolescence, 16-19 years, and (6) adults 20 years and above.

A control sample of normal caucasian individuals approximately matching the Trisomy sample in age and sex was collected. The Control sample consisted of 137 individuals, which included 67 males and 70 females. All the subjects were chosen at random from the files of the University of Manitoba and were all residing in the Winnipeg area. A complete distribution of the sample has been shown in Tables I, II, and III.

Records

Postero-anterior cephalometric radiographs of the Trisomy 21 and the Control groups were obtained by using the technique described by Broadbent in 1931.

These P.A. radiographs were utilized for the following:

1. Studying the skeletal changes in width between various bilateral craniofacial structures.
2. Assessing the asymmetry of various bilateral structures from a constructed midline which was erected as a perpendicular to the supra-orbital plane and passed through the base of crista galli.
3. Subjective assessment of the presence of patent metopic sutures and the presence of wormian bones

TABLE I

AGE DISTRIBUTION OF THE SAMPLE

Age Range (in years)	Trisomy 21	Control
3-5	7	17
6-8	7	19
9-11	14	21
12-15	32	30
16-19	29	20
Adult	38	30
Total	127	137

TABLE II

AGE DISTRIBUTION OF THE MALES

Age Range (in years)	Trisomy 21	Control
3-5	4	9
6-8	3	8
9-11	8	10
12-15	20	16
16-19	17	10
Adult	19	14
Total	71	67

TABLE III

AGE DISTRIBUTION OF THE FEMALES

Age Range (in years)	Trisomy 21	Control
3-5	3	8
6-8	4	11
9-11	6	11
12-15	12	14
16-19	12	10
Adult	19	16
Total	56	70

in the cranial sutures of the Trisomy 21 and Control groups.

4. Assessment of orbital hypo or hypertelorism in the Trisomy 21 group as compared with the Control group.

In addition to the P.A. radiographs, soft tissue measurements were taken of the inter-endocanthal width, the inter-pupillary width, and the inter-ectocanthal width of each individual in the sample. These soft tissue measurements were utilized for the assessment of occular and pupillary hypo or hypertelorism in the Trisomy 21 group as compared with the Control group.

Cephalometric Technique

The P.A. cephalometric radiographs for the Trisomy 21 group were obtained by the use of two cephalometric machines. A small portion of the Trisomy 21 sample (7.18%) was collected by using a portable cephalometer which has been described by Ghiz (1968) and Frostad (1969). This portable cephalometer was built along the lines of a conventional cephalometer utilizing a General Electric* 90 KV x-ray head, a control panel, a standard cephalostat for head positioning, and an easily dismantled plywood base. The P.A. radiographs for the remaining portion of the Trisomy 21 sample (92.82%) and all the P.A. radiographs of the Control sample were

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* General Electric of Canada Limited, Toronto, Ontario, Canada.

obtained by using the cephalometrix* cephalometer in the orthodontic department at the University of Manitoba.

The subject's head was positioned in the cephalostat, facing the film cassette in the position of distant vision, with the Frankfort plane approximately parallel to the floor. In this position, the X-ray beams passed through the head parallel to the midsagittal plane and at right angles to the transmeatal axis.

The anode to the transmeatal axis distance remained fixed at 5 feet 6 inches for both machines, and the transmeatal axis to the film distance was fixed at 150 millimeters. The films were produced using an exposure of 15 milliampere seconds (mAs) and a kilovolt potential of 90 KVp. The time was altered depending on the size of the head and age of the subject.

Magnification for the portable cephalometer with the fixed focal length and midsagittal plane to film distance was determined previously by Frostad (1969). A plastic gauge having radio-opaque millimeter markings was made. Projection onto the films of this plastic gauge placed at the transmeatal axis enabled calculation of the magnification factor for the cephalometrix machine. The magnification factor for the portable cephalometer and the cephalometrix cephalometer was found to be seven per cent and nine per cent, respectively, at the transmeatal axis.

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* Moss Corporation, Chicago, Illinois, U.S.A.

Since skeletal structures lying anterior to the transmeatal axis will be magnified less, as compared to structures posterior to the transmeatal axis, the plastic gauge was used to determine the percentage of magnification to be expected for any similar distances between the same bilateral structures lying in two different coronal planes approximately 10 millimeters apart. The difference in magnification for the distance lying in the coronal plane 10 millimeters anteriorly was found to be 0.6 per cent less when compared to the distance lying posterior to it.

Since the magnification error in any measurement was insignificant (i.e., 0.6 per cent) in comparison with the difference between the mean measurements for the same distance between the same bilateral structures in the two groups, no correction for magnification was made. A graphic description of the magnification factor to be expected is shown in Figure 4.

Soft Tissue Measurement Technique

The inter-endocanthal width, the inter-pupillary width and the inter-ectocanthal width were determined by using a vernier caliper accurate to one-tenth of a millimeter (Figure 5).

The subject was seated in a comfortable upright position on a dental chair and was asked to look straight ahead. Measurements of the inter-endocanthal and inter-ectocanthal widths were made in direct contact with the endocanthions and ectocanthions, in order to eliminate the

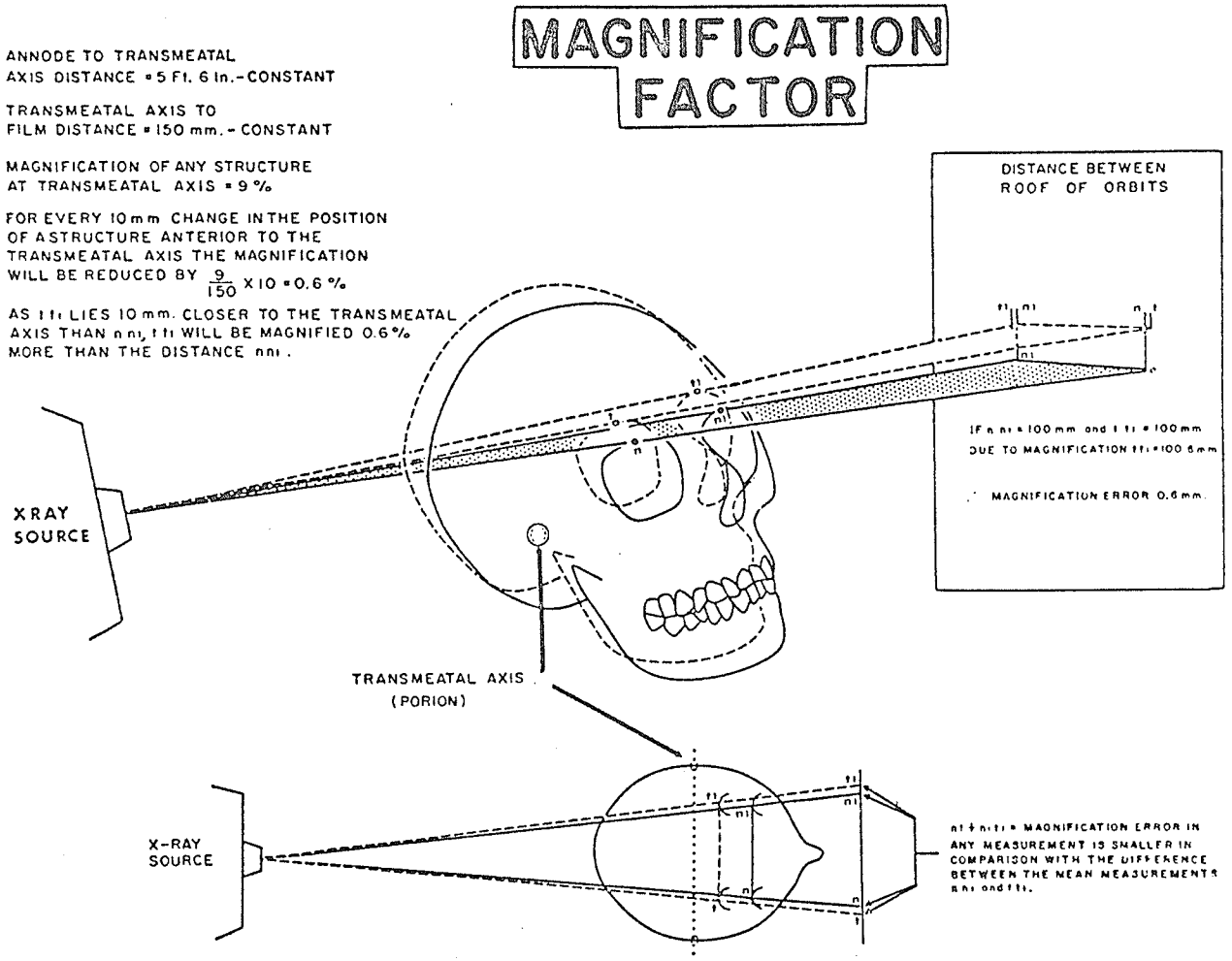


Figure 4. Schematic diagram to explain magnification error.

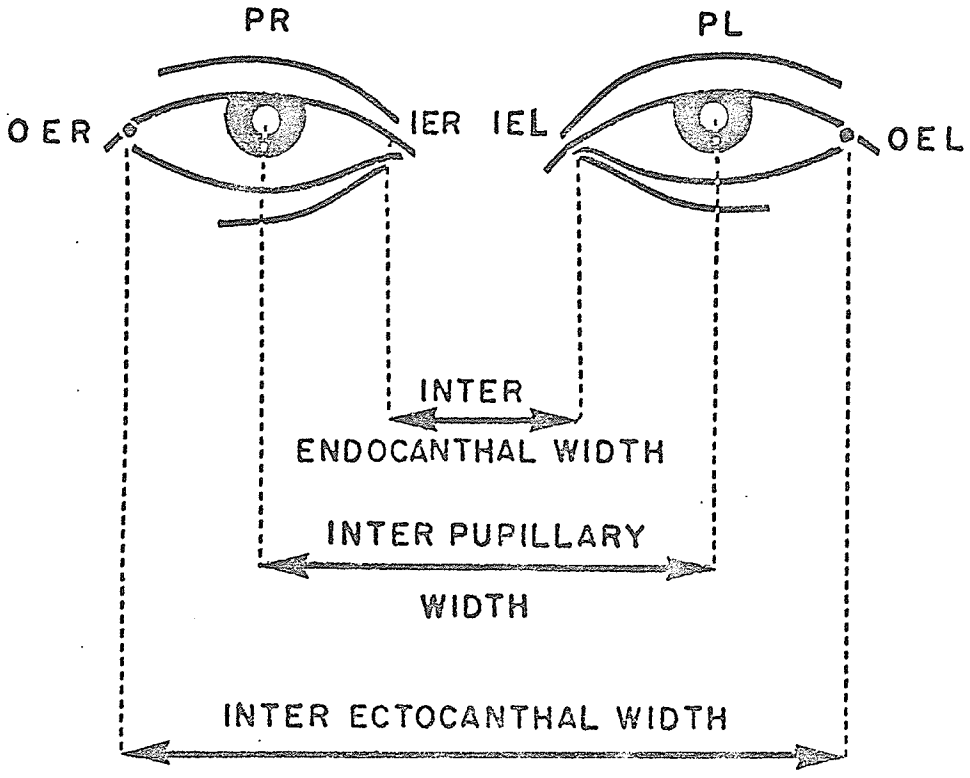


Figure 5. Illustration of the soft tissue landmarks and distances used in this study.

parallax error. The inter-pupillary width was taken in the same position with the beaks of the vernier caliper as close as possible to the center of the pupils, so as to reduce the parallax error to a minimum. Any subjects that showed clinical evidence of strabismus were not measured.

Selection of Landmarks

Since the P.A. radiographs are not used routinely, and there is a considerable amount of superimposition of craniofacial structures, a pilot study was done on five skulls to identify the craniofacial structures as seen on the postero-anterior cephalometric radiographs.

The parasagittal and bilateral structures to be used in the study were identified and marked on the left side of the skull with pinpoint daps of radio-opaque barium paste injected from a 2 cc. syringe with a 25 gauge needle.

Postero-anterior radiographs of the skulls were taken by the same method described previously with the Frankfort plane parallel to the floor. The exposure time was reduced to one-twentieth of a second to obtain suitable P.A. radiographs of the skull.

These postero-anterior radiographs of the skull were studied. The paired bilateral structures on the right side were identified without looking at the paired radio-opaque barium paste markings on the left side. After a careful study of these radiographs, 47 landmarks were selected to

be digitized from the radiographs of the Control and Trisomy 21 sample. A detailed description of all the landmarks used in this study may be found in the Glossary, and the order of digitization of the landmarks is illustrated in Figure 6.

Plotting of Landmarks

The radiographs of each of the subjects in the Trisomy 21 and Control groups were placed on the viewing screen of a modified Tagarno motion analyzer specially adapted to accept a standard sized 8 X 10 inch postero-anterior film. Only films of good quality and acceptable clarity were selected for digitizing the chosen landmarks. When a landmark was missing or could not be identified easily, it was omitted for that subject. This procedure eliminated the possibility of computing a linear measurement dependent upon the missing landmark for that subject. Any measurement, dependent upon a landmark missing too frequently, was not taken into consideration in this study. The sample size in each age range was large enough to absorb a small amount of missing data without significantly affecting the mean values.

After having assessed the radiograph for its quality, the uppermostpoints on theroofs of the orbits and the base of crista galli were identified and marked with a fine point number 6 SE Piano wire explorer. An acetate template with two lines intersecting exactly at right angles was

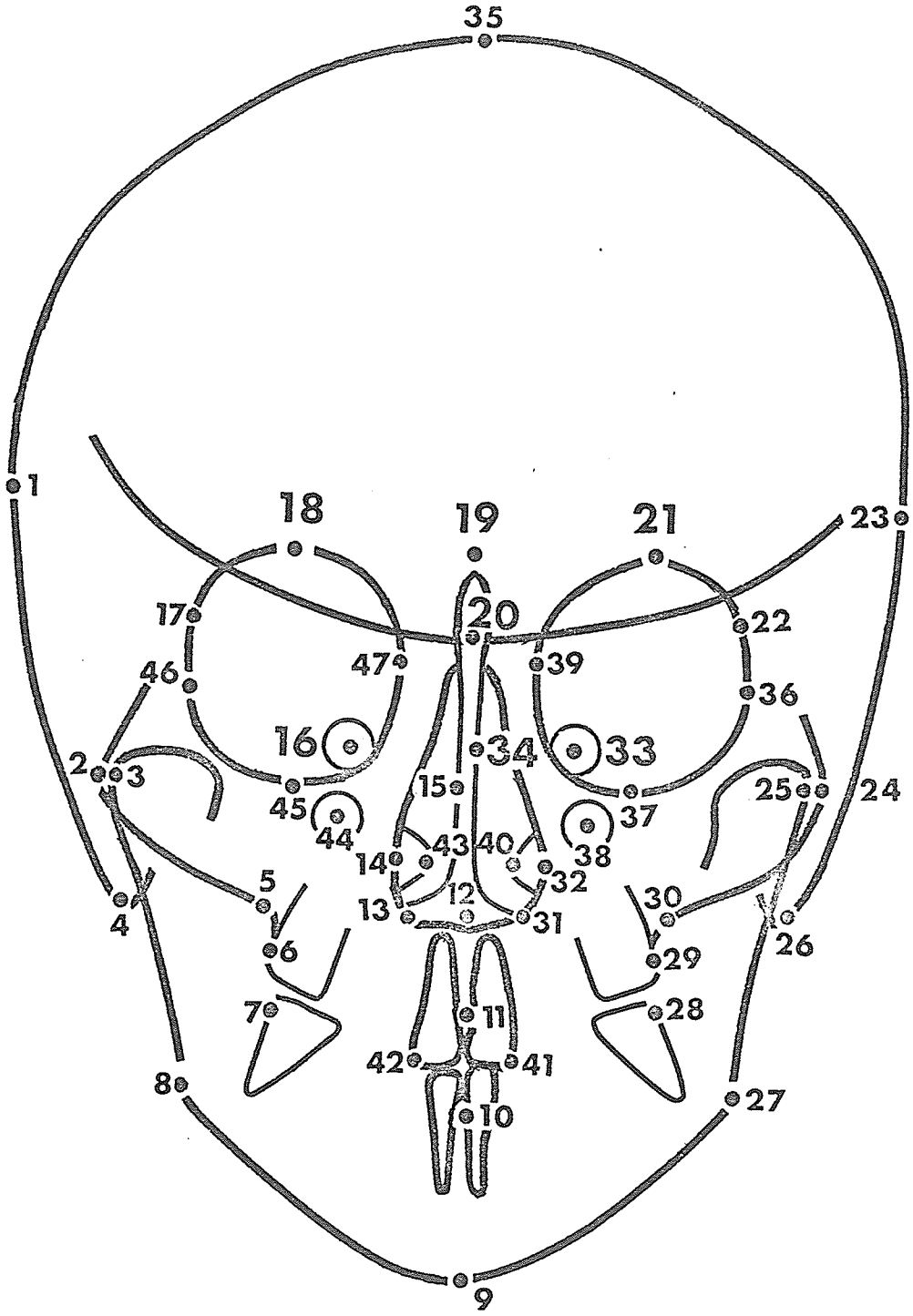


Figure 6. Order of digitization of landmarks on the P.A. radiographs.

placed over the P.A. radiograph.

The use of the template was necessary as the various radiographs of each subject were mathematically superimposed, following the computerized method of co-ordinate analysis described by Cleall and Chebib in 1971. This method required a point of origin and the definition of a line for the superimposition of the radiographs.

In order to obtain a suitable point of origin, designated as site 19 in Figure 6, one of the intersecting lines of the template was placed on the uppermost points on the roofs of the orbits (sites 18 and 21), and the other line on the template passed through the base of crista galli, which is site 20. The junction was considered to be the point of origin (site 19), while the perpendicular line passing through sites 19 and 20 served as the direction for the computer analysis. This perpendicular line also served as the midline of the skull for the assessment of asymmetries. The line passing through sites 18-20 will be referred to as the supraorbital plane.

The co-ordinates for each of the 47 chosen landmarks were plotted in a pre-selected order and transferred to IBM 80 column computer punch cards, by means of a Ruscom logistics strip chart digitizer*, illustrated in Figure 7. Information from the punch cards was loaded into the University of Manitoba IBM 360-65 computer system, which mathematically computed all the linear measurements used in

* Ruscom Logistics Ltd., Toronto, Ontario, Canada.

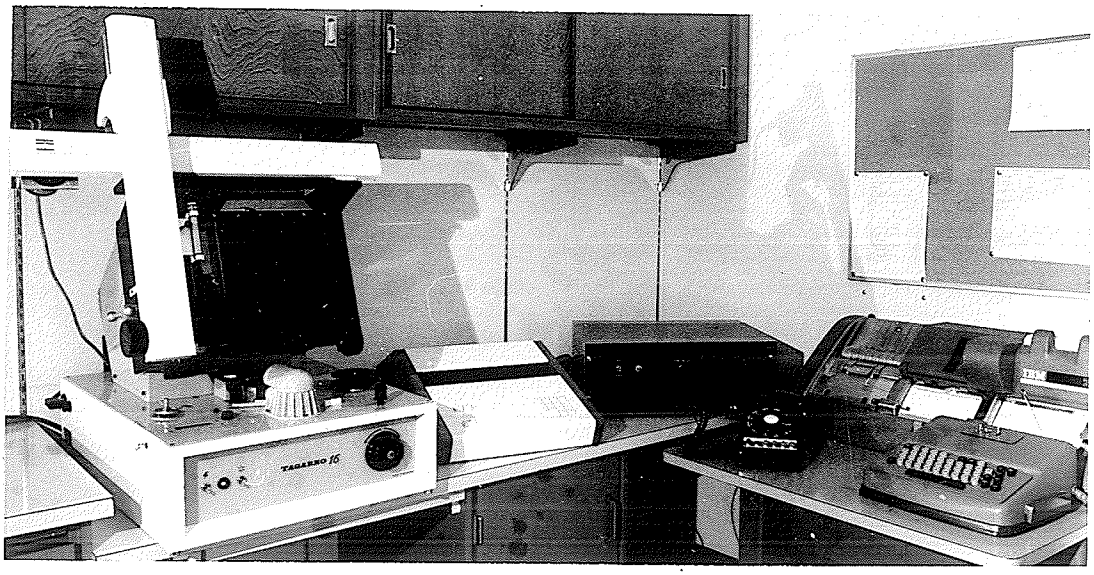


Figure 7. Digitizer used to record the co-ordinates of the landmarks from the P.A. cephalometric radiographs.

this study, according to the method described by Cleall and Chebib (1971).

Measurement Errors

It was recognized in this study that the measurement error associated with the different measurements in various areas of the skull may be different. Some of these errors could be dependent upon a combination of various sources of errors, which have been discussed in the Review of Literature in the section dealing with errors associated with cephalometric roentgenography. The error associated with each measurement to be used in the skeletal analysis was therefore calculated separately.

In order to obtain the measurement error for each of the distances used in the skeletal analysis, each of ten randomly selected radiographs were digitized three times. The values of the selected distances were calculated from each of the 30 data sets and were used to estimate the measurement errors associated with each variable. The method of digitization and calculation of the various variables was the same as that employed in the actual study.

The measurement errors were estimated for each variable as the maximum errors associated with 95 or 99 per cent of the measurements as described by Chebib and Burdick (1973).

The formula used to estimate the standard deviation of the error was as follows:

$$S = \frac{\sum_{i=1}^{n} \sum_{j=1}^{m} (X_{ij} - \bar{X}_i)^2}{\sum_{i=1}^{n} (m - 1)}$$

where X_{ij} = the jth repeated measure taken on the ith subject,

$\bar{X}_i$ = the mean of repeated measures for the ith subject,

m_i = the number of repeated measures taken for the ith subject, and

n = the number of subjects.

The maximum error associated with a certain percentage of the measurements (p) was calculated as follows:

$$\text{maximum error} = t_{(p.df)}S$$

where S = the standard deviation of the error as shown above,

t = the theoretical t value for probability p, and df degrees of freedom, and

df = the degrees of freedom associated with the standard deviation of the error.

The values of the standard deviations of the measurement error and the maximum errors associated with 95 to 99 per cent of the measurements for each variable are listed in Table XXXVI in the Appendix.

The largest errors occurred with the width of the floor of the nasal cavity, the bicondylar width, and the bilatero-orbital width. The error in these measurements was not more than 2.6 mm., while the maximum error associated with all the other measurements ranged from 0.41 mm. to 1.88 mm. for 95 per cent of the data. This degree of measurement error was of such magnitude that it did not warrant correction in the statistical analysis.

Skeletal Analysis

For the skeletal analysis, the landmarks, the supra-orbital plane and the midline used in this study are illustrated in Figure 8. It was possible to obtain measurements between any two landmarks; however, in order to minimize the effects of craniofacial asymmetry, widths between any two structures were not measured directly from one landmark to another, but rather as their projections on the supraorbital plane (RoR-RoL) extending from the roof of the right orbit (RoR) to the roof of the left orbit (RoL). These width measurements will be referred to as horizontal projection distances "H".

On the same basis, all the vertical linear measurements were projected onto the chosen midline (X-Cg), represented by a perpendicular line erected from the supraorbital plane and passing through the base of crista galli. These vertical measurements will be referred to as vertical projection distances "V".

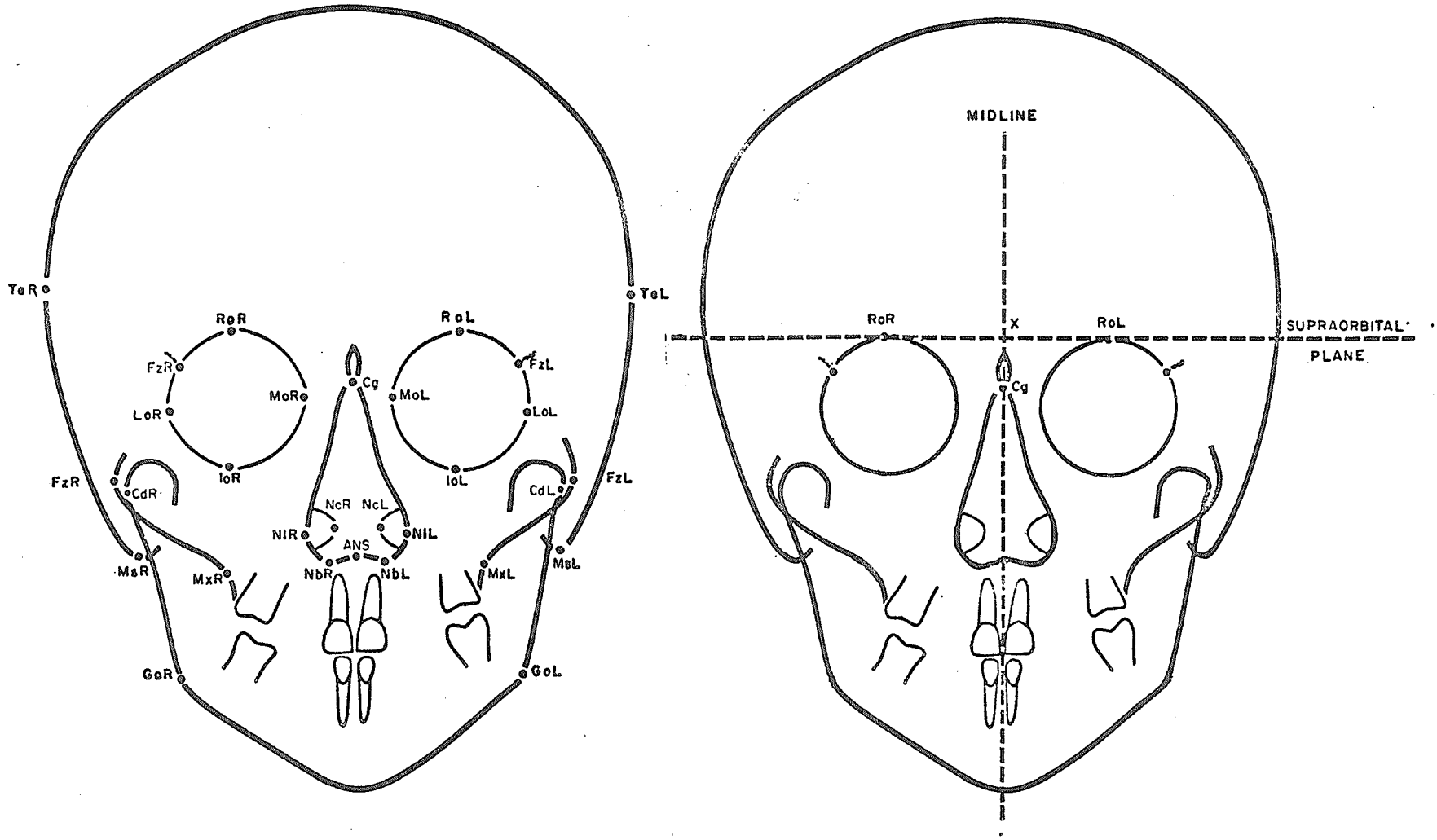


Figure 8. The landmarks, the midline and the supraorbital plane used in the skeletal analysis.

The method of measuring these horizontal and vertical projection distances is illustrated in Figure 9. A total of 21 horizontal and vertical projection measurements were used to assess and compare the morphological and developmental changes in the craniofacial complex of the Trisomy 21 and Control samples. These measurements were as follows (Figure 10):

A. CRANIUM

TeR-TeL: This measurement represents the width of the cranium.

MsR-MsL: This measurement represents the bimastoid width and measures the distance between the mastoid processes of the temporal bones.

B. UPPER FACE

ZyR-ZyL: This measurement represents the bizygomatic width and is indicative of the width of the face.

MxR-MxL: This measurement represents the bimaxillary width at the level of the key ridge.

NlR-NlL: This measurement represents the width of the nasal cavity at its widest part.

NbR-NbL: This measurement represents the width of the floor of the nose in its anterior part.

NcR-NcL: This measurement represents the horizontal separation between the inferior nasal conchae.

Cg-ANS: This measurement represents the height of the nasal cavity.

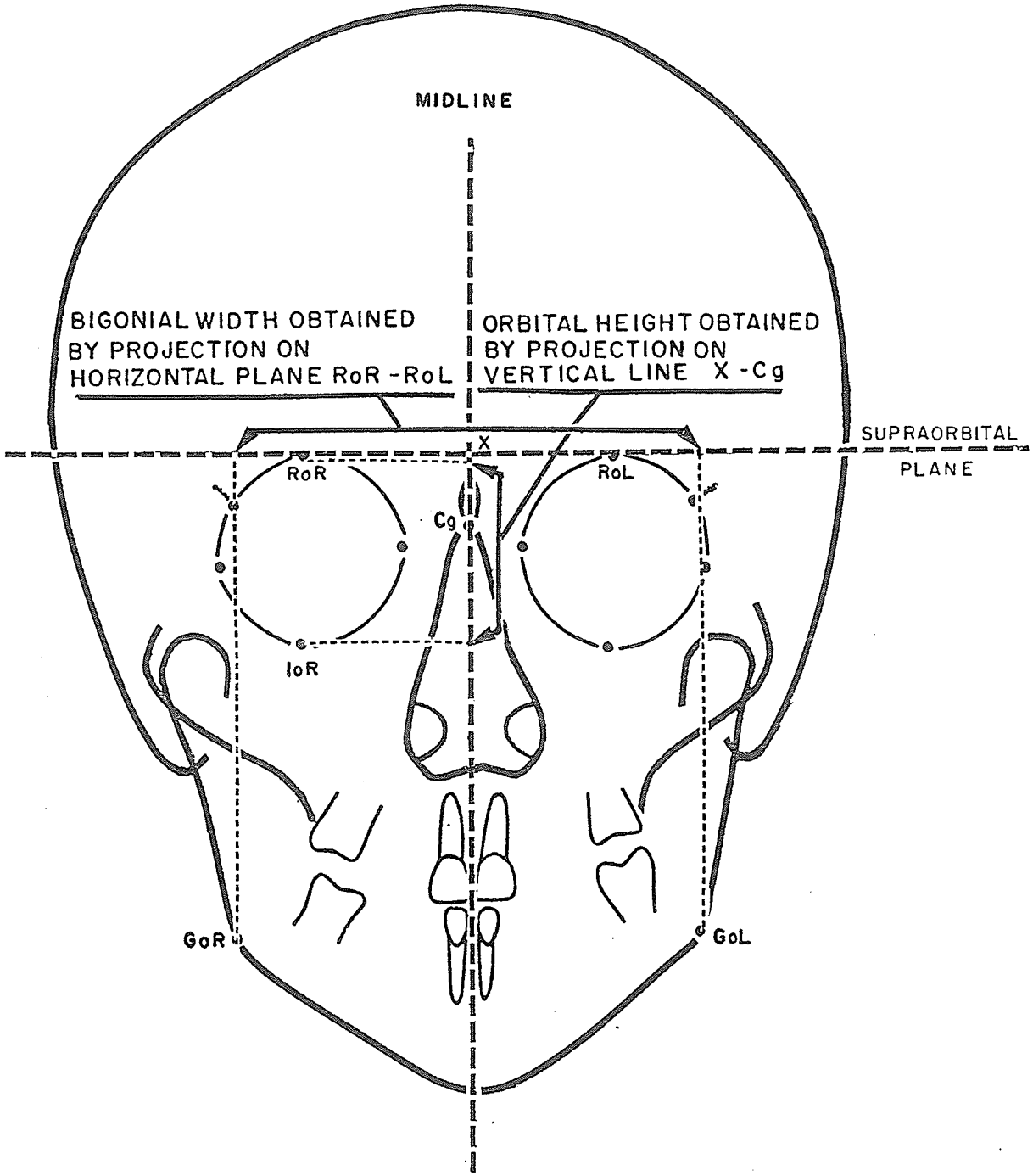


Figure 9. Method of obtaining Horizontal and Vertical projection distances from the P.A. radiograph. Note: Bigonial width is a Horizontal projection distance and Orbital height is a Vertical projection distance.

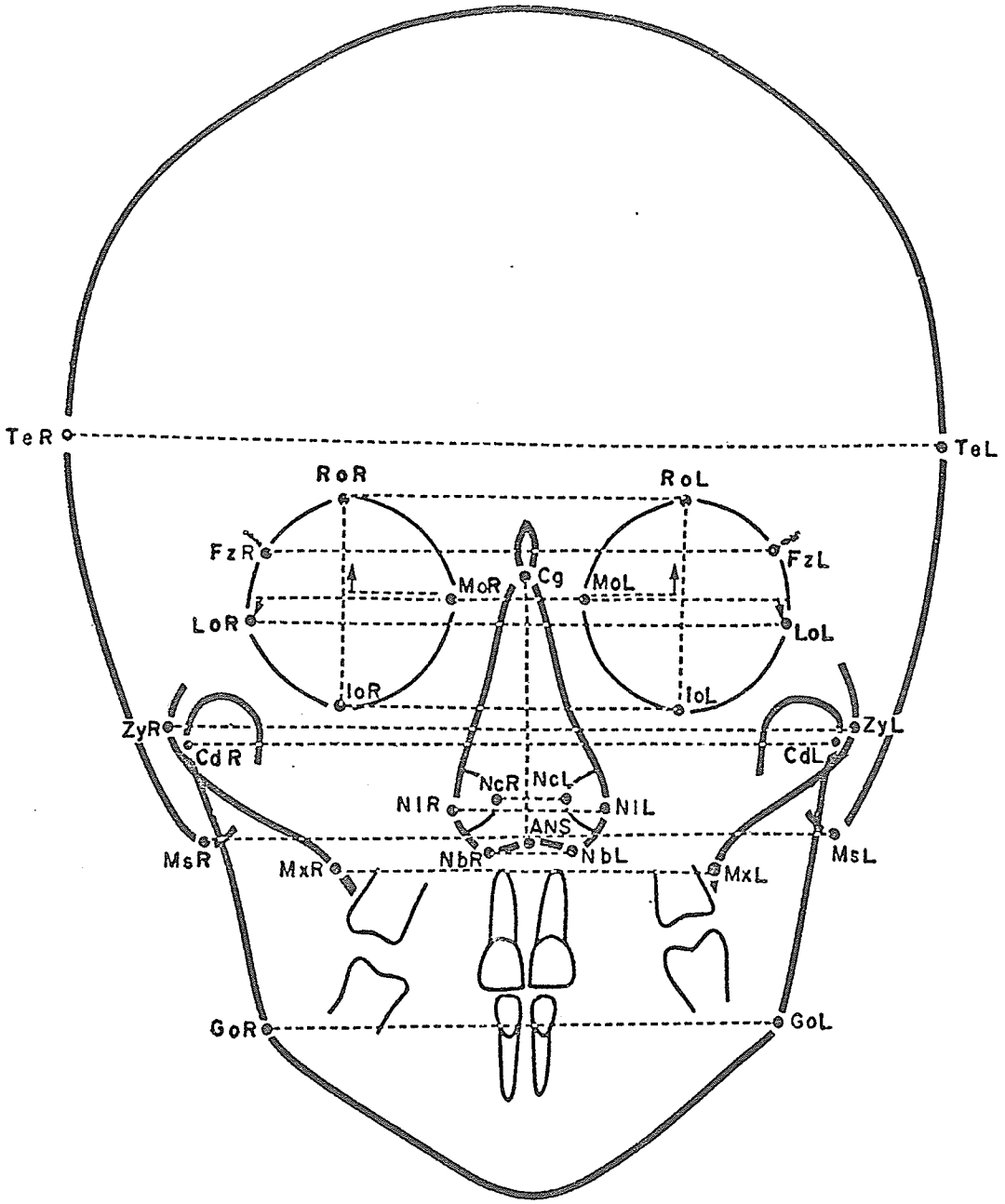


Figure 10. Illustration of the Horizontal and Vertical projection measurements obtained from the P.A. radiograph for the skeletal analysis.

MoR-MoL: This measurement represents the horizontal separation between the orbits.

RoR-RoL: This measurement represents the horizontal separation between the most superior point on each orbital margin as seen on the P.A. film and is located on the roof of each orbit.

MoR-RoR: This measurement represents the horizontal distance between the right medio-orbitale and the roof of the right orbit.

MoL-RoL: This measurement represents the horizontal distance between the left medio-orbitale and the roof of the left orbit.

IoR-IoL: This measurement represents the distance between the most inferior point on the orbital margin of each orbit.

FzR-FzL: This measurement represents the distance between the most medial point on each fronto-zygomatic suture.

LoR-LoL: This measurement represents the distance between the most lateral point on the lateral orbital margin of each orbit.

MoR-LoR: This measurement represents the width of the right orbit.

RoR-IoR: This measurement represents the height of the right orbit.

RoL-IoL: This measurement represents the height of the left orbit.

C. LOWER FACE

CdR-CdL: This measurement represents the distance between the outermost point on each condylar process of the mandible and represents the bicondylar width.

GoR-GoL: This measurement represents the bigonial width of the mandible.

Analysis of Asymmetries

In order to assess the asymmetries in the craniofacial complex of the Trisomy 21 and Control groups, it was necessary to select a midline of the skull, so that the distances from bilateral structures to this chosen midline could be compared.

The template technique, utilized to obtain this midline, has already been described under the section dealing with the plotting of landmarks. It is realized that this midline could be affected by any asymmetries between the roof of the right and left orbit. Furthermore, the landmark crista galli may not be in the true midline. By the very nature of growth, it is doubtful whether any of these landmarks or any other landmark or plane in the craniofacial complex is truly stable. This midline was, however, chosen because it was felt that the growth of the orbits and the anterior cranial base area ceased early in life, and therefore, the position of this midline would be affected to a relatively lesser degree. This midline plane (X-Cg) was selected to analyze the asymmetries of the

craniofacial skeleton, realizing its limitations.

The asymmetries of the craniofacial complex in the Trisomy 21 and Control groups were studied by comparing 28 measurements from 14 bilateral structures to the midline (X-Cg). In addition to the above, the width of the right orbit and width of the left orbit were compared. These 30 measurements are illustrated in Figure 11, and were as follows:

A. CRANIUM

TeR and TeL to X-Cg: These two measurements represent the distance of the right temporal landmark and the left temporal landmark from the midline.

MsR and MsL to X-Cg: These two measurements record the distance of the right mastoid process and the left mastoid process from the midline.

B. UPPER FACE

ZyR and ZyL to X-Cg: These two measurements represent the distance of the right zygomatic process and left zygomatic process from the midline.

MxR and MxL to X-Cg: These two measurements record the distance of the right side of the maxilla and the left side of the maxilla from the midline.

NlR and NlL to X-Cg: These two measurements record the distance from the right lateral wall of the nasal cavity and the left lateral wall of the nasal cavity from the midline.

NbR and NbL to X-Cg: These two measurements record

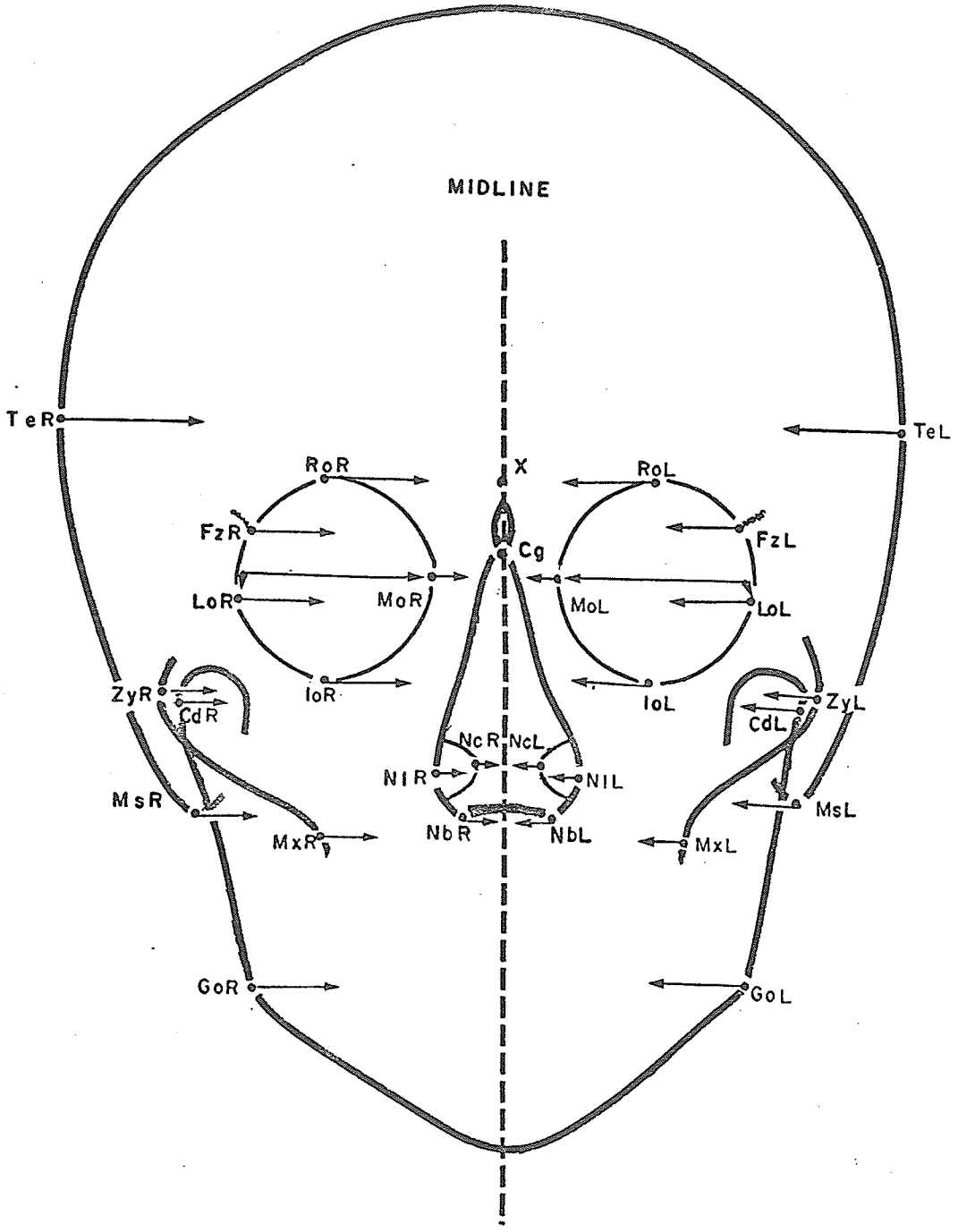


Figure 11. Illustration of the measurements obtained from the P.A. radiograph for the analysis of asymmetry.

the distance of the right nasal base landmark and of the left nasal base landmark from the midline.

NcR and NcL to X-Cg: These two measurements record the distance of the right inferior nasal concha and left inferior nasal concha from the midline.

RoR and RoL to X-Cg: These two measurements represent the distance of the roof of the right orbit and the roof of the left orbit from the midline.

FzR and FzL to X-Cg: These two measurements represent the distance of the right fronto-zygomatic suture and the left fronto-zygomatic suture from the midline.

LoR and LoL to X-Cg: These two measurements represent the distance of the right lateral orbital margin and left lateral orbital margin from the midline.

IoR and IoL to X-Cg: These two measurements record the distance of the most inferior point on the right orbital margin and the left orbital margin from the midline.

MoR and MoL to X-Cg: These two measurements record the distance of the most medial point on the right orbital margin and the left orbital margin from the midline.

MoR-LoR and MoL-LoL: These two measurements record the width of the right orbit and the width of the left orbit.

C. LOWER FACE

CdR and CdL to X-Cg: These two measurements record the distance of the right mandibular condyle and left

mandibular condyle to the midline.

GoR and GoL to X-Cg: These two measurements record the distance of the right gonial landmark and left gonial landmark from the midline.

Assessment of the Distance Between the Orbits, the Pupils and the Eyes

The word hypertelorism is derived from the Greek hyper (over, above), telouros (distant), and ismos (condition). Although hypertelorism is defined as an excessive distance between any paired organs (Dorland, 1965), in actual use, the term is confined to the excessive spacing between the orbits or the eyes. Conversely, the term hypotelorism is used to designate the decreased spacing between the orbits or the eyes.

There has existed considerable confusion in the literature as regards the application of the words "orbital" and "occular" hypertelorism. These two terms have been used synonymously to designate the excessive spacing between the bony orbits and the endocanthions of the eyes. Furthermore, the term "occular hypertelorism" has also been used to designate the excessive spacing between the pupils.

In this study, the term orbital hypertelorism has been used to designate the excessive spacing between the orbits. The term occular hypertelorism refers to the excessive spacing between the eyes, using the distance

between the right and left endocanthions, while the term pupillary hypertelorism refers to the excessive spacing between the pupils.

It was the opinion of the author that the presence of orbital, pupillary, and occular hypo or hypertelorism in Trisomy 21 individuals should be made by taking the width of their faces into consideration, as the overall dimensions of the Trisomy 21 individuals are believed to be smaller than in normal subjects.

In this study, the skeletal bizygomatic width (ZyR-ZyL) was used to represent the width of the face (Sassouni, 1962). The assessment of orbital, pupillary, and occular hypo or hypertelorism was made by statistically comparing the following ratios for each individual, in the Trisomy 21 and Control groups, among the six age ranges.

MoR-MoL/ZyR-ZyL: This ratio of the inter-orbital distance (MoR-MoL) over the skeletal bizygomatic width (ZyR-ZyL) was used to assess orbital hypo or hypertelorism in the Trisomy 21 group, when compared with the Control group.

PR-PL/ZyR-ZyL: This ratio of the distance between the pupils (PR-PL) over the skeletal bizygomatic width, was used to assess the presence of pupillary hypo or hypertelorism in the Trisomy 21 group, when compared with the Control group.

IER-IEL/ZyR-ZyL: This ratio of the inter-endocanthal

distance (IER-IEL) over the skeletal bizygomatic width, was used to assess the presence of occular hypo- or hypertelorism in the Trisomy 21 group, when compared with the Control group.

As a second term of reference, the Canthus index was used to determine the degree of occular hypertelorism. The Canthus index was obtained by the ratio of the inter-endocanthal distance (IER-IEL) over the inter-ectocanthal distance (OER-OEL), multiplied by 100. According to the Canthus index, a score of 38 is considered to be the upper limits of normality. A score between 38 and 42 is an intermediate condition known as Euryopia, while a score above 42 is considered to be the condition known as hypertelorism, as mentioned by Gaard (1961).

Statistical Analysis of the Data

The raw data was checked for errors by measuring the dispersion about the means. By the use of the co-ordinate analysis program, described by Cleall and Chebib (1971), the values for each of the selected distances shown on pages 66, 69 and 70, were calculated for each individual in the Trisomy 21 and Control sample, and the means and standard deviations were produced according to group, sex, and age.

To study 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 263 degrees of freedom among the 264 subjects were allocated as shown in Table IV. All the main effects and interactions were tested for significance by the variance ratio "F" tables (Snedicor, 1946).

TABLE IV

DEGREES OF FREEDOM FOR

EIGHT SOURCES OF VARIATION FOR THE 264 SUBJECTS

Source of Variation	Degrees of Freedom
Between groups	1
Between sexes	1
Among age groups	5
Group x sex	1
Group x age	5
Sex x age	5
Group x sex x age	5
Experimental error	240
Total	263

A similar statistical analysis was done on all the ratios utilized to assess the presence of orbital, occular, and pupillary hypo or hypertelorism in the Trisomy 21 and Control groups.

For the asymmetry part of the study, the raw data was again checked for errors by measuring the dispersion about the means. By the use of the co-ordinate analysis

program, each of the selected distances from the bilateral landmarks to the midline and the width of each orbit were calculated for each individual in both samples, and the means and standard deviations were produced according to group, sex, age, and side.

To study the actual asymmetry in the craniofacial complex and how it is affected by group, sex, and age, a 4-factor mixed factorial analysis of variance was performed according to the method suggested by Becker and Chebib (1969). The independent factors were group, sex, and age, and the dependent factor was side. The allocation of the degrees of freedom is shown in Table V. All the main effects and interactions were tested for significance.

Assessment of the Presence of Patent Metopic Sutures

At the time of selection of postero-anterior radiographs for this study, it was noticed that some of the Trisomy 21 subjects showed a patent metopic suture. It was felt that it would be interesting to assess the percentage of individuals showing patent or partially patent metopic sutures, as no such reports were found to exist for such a large group of Trisomy 21 individuals living on the North American continent.

The criteria used to assess the existence of a patent metopic suture was the presence of a radiolucent line being present in the anatomical region of the metopic suture.

TABLE V

ALLOCATION OF THE DEGREES OF FREEDOM

FOR THE MIXED ANALYSIS OF VARIANCE

FOR THE CRANIOFACIAL ASYMMETRIES

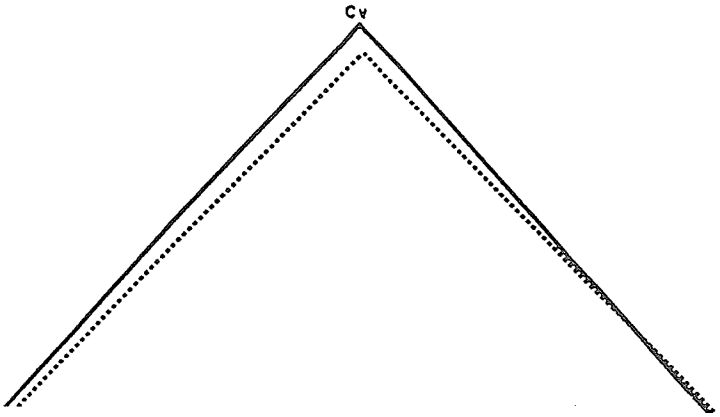
Source of Variation	Degrees of Freedom
Between groups	1
Between sexes	1
Among age groups	5
Group x sex	1
Group x age	5
Sex x age	5
Group x sex x age	5
Between subject error	240
Between sides	1
Group x side	1
Sex x side	1
Age x side	5
Group x sex x side	1
Group x age x side	5
Sex x age x side	5
Group x sex x age x side	5
Within subject error	240
Total	527

Normally, the metopic suture closes early in life (Davies and Davies, 1962). Thereafter, no radiolucent line should be observed in this region on the postero-anterior radiographs. It is realized that the presence of a radiolucent line, however, does not necessarily indicate the complete patency of the metopic suture at a histological level, because some minute bony fusions in the suture would be unidentifiable on a radiograph.

The incidence of patent metopic sutures within each age range was investigated in both sexes of the Trisomy 21 and Control groups.

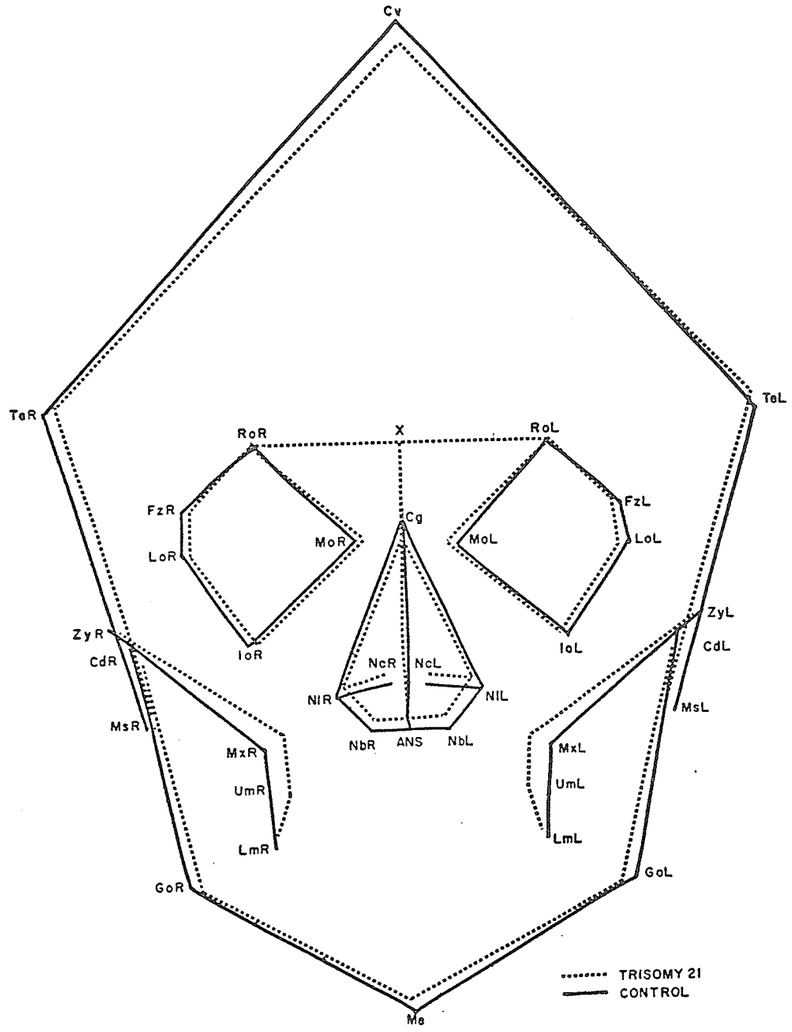
Assessment of the Incidence of Sutural Bones (Wormian) Present in the Cranial Sutures

The incidence of sutural bones within the metopic, inter-parietal, coronal, and lambdoid sutures was studied in the Trisomy 21 and Control groups. Regardless of the actual numbers of sutural bones observed per case, in the calculation of the data, no account was taken of the number of wormian bones present, rather, only the percentage of individuals showing the presence of wormian bones within the cranial sutures has been reported.



Duplicates of Figures 5, 10 and 11 may be helpful in the reading of the Results.

Duplicates of Figure 63 and Table VIII may be helpful during the reading of the Discussion.



IV. COMPUTER POLYGONAL PLOT FOR THE TRISOMY 21 AND CONTROL SAMPLES

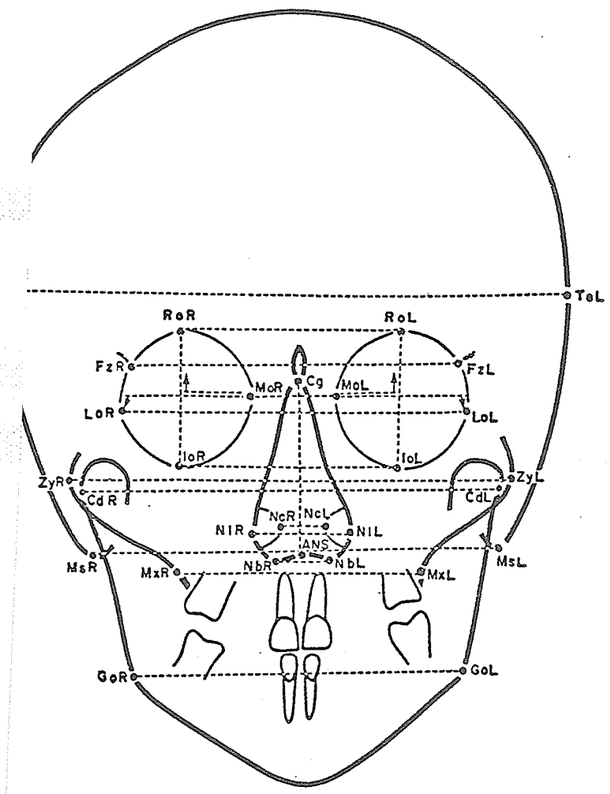
(Figure 63)

TABLE VIII

PERCENTAGE OF WIDTH ATTAINED BY THE TRISOMY 21 GROUP, USING THE MEAN MEASUREMENTS OF THE CONTROL AND TRISOMY 21 GROUPS FOR 21 VARIABLES

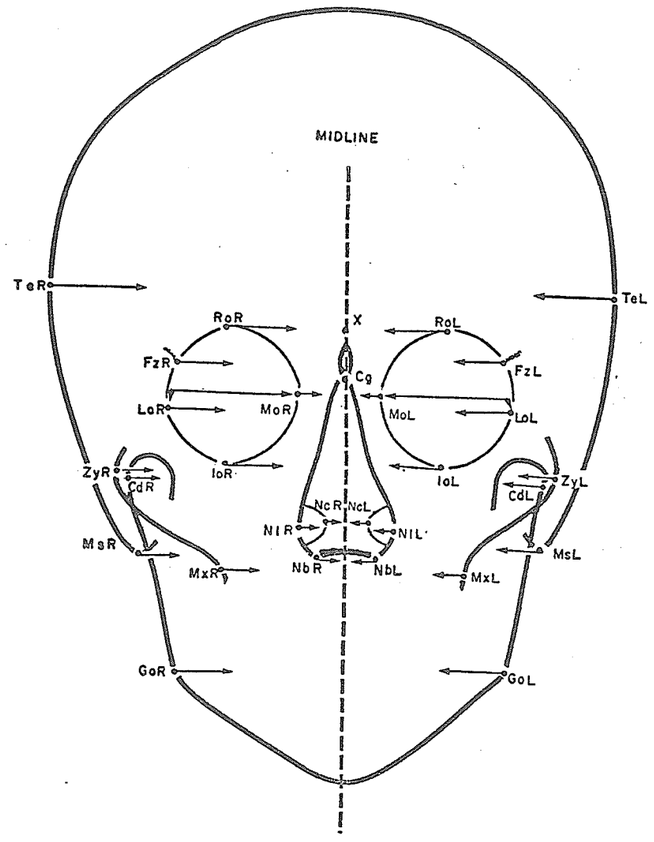
VARIABLE	TRISOMY 21 Mean Width mm.	CONTROL Mean Width mm.	PER CENT TRISOMY 21 TO CONTROL
"H" MoR-MoL	17.1	20.9	81.8
"V" Cg-ANS	39.0	45.5	83.5
"H" MxR-MxL	51.6	61.2	84.3
"H" NbR-NbL	14.5	16.1	90.0
"H" NlR-NlL	28.1	30.8	91.2
"H" GoR-GoL	88.8	94.8	93.6
"H" IoR-IoL	64.2	67.4	95.2
"H" MsR-MsL	105.7	110.9	95.3
"H" FzR-FzL	89.0	92.9	95.8
"H" LoR-LoL	91.1	94.4	96.5
"H" ZyR-ZyL	123.5	126.8	97.3
"H" TeR-TeL	147.6	151.3	97.5
"H" CdR-CdL	113.6	116.4	97.5
"V" RoR-IoR	41.9	42.4	98.8
"V" RoL-IoL	41.7	41.9	99.5
"H" MoR-LoR	37.0	36.8	100.5
"H" MoL-LoL	37.0	36.7	100.8
"H" RoR-RoL	63.4	62.2	101.9
"H" MoR-RoR	23.4	21.2	110.3
"H" MoL-RoL	22.9	20.1	113.9
"H" NcR-NcL	8.9	6.2	143.5

V. TABLE VIII



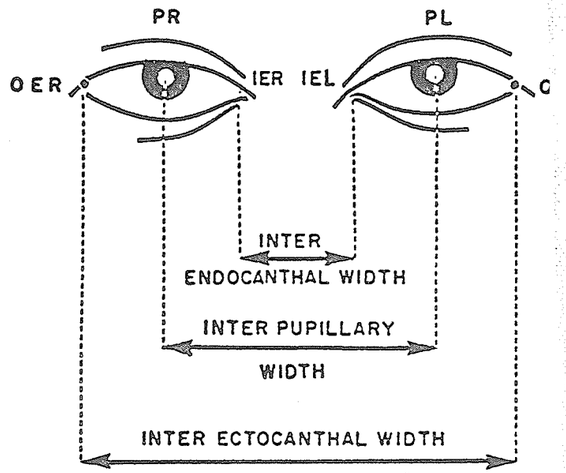
I. MEASUREMENTS USED IN THE SKELETAL ANALYSIS

(Figure 10)



II. MEASUREMENTS USED FOR THE ANALYSIS OF ASYMMETRY

(Figure 11)



III. SOFT TISSUE MEASUREMENTS

(Figure 5)

CHAPTER IV

RESULTS

Horizontal "H" and Vertical "V" projection distances to the supraorbital plane (RoR-RoL) and midline (X-Cg) respectively, were used to evaluate the craniofacial morphology and developmental changes, which occur through six age ranges in the Trisomy 21 and Control groups.

It is to be understood that the distance measured on the postero-anterior radiographs do not represent the actual 1:1 linear measurement between any two landmarks. This is because there is divergence of the rays of radiation. The distances recorded, are measures of the positions of the landmarks multiplied by a factor which varies directly with the distance of the point from the film and from the central ray. However, within the Control and Trisomy 21 groups under study, similar landmarks are sufficiently close to each other in the antero-posterior dimension, so that the increase in size due to magnification of any distance between similar structures in the two groups would be minimal. This was explained in Figure 4, in Methods and Materials. Hence, comparisons in the Trisomy 21 and Control groups can be made for only the same width, that is, bigonial width in the Trisomy 21 group can be compared with bigonial width in the Control group, as they lie approximately in the same coronal plane and would have similar magnifications.

It is also to be realized, that the effects of magnification will cause a minimal change in the measurement of the width between bilateral structures due to antero-posterior growth. Using Figure 4, the effects of magnification on width measurements, due to antero-posterior growth can be explained, if it can be imagined that the width between two landmarks was a certain value, as measured on the postero-anterior radiograph, which is a two dimensional image. Then, if for a moment we now consider that only antero-posterior growth was occurring, so that these two landmarks were translated forwards without any change in the position of these landmarks relative to each other, the only change would be that they are now located in a plane that lies anteriorly and, of course, closer to the film.

The magnification of any structure is dependent upon its distance from the film, therefore, growth changes which involve an alteration of that separation from the film incur a magnification error. This error has been calculated to be 0.6% over a distance of 10 mm. Thus, an observed increase during growth for structures located in front of the transmeatal axis would have to be reduced by a certain percentage in order to obtain the true change, and conversely, increased by a certain percentage in the case of changes behind the transmeatal axis. Thus, over a range of 20 mm., which is the maximum possible growth change that the subject could incur (Colby, 1972), the error due to magnification could be as large as 1.2% in the parameter measured.

It has been shown by Colby (1972) that the total antero-posterior growth from the age of 3 years to adulthood in this group of controls does not exceed 20 mm. Frostad (1969) and Ghiz (1968) have also shown that although the antero-posterior distance between given points in Trisomy 21 individuals is smaller than the normal group, the rate and direction of growth remains the same as that of the normal sample after the age of 4 years. From the work of these researchers, it may be said that, if a reduction in width was noticed when measured on the postero-anterior film, a reduction in the order of 1.2% may be attributed to the anterior growth of these structures. However, if there was an increase in width over and above the 1.2% decrease attributed to antero-posterior growth, then a true increase in width between the two bilateral landmarks had occurred.

For ease of comprehension, the results have been placed under five main headings, as follows: (1) skeletal analysis, (2) asymmetries of the craniofacial skeleton, (3) distance between the orbital cavities, the pupils, and the eyes, (4) differences observed in the presence of patent metopic sutures, and (5) differences observed in the presence of sutural bones. The means and standard errors for all the variables used in the skeletal analysis have been presented in the Appendix in Tables XV to XXXV.

The various linear and vertical distances used in this study were statistically analysed using the analysis of variance, which permitted the study of some of the various

parameters affecting craniofacial growth. The parameters considered in this study were groups (Trisomy versus Normal), sex (male versus female), age range (six age ranges described previously), and in the asymmetry part of the study, side (right versus left) was used as an additional factor. The above four factors are considered to be the main effects or parameters studied. This statistical test not only permits detection of significant differences between the means of the factors, but also permits the study of the interaction among the various factors. A significant group x sex interaction would indicate that the effect of the group on the variable studied was not similar for the two sexes, or that the difference between the means in the two sexes was not similar in the two groups. These interactions are termed second order interactions.

Third order interactions could involve any of the three parameters, that is group x sex x age. In the section dealing with the skeletal analysis, no third order interactions were significant, however, in the section dealing with the results pertaining to asymmetries a group x side x age, interaction was significant for some variables and these third order interactions have been explained under that section. No fourth order interactions were significant and hence, were not considered in this study.

The levels of significance for the various variables in the skeletal analysis have been presented in Table VI. Similar levels of significance for the 30 variables in the

TABLE VI

LEVELS OF SIGNIFICANCE REVEALED BY THE ANALYSIS OF VARIANCE FOR 21 LINEAR VARIABLES AND 4 SOFT TISSUE RATIOS

Source of Variation	Between Groups (Trisomy or Control)	Between Sexes (Male or Female)	Among Ages (6 age ranges)	Group x Sex	Group x Age	Sex x Age	Group x Sex x Age
A. CRANIUM							
TeR-TeL	**	**	**				
MsR-MsL	**	**	**				
B. UPPER FACE							
ZyR-ZyL	**	**	**			**	
MxR-MxL	**	**	**		**	**	
NlR-NlL	**		**				
NbR-NbL	**		**				
NcR-NcL	**		**				
Cg-ANS	**	**	**		**	*	
MoR-MoL	**		**		**		
RoR-RoL	*		**		*		
MoR-RoR	**						
MoL-RoL	**						
IoR-IoL	**	**	**		*	*	
FzR-FzL	**	**	**			*	
LoR-LoL	**	**	**				
MoR-LoR		**	**				
MoL-LoL		**	**				
RoR-IoR		**	**				
RoL-IoL		**	**				
C. LOWER FACE							
CdR-CdL	**	**	**			*	
GoR-GoL	**	**	**			**	
D. RATIOS							
MoR-MoL/ZyR-ZyL	**	**	**		*		
PR-PL/ZyR-ZyL	**						
IER-IEL/ZyR-ZyL	**		**				
OER-OEL/IER-IEL	**	**	**				

* Significant at the 5% level.
** Significant at the 1% level.

TABLE VII

LEVELS OF SIGNIFICANCE REVEALED BY MIXED ANALYSIS OF VARIANCE FOR 30 LINEAR VARIABLES REPRESENTING HORIZONTAL ASYMMETRIES OF THE CRANIOFACIAL SKELETON

SOURCE OF VARIATION	CRANIUM		UPPER FACE											LOWER FACE	
	TeR & TeL	MsR & MsL	ZyR & ZyL	MxR & MxL	N1R & N1L	NbR & NbL	NcR & NcL	RoR & RoL	FzR & FzL	LoR & LoL	IoR & IoL	MoR & MoL	MoR-Lor & MoL-LoL	CdR & CdL	GoR & GoL
Among Ages	**	**	**	**	**	**	**	**		**	**	**	**	**	**
Between Groups	**	**	**	**	**	**	**	**	**	**	**	**		**	**
Between Sexes	**	**	**	**					**	**	**		**	**	**
Between Sides	**	**	**		**	**		*	**	**	**	**		**	**
Group x Age				**				*		*		*			
Group x Sex															
Group x Side	**	**	**											**	
Sex x Age			**	**					*	*				*	**
Sex x Side															
Age x Side	**	**	**											**	**
Group x Age x Side	**	**	*											**	*
Group x Sex x Side	**														
Group x Sex x Age															
Sex x Age x Side															
Group x Sex x Age x Side															

* Significant at the 5% level.
** Significant at the 1% level.

asymmetry part of the study have been presented in Table VII. Only those main effects and interactions that were significant at the 1% and 5% levels have been discussed, as these levels of significance are acceptable for biological data.

I. SKELETAL ANALYSIS

A. CRANIUM

Width of the cranial vault

The width of the cranial vault was measured by the horizontal projected distance, TeR-TeL. A difference significant at the 1% level was found between the two groups and among the sexes. The Trisomy 21 individual was smaller than the Control. The mean width of the cranial vault was 147.6 mm. and was 151.3 mm. for the Trisomy 21 and the Control samples respectively. Males had significantly larger cranial widths than females. The average cranial width for the males was 151.2 mm. and for the females was 147.6 mm.

The width of the cranial vault was also significantly different at the 1% level among the age ranges (Figure 12). A nearly linear growth pattern was observed from the age range of 3-5 to 12-15 years, which was followed by diminished incremental growth up to the age range of 16-19. After this age range, no significant changes were observed in this measurement. Since no significant group x age, or sex x age interactions were detected, it can be said that the development

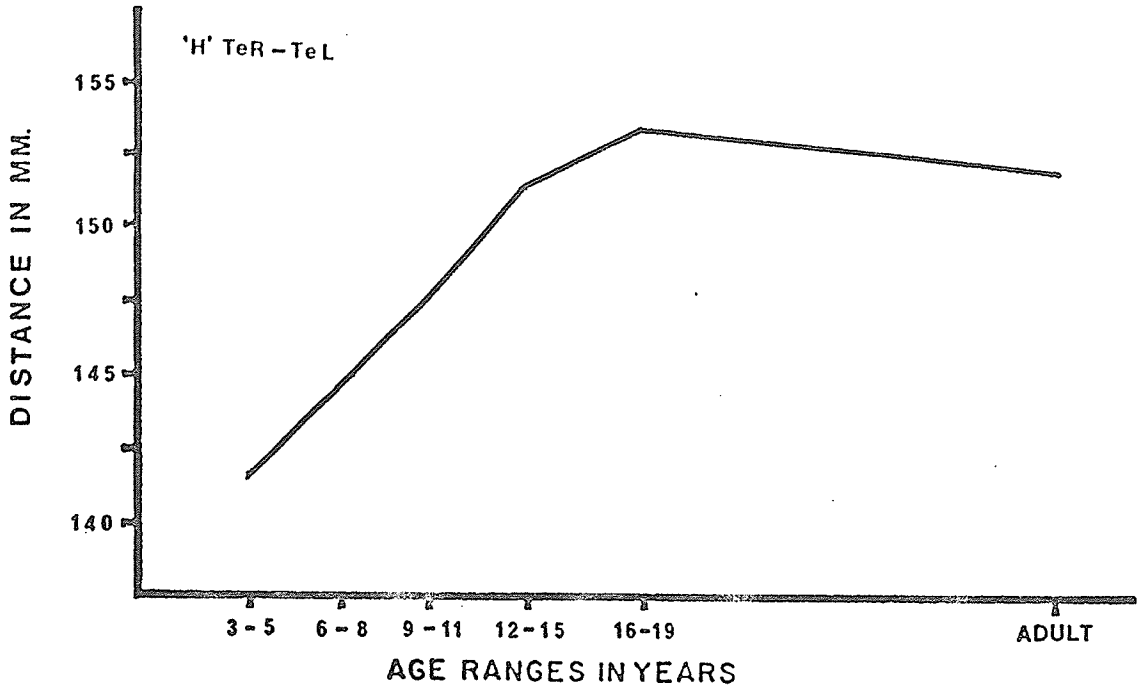


Figure 12. Main effect of age on the linear distance TeR-TeL.

of this dimension was parallel in the Trisomy 21 and Control groups and in both the sexes. Therefore, the illustration of the main effect of age was considered representative of both groups for this variable. Examination of the mean measurements of this variable in the two groups, at different ages, indicated that the Trisomy 21 individual was small in the age range of 3-5 years, and this smallness persisted throughout the age ranges studied.

Bimastoid width MsR-MsL

The linear measurement, MsR-MsL, representing the width between the mastoid process of each temporal bone, showed significant differences to exist at the 1% level when the main effects of the group, age, and sex were considered.

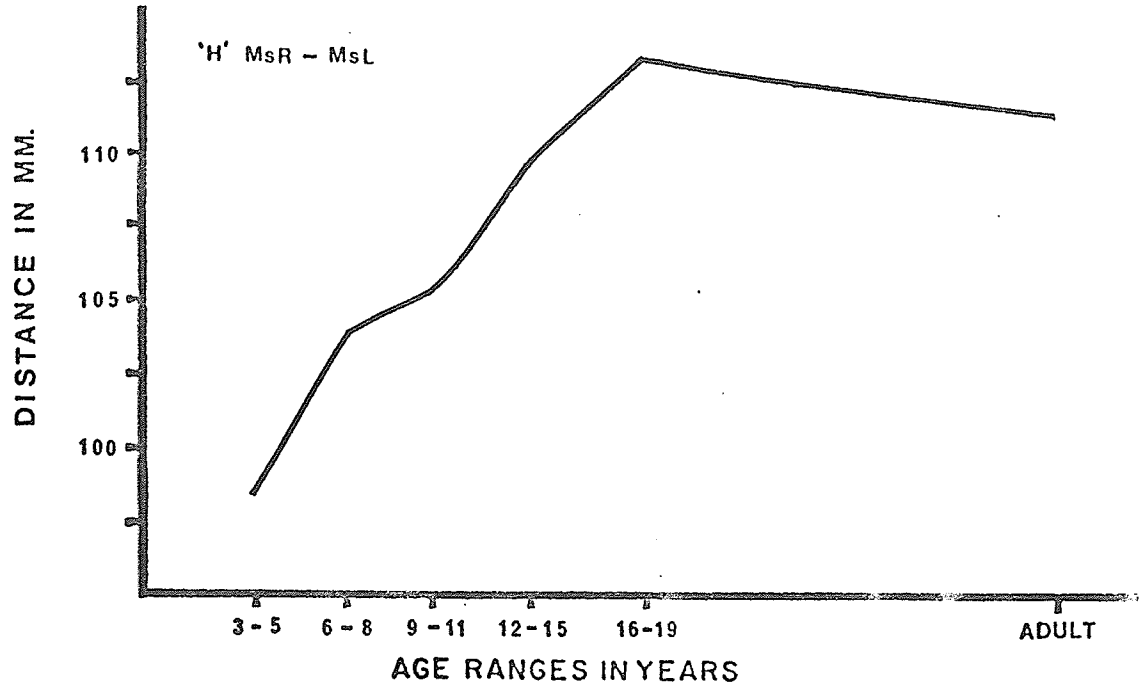


Figure 13. Main effect of age on the linear distance MsR-MsL.

The mean bimastoid width in the Trisomy 21 group was 105.7 mm. while that in the Control was 110.9 mm. The main effect of sex indicated a mean measurement of 106.1 mm. in the females, while it was 110.5 mm. in the males.

The main effect of age is illustrated in Figure 13. The difference between the age ranges was significant at the 1% level. Since no group x age or group x sex interactions were detected, this observation indicates that the increase in this dimension was parallel in the two groups and sexes.

Appreciably large increments occurred in this measurement between the age ranges of 3-5 years to 6-8 years and between the age ranges of 9-11 to 16-19 years. A diminished incremental growth was noted between the age ranges of 6-8 years to 9-11 years. A slight decrease in this measurement

was noted after the age range of 16-19 years.

In summary, parallel developmental changes were observed in the cranial measurements of both groups, however, the Trisomy 21 individual started out smaller in this measurement and stayed smaller throughout the age ranges studied.

B. UPPER FACE

Bizygomatic width

The linear dimension between the two zygomatic arches (ZyR-ZyL) showed a group effect significant at the 1% level, with the average values for the Control being larger than that of the Trisomy group. The average values for the Trisomy group was 123.5 mm. and the Control group was 126.8 mm.

The bizygomatic width was significantly different at the 1% level among the different age ranges (Figure 14). A nearly linear growth pattern was shown by both populations up to 12-15 years which was followed by a diminished incremental growth in the older age groups. No significant group x age interaction was detected implying that this measurement behaved the same in both groups.

A significant main effect of sex showed the females to be smaller than the males in both groups combined. The mean bizygomatic width for the males was 127.8 mm. and for the females was 122.3 mm. However, an age x sex interaction (Figure 15) indicated that though the females were smaller in the age range of 3-5 years, they tended to approach the

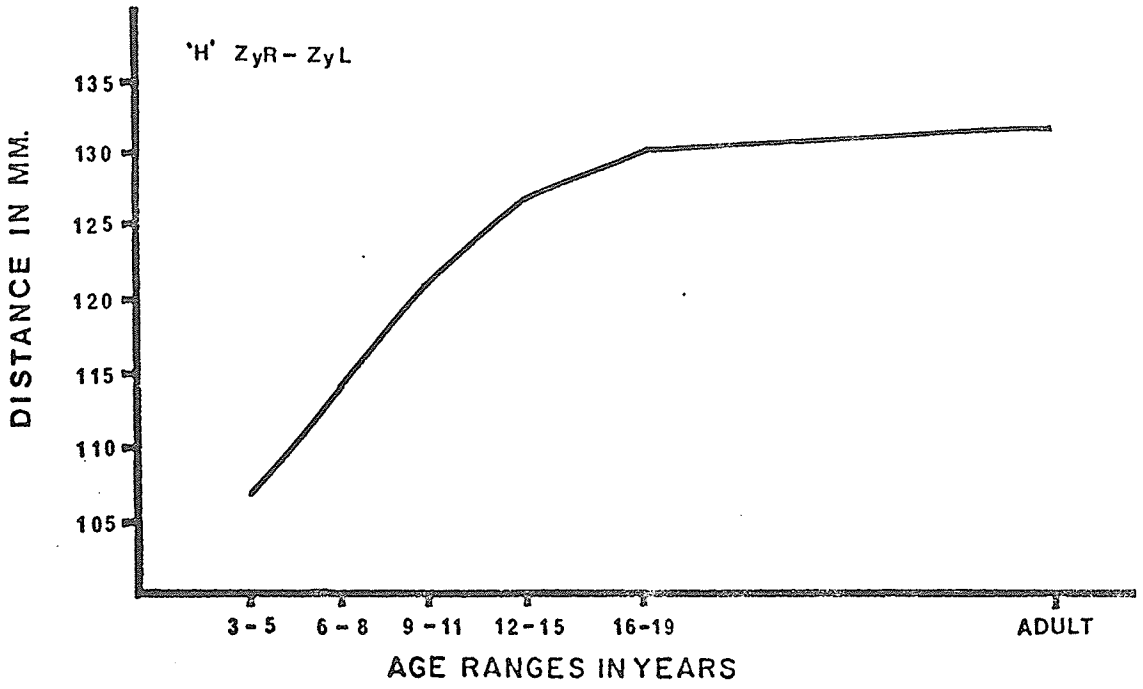


Figure 14. Main effect of age on the linear distance ZyR-ZyL.

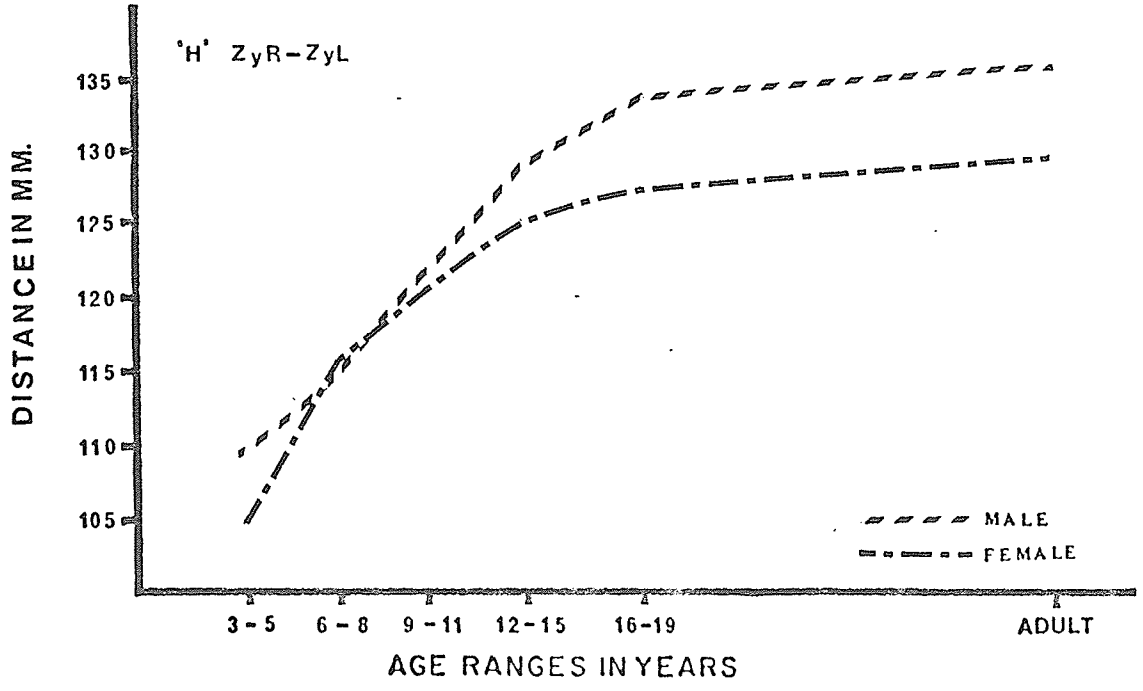


Figure 15. Effect of age on the linear distance, ZyR-ZyL, for the males and females of both groups.

male measurements in between the ranges of 6-8 years and 9-11 years. In the age range of 12-15 years, the males showed a greater incremental increase than the females, leading to a larger bizygomatic width in the males than in the females in the age range from 12-15 years and above.

Width of the maxilla

Bimaxillary width, represented by the linear measurement MxR-MxL, was significantly greater at the 1% level in the Control group than in the Trisomy 21 group. The mean measurement for the Control group was 61.2 mm. and for the Trisomy 21 group was 51.6 mm. A significant effect of group x age shown in Figure 16, indicated that a continual increase in this measurement occurred until the age range of 16-19 years in the Control group, but the Trisomy 21 group showed no significant increase in this width between the age ranges of 6-8 years to 9-11 years, however, there was a slight increase in this measurement between the age ranges of 9-11 years to 12-15 years.

Furthermore, the difference in width of maxilla of the Trisomy 21 and Control groups at the age range of 3-5 years was smaller than the difference in maxillary width at older ages in the two groups. It is interesting to note that the mean width of the maxilla in any age range in the Trisomy 21 group does not approach the values of the width of the maxilla as seen in the Control group, even at the age range of 3-5 years.

The males were generally larger in both samples than

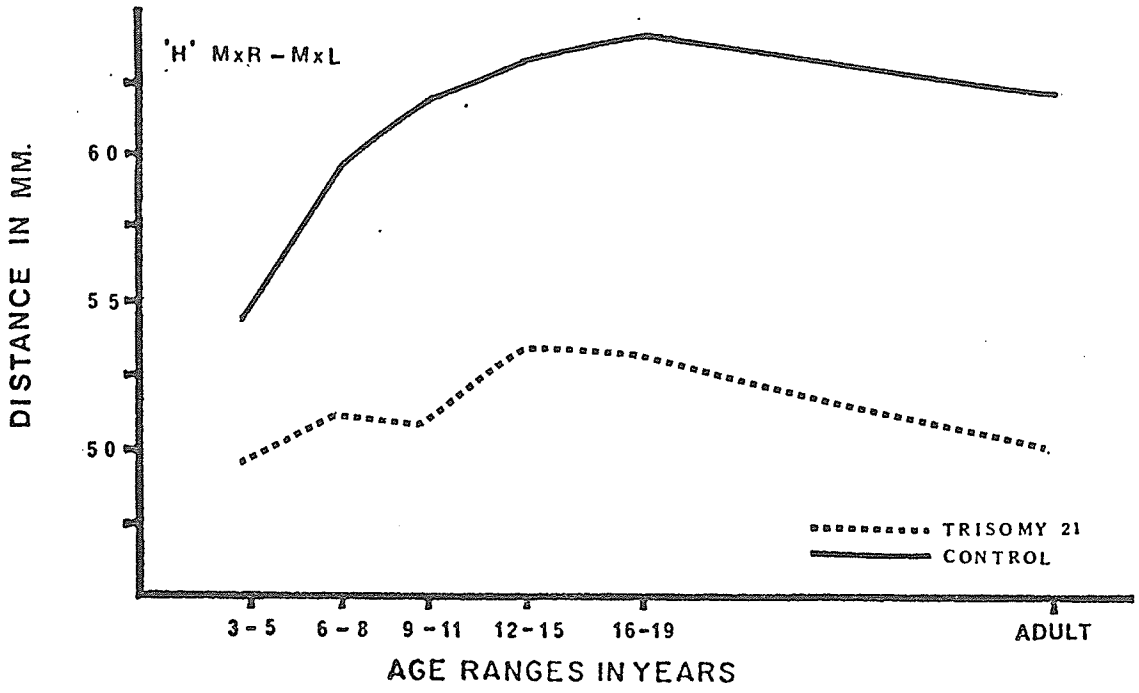


Figure 16. Effect of age on the linear distance MxR-MxL for the Trisomy 21 and Control groups.

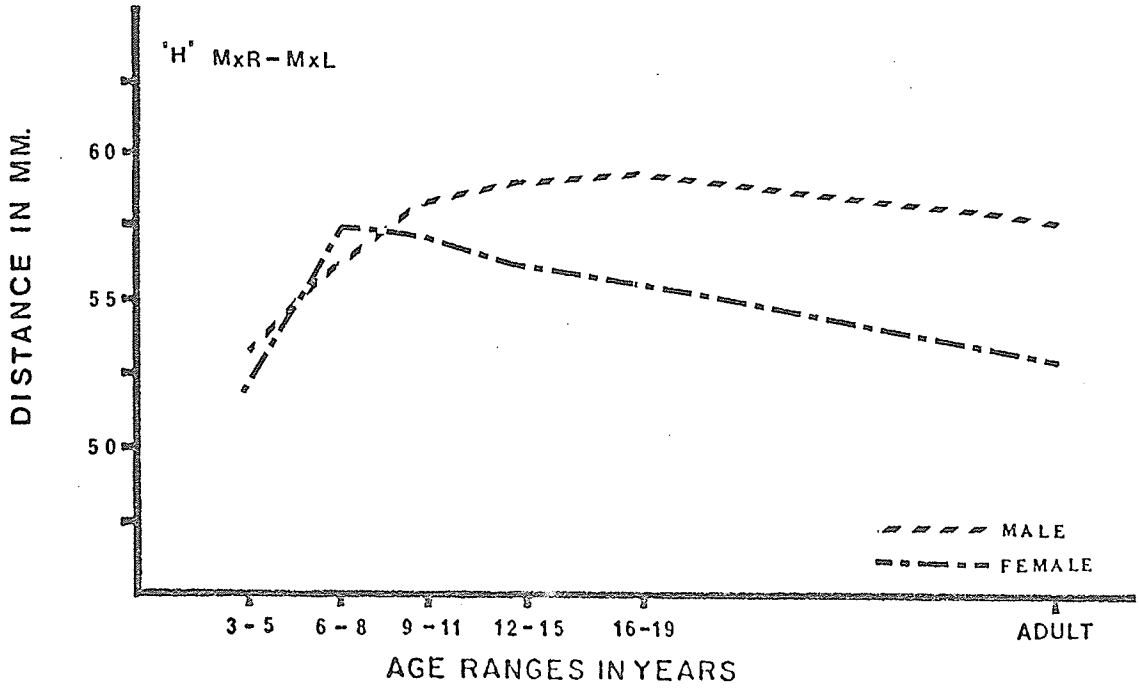


Figure 17. Effect of age on the linear distance MxR-MxL for the males and females of both groups.

the females. The mean figures for the Control males, Trisomy males, Control females, and Trisomy females were 65.6 mm., 60.0 mm., 53.3 mm., and 49.4 mm., respectively. A sex x age effect significant at the 1% level indicated that the males and females were different in the development of this measurement. As can be seen from Figure 17, the females of both groups tended to achieve their maximum maxillary widths by the age range of 6-8 years and the males tended to achieve their maximum maxillary width by the age range of 9-11 years.

Width of the Nasal Cavity

The width of the lower part of the nasal cavity was assessed by the measurement N1R-N1L. A between group effect was significant at the 1% level and showed that the nasal cavity was smaller in the Trisomy 21 than in the Control. The mean for the Control was 30.8 mm. and for the Trisomy was 28.1 mm. Among the different age ranges a significant difference at the 1% level was observed (Figure 18). A linear increase was found to occur from the age range of 3-5 years to 12-15 years.

A smaller amount of incremental growth was observed from the age range of 12-15 years to 16-19 years and very little change was noted thereafter. No interactions were present and examination of the mean measurements showed that parallel growth was observed between the Trisomy 21 and Control groups until the age range of 16-19 years, as illustrated in Figure 19.

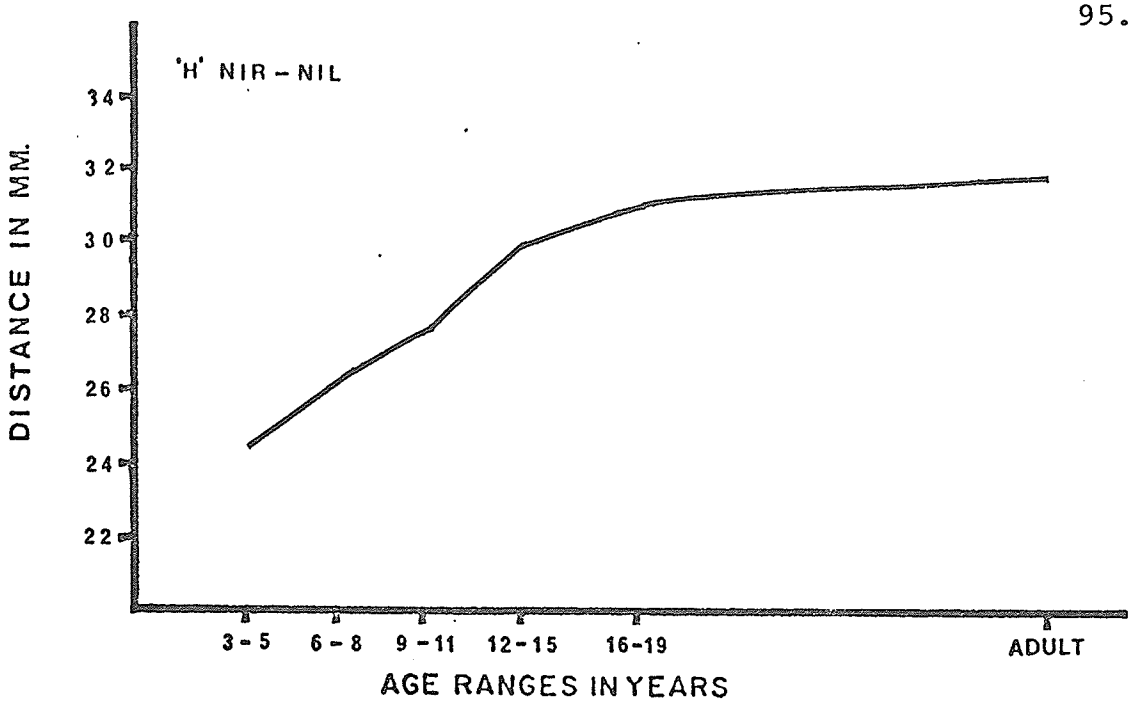


Figure 18. Main effect of age on the linear distance N1R-N1L.

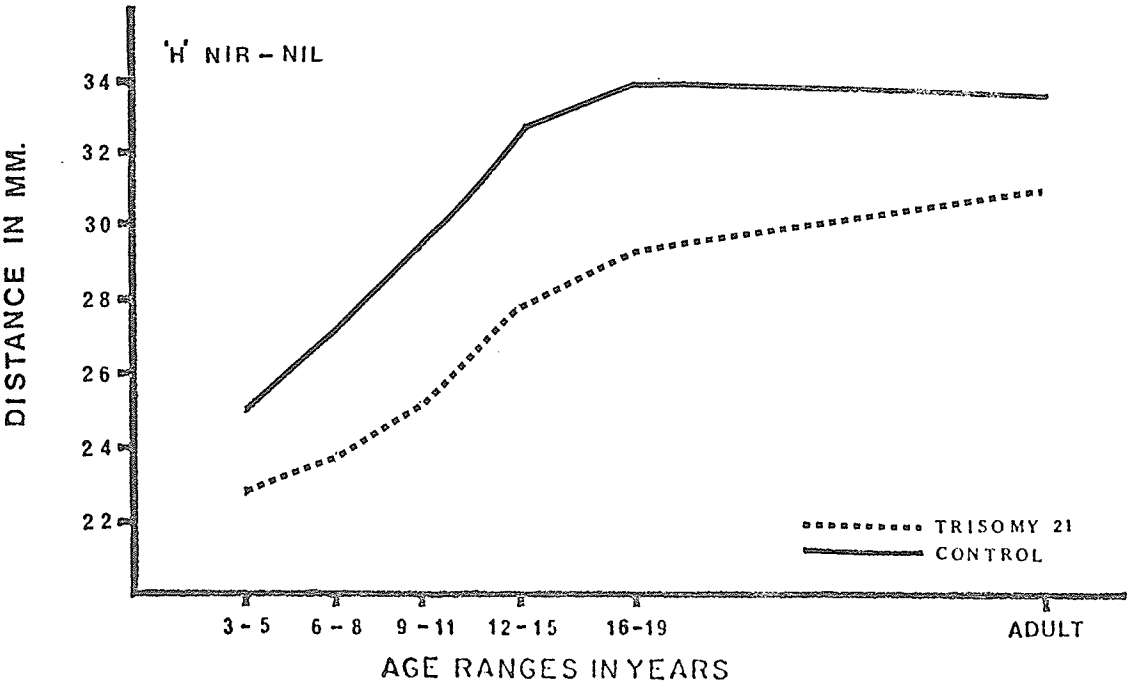


Figure 19. Effect of age on the linear distance N1R-N1L for the Trisomy 21 and Control groups.

Nasal base width

The width at the base of the nasal cavity was assessed by the measurement NbR-NbL. A between group effect was significant at the 1% level, and showed that the nasal base was smaller in the Trisomy 21 than in the Control. The mean for the Control was 16.1 mm. and the Trisomy 21 was 14.5 mm.

The main effect of age was significant at the 1% level and is shown in Figure 20. Significantly larger increments occurred in this measurement between the age ranges of 3-5 to 6-8 years and between the age ranges of 9-11 to 16-19 years. The rate of increase was diminished between the age ranges of 6-8 to 9-11 years and between the age ranges of 12-15 to 16-19 years. No group x age interactions were significant, therefore, the illustration of the main effect of age was considered representative of both groups for this variable.

Width between the inferior nasal conchae

The distance NcR-NcL was used to measure the separation between the inferior nasal conchae. This distance was significantly different between groups at the 1% level, and showed that the Trisomy 21 group had a larger separation between the inferior nasal conchae than the Control group. The mean measurement for the Trisomy 21 was 8.9 mm. and that of the Control was only 6.2 mm.

Among the six age ranges, a significant difference at the 1% level was found (Figure 21). The changes observed with age in this distance indicated that very little separation

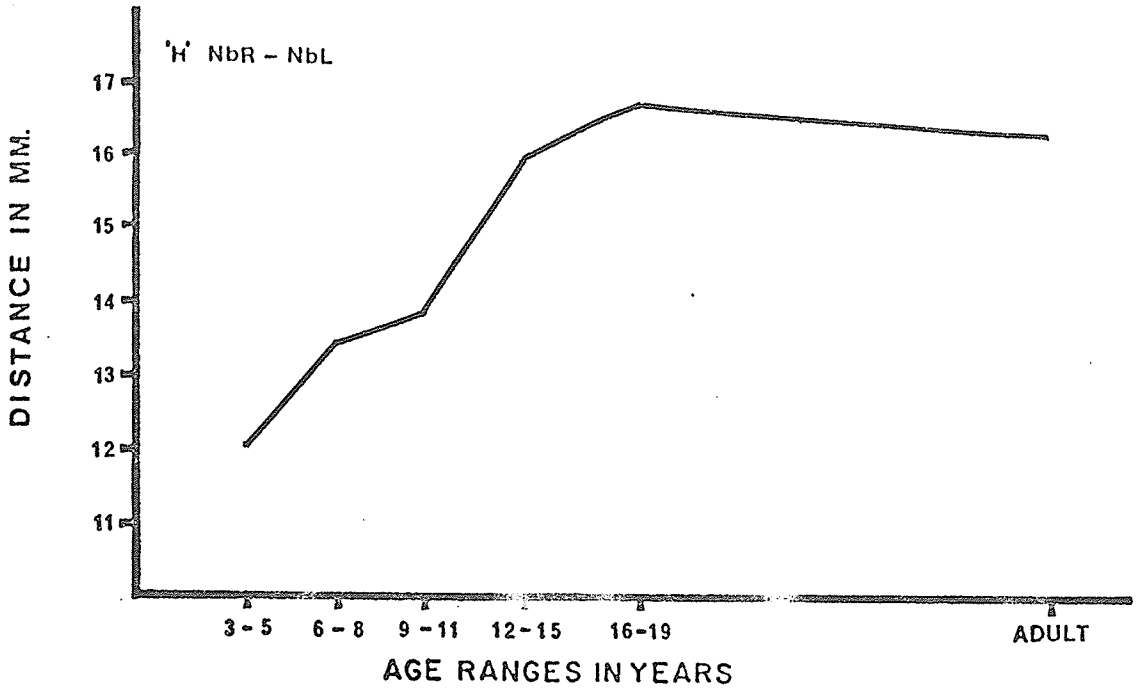


Figure 20. Main effect of age on the linear distance NbR-NbL.

between the inferior nasal conchae occurred between the age ranges of 3-5 to 9-11 years. However, a linear increase was observed between the age ranges of 9-11 to 16-19 years. After the age range of 16-19 years, no increase in this measurement occurred.

No group x age effects were significant and examination of the mean measurements at the six age ranges indicated that the Trisomy 21 group showed a wider separation between the inferior nasal conchae at all age ranges (Figure 22).

Height of the nasal cavity

The nasal cavity height was measured as the vertical projection distance, Cg-ANS. This measurement showed significant differences at the 1% level among the six age ranges, between groups, between sexes, and group x age. A sex x age

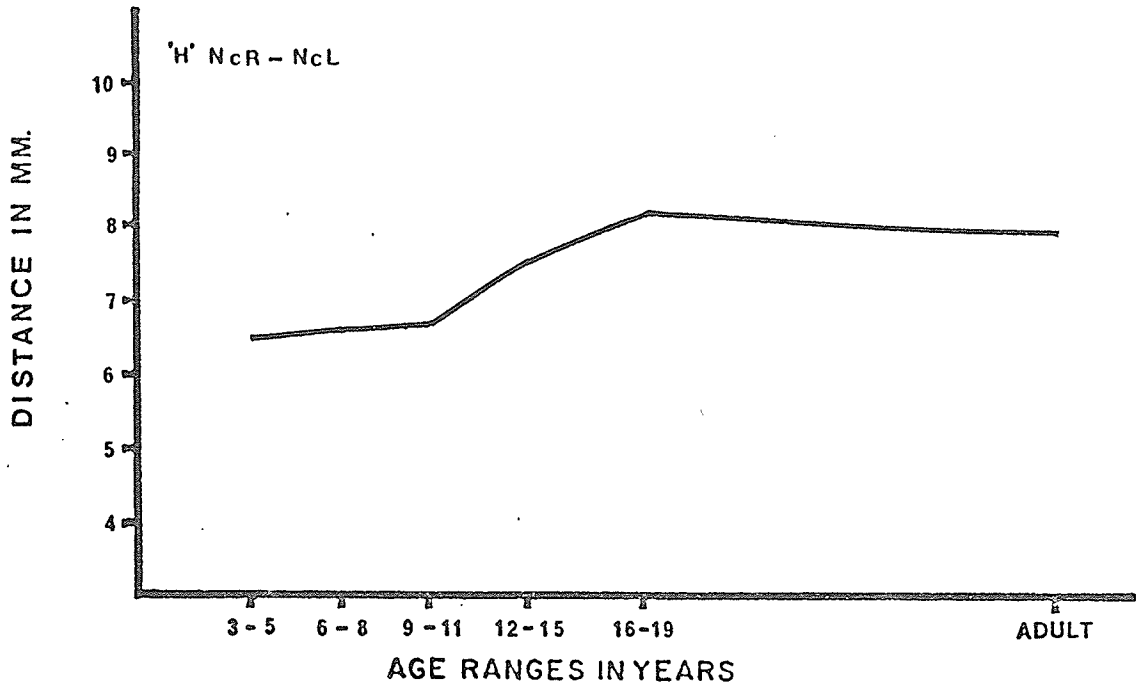


Figure 21. Main effect of age on the linear distance NcR-NcL.

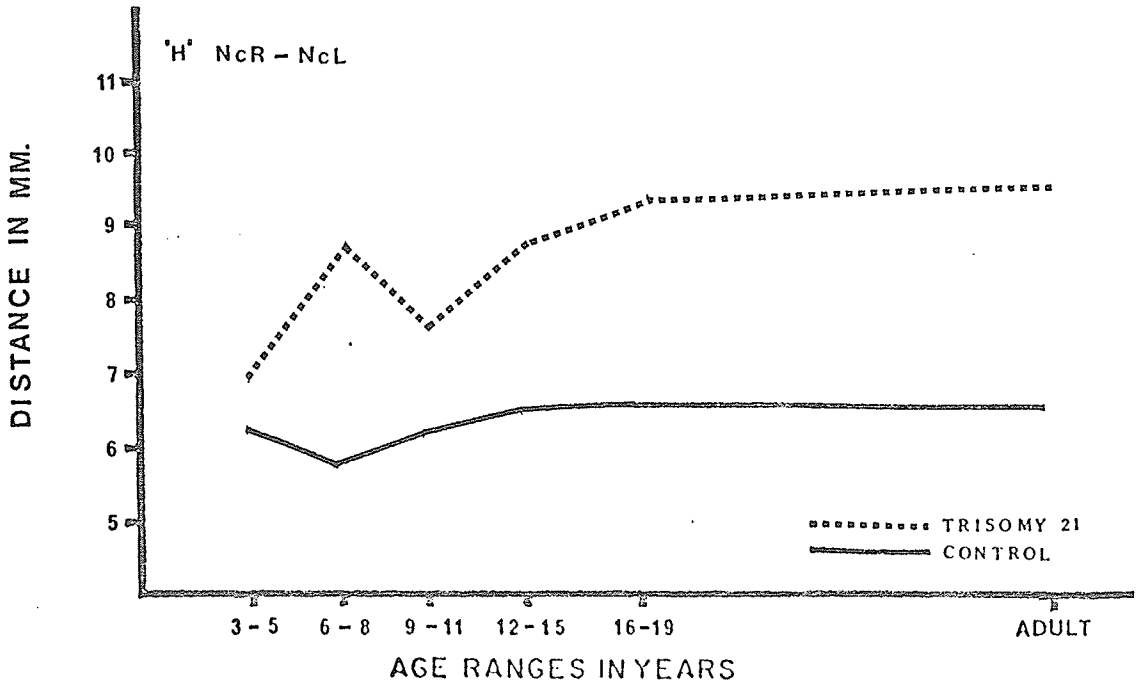


Figure 22. Effect of age on the linear distance NcR-NcL for the Trisomy 21 and Control groups.

interaction was significant at the 5% level.

The significant main effect of group showed that the Trisomy 21 individual was considerably smaller than the Control. The mean measurement for the Trisomy 21 was 39.0 mm. and 45.5 mm. for the Control. The significant group x age effect (Figure 23), showed that in the Controls a nearly linear increase occurred in this measurement from the age range of 3-5 to 16-19 years and no incremental growth occurred after the age range of 16-19 years.

In the Trisomy 21 group, no significant increases in the nasal cavity height were observed between the age ranges of 3-5 years to 6-8 years and between the age ranges of 12-15 years to 20-56 years, but a significant linear increase occurred between the age ranges of 6-8 years to 12-15 years.

Due to the larger incremental growth in the Control, the Trisomy 21 individual was not only 3.5 mm. smaller than the Control at the age range of 3-5 years but, at the age range of 20-56 years, this difference in the nasal cavity height between the Trisomy 21 and Control was 11.2 mm. This suggests a retardation in growth of the nasal cavity height of the Trisomy 21 individuals.

The main effect of sex, again indicated that females were smaller than the males with the mean measurement for the males being 43.3 mm. and 41.4 mm. for the females.

A sex x age interaction (Figure 24) showed that females paralleled the developmental pattern of the males until the age range of 12-15 years but between the age ranges of 12-15

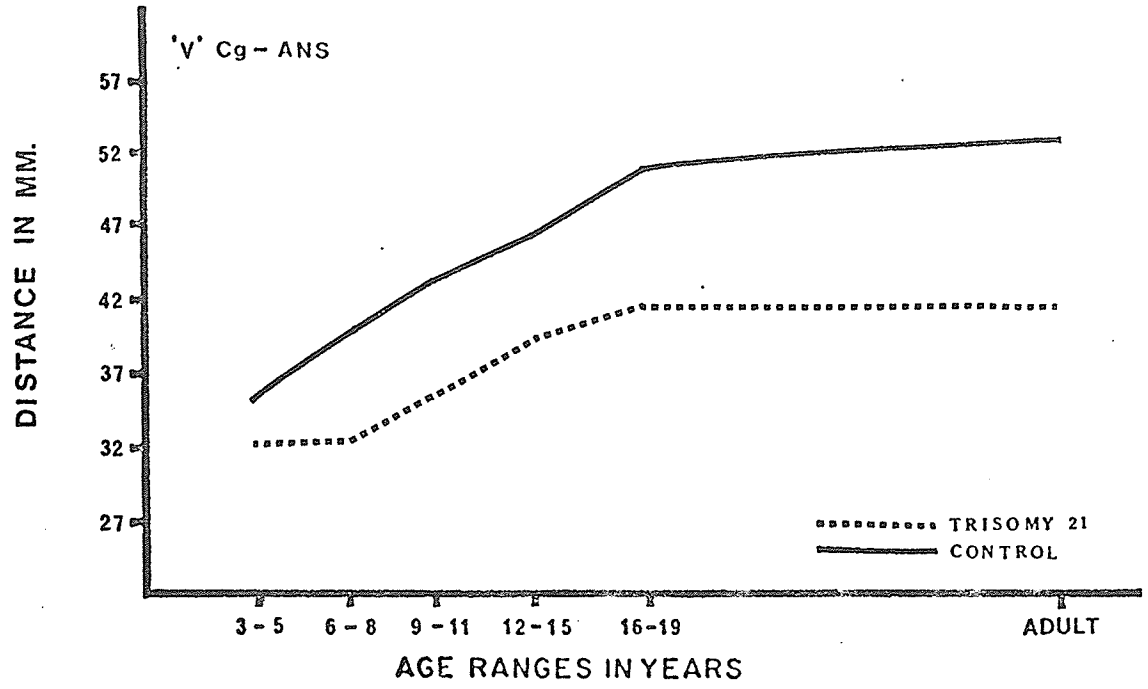


Figure 23. Effect of age on the linear distance Cg-ANS for the Trisomy 21 and Control groups.

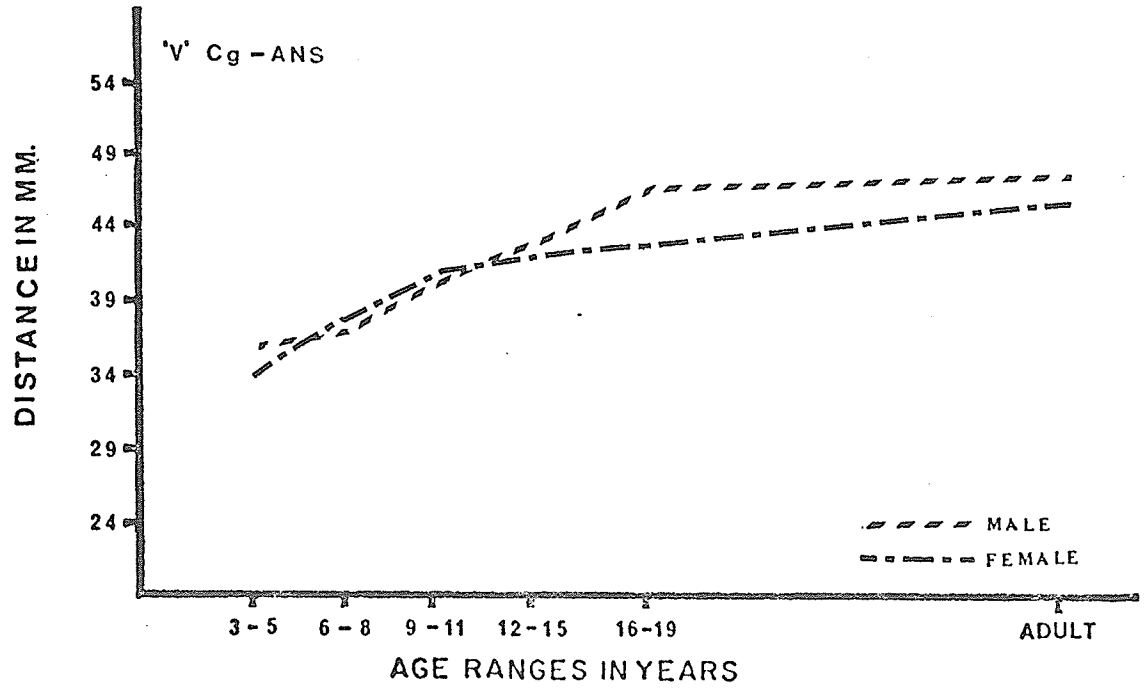


Figure 24. Effect of age on the linear distance Cg-ANS for the males and females of both groups.

years to 16-19 years the males showed larger growth increments than the females.

Width between the orbits

The inter-orbital width was represented by the linear distance MoR-MoL. The main effect of group was significant at the 1% level and indicated that in the Trisomy 21 group, the distance between the orbits was smaller than in the Control population. The mean measurement for the Trisomy 21 sample was 17.1 mm. and that of the Control sample was 20.9 mm.

A group x age effect was observed to be significant at the 5% level and is illustrated in Figure 25. This figure indicates that there was a linear increase in this measurement in the Control group until the age range of 12-15 years, with a reduced rate of increase thereafter. The Trisomy 21 individuals, however, showed appreciable increases between the age ranges of 3-5 years to 6-8 years and between the age ranges of 9-11 years to 12-15 years. No significant increases were observed between the age ranges of 6-8 years to 9-11 years and after the age range of 12-15 years.

Supraorbital width

The changes in the distance between the most superior point on the superior orbital margin of the two orbits, was studied by the linear dimension RoR-RoL. A between group effect was significant at the 5% level, with the Trisomy 21 group being larger than the Control. The mean for the

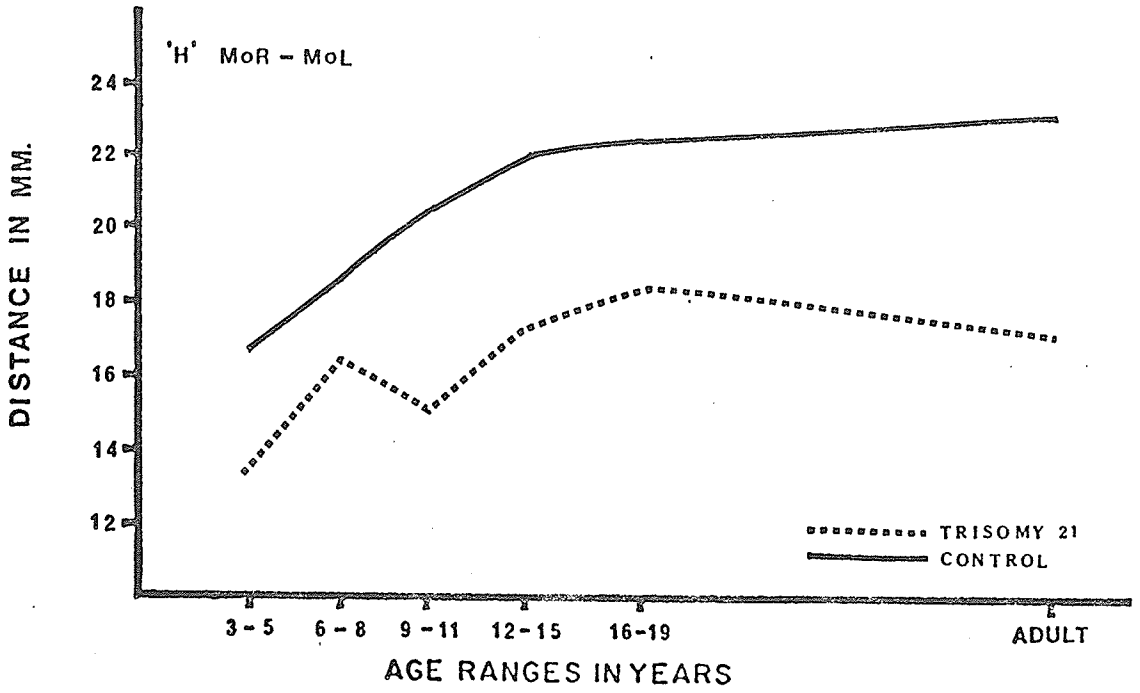


Figure 25. Effect of age on the linear distance MoR-MoL for the Trisomy 21 and Control groups.

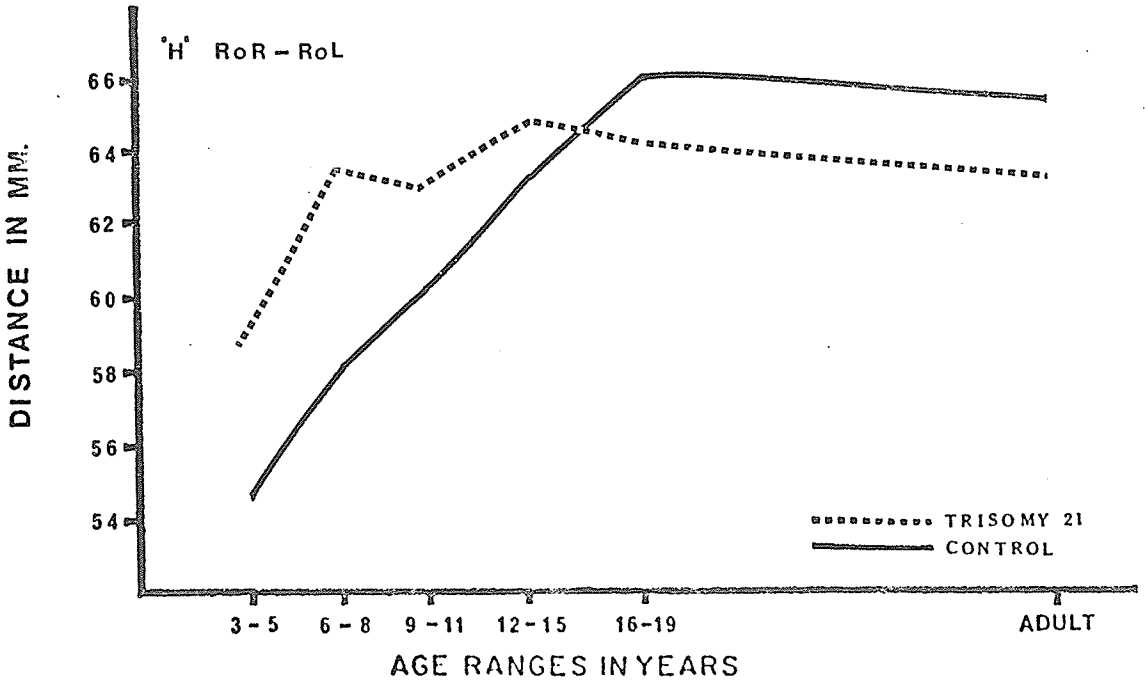


Figure 26. Effect of age on the linear distance RoR-RoL for the Trisomy 21 and Control groups.

Trisomy 21 group was 63.4 mm., while the mean for the Normal group was 62.2 mm. The separation between the most superior points on the roofs of the orbits was significantly different at the 1% level among the age ranges. However, a group x age interaction (Figure 26), significant at the 5% level, indicated that in the Trisomy 21 group the most superior points on the roofs of the orbits were located further apart until the age range of 12-15 years. Between the age ranges of 12-15 to 16-19 years an interaction occurred when the measurements for the Trisomy 21 group were smaller than the Control. The Control sample showed a linear increase in this measurement until the age range of 16-19 years, and no increases were seen thereafter.

This measurement, representing the horizontal separation between the most superior points on the superior orbital margins, when compared with the changes seen in the inter-orbital width, tend to indicate that at least up to the age range of 12-15 years, the most superior points on the superior orbital margins are located further laterally in the Trisomy 21 individuals. This is because the inter-orbital width, as seen in Figure 25, is smaller in the Trisomy 21 group as compared to the Control at all age ranges, but the width between the most superior points on the superior orbital margins in the Trisomy 21 individuals is larger than the Control, until the age range of 12-15 years (Figure 26).

Position of the roof of the orbit within each orbit relative to the medial orbital margin (MoR-RoR and MoL-RoL)

To further substantiate the finding that the most superior point on the orbital margin is located further laterally in the Trisomy 21 individual, the changes within each orbit were considered individually by taking the projection distance from the most medial point on the medial orbital margin to the most superior point on the superior orbital margin. This measurement for the right orbit was represented by the linear distance MoR-RoR. The only significant effect was a group effect, which showed the mean measurement to be 23.4 mm. in the Trisomy 21 sample and 21.2 mm. in the Control population.

The findings for the similar measurement in the left orbit obtained by the horizontal projection distance, MoL-RoL, showed a group effect significant at the 1% level. The measurement for this distance was again larger in the Trisomy 21 group as compared to that of the Control group. The mean measurement for the Trisomy 21 sample was 22.9 mm. and 20.1 mm. in the Control sample.

It would seem, therefore, that the most superior point on the superior orbital margin in the Trisomy 21 individual is located further laterally than in the Control. No group x age effects were significant and examination of the mean measurements at the six age ranges indicated some decrease in these measurements with age in the Trisomy, while an increase with age was observed in the Control group.

This measurement, however, remained higher in the Trisomy 21 at all age ranges (Figures 27, 28).

Frostad (1969) and Benda (1946, 1969), from their subjective evaluations of the orbital outlines in Trisomy 21 individuals, felt that the most superior points on the superior orbital outlines were located further laterally in these individuals. The objective measurements pertaining to this area described above, would tend to support the contention of Frostad and Benda.

Both these authors from their subjective observations on the superior orbital outlines, concluded that the shape of the complete orbital outline was egg shaped or oval in shape. Frostad also stated that the orbits had a lateral slant and appeared to be obliquely situated.

Spitzer, Rabinowitch and Wybar (1961) do not accept this contention of Benda (1946) even though they mention that subjective evaluation of their sample showed that 51% of the Trisomy 21 individuals had oval orbital outlines. One of the methods to look at the changes in the shape of the orbital outlines would be to look at the changes occurring at the inferior, lateral, and superior orbital margins. Also changes in the slant of the orbits could be studied by the changes occurring at inferior and superior orbital margins.

The changes occurring at the inferior orbital margins were observed by noting the changes in the IoR-IoL measurement. The changes in the lateral orbital margins were observed by the FzR-FzL and LoR-LoL measurements, which represent the distance between the fronto-zygomatic sutures and the most

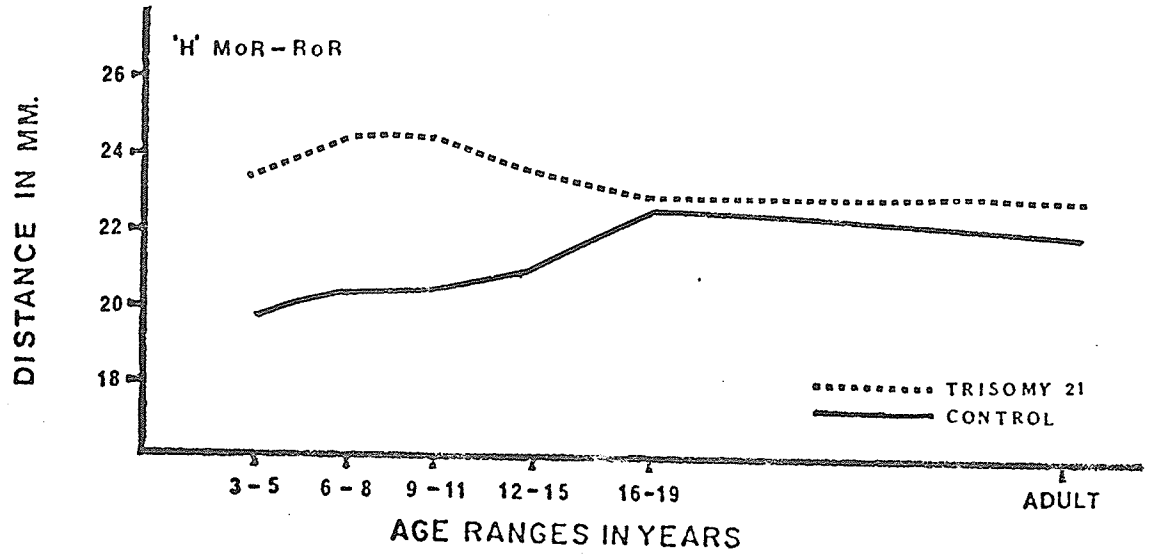


Figure 27. Effect of age on the linear distance MoR-RoR for the Trisomy 21 and Control groups.

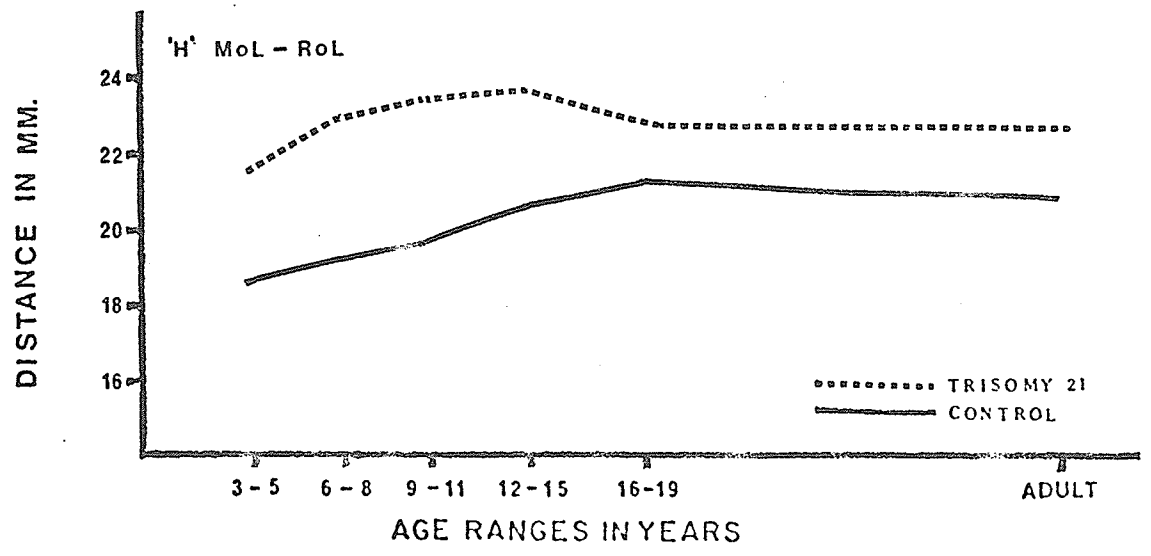


Figure 28. Effect of age on the linear distance MoL-RoL for the Trisomy 21 and Control groups.

lateral points on the lateral orbital outlines, respectively.

Bi-inferior orbital width (IoR-IoL)

Measurement of the horizontal separation between the lowermost points on the inferior orbital margins revealed significant differences for the main effects of age, sex, and between groups at the 1% level. The second order interactions of age x group and group x sex were significant at the 5% level.

The mean measurement for the Control group was 67.4 mm. and that for the Trisomy 21 group was 64.2 mm. A group x age effect was significant at the 5% level (Figure 29) and indicated that in the Control, some separation occurred between the lowermost points on the inferior orbital outlines between the age ranges of 3-5 years to 6-8 years and, thereafter, a linear increase occurred up to the age range of 12-15 years. No significant increases were noted after the age range of 12-15 years. In the Trisomy 21 sample the largest separation between the landmarks, IoR-IoL, occurred between the age ranges of 3-5 years to 6-8 years and a decrease was noted between the age ranges of 6-8 years to 9-11 years. A similar increment, as seen in the Control, was noted between the age ranges 9-11 years to 12-15 years. Thereafter, only a slight increase was noted until the age range of 16-19 years. No increases were seen thereafter.

The main effect of sex indicated that males were

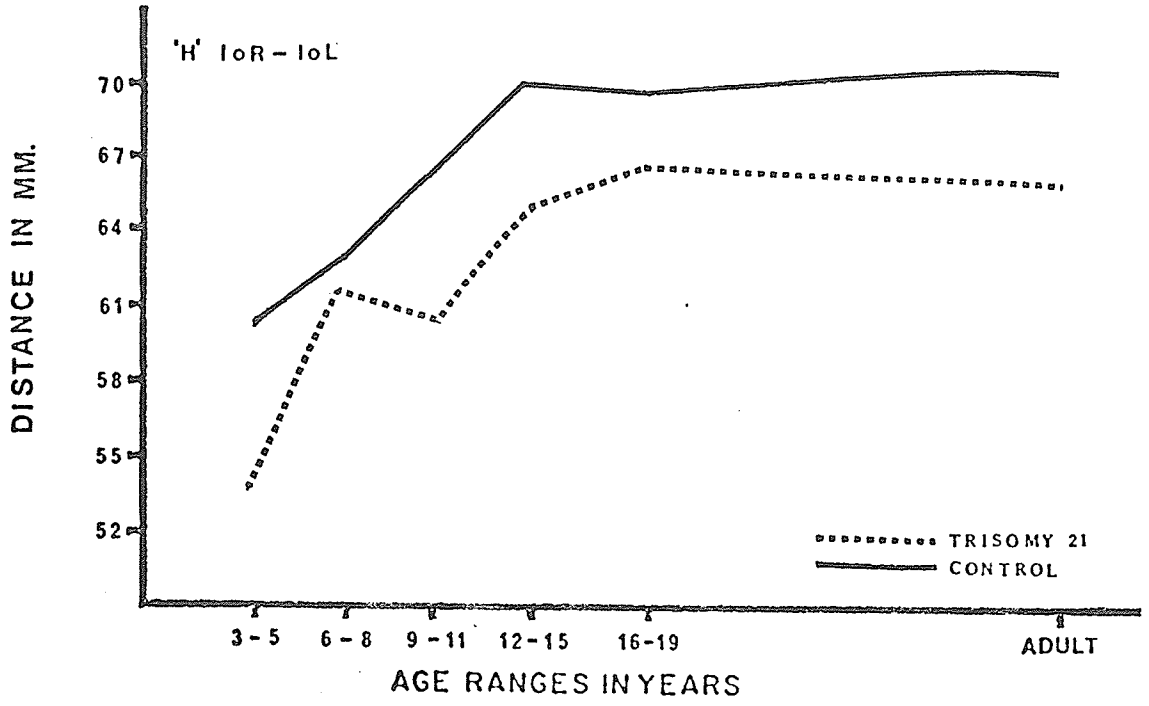


Figure 29. Effect of age on the linear distance IoR-IoL for the Trisomy 21 and Control groups.

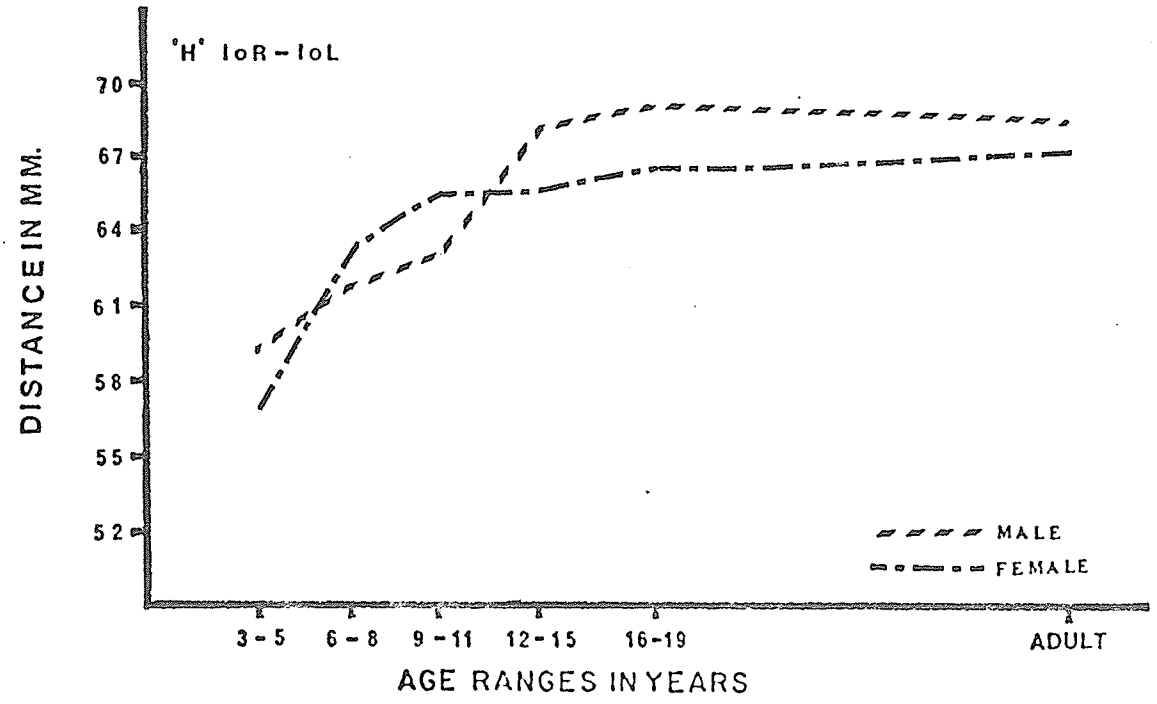


Figure 30. Effect of age on the linear distance IoR-IoL for the males and females of both groups.

larger than females. The mean measurement for the males was 66.8 mm. and for the females was 64.8 mm. A sex x age interaction (Figure 30) indicated that the females were smaller in this measurement at the age range of 3-5 years, but tended to show a larger separation between the inferior orbital margins from the age range of 6-8 years to 9-11 years. However, the males showed a larger increment than the females between the age ranges of 9-11 years to 12-15 years, leading again to a wider separation between the most inferior points on the orbital margins of the two orbits. Beyond the age of 12-15 years, males and females showed parallel development until adulthood. Since no group x sex measurements were significant, it can be stated that the males and females were different in their developmental patterns and showed similar differences in the Trisomy 21 and Control groups.

The fact, that the most superior point on the superior orbital margin is located further laterally in the Trisomy 21 individuals, has already been mentioned. To analyze the changes in the slant of the orbits, the changes occurring at the superior orbital margin have to be viewed concomitantly with the changes occurring at the inferior orbital margin. The RoR-RoL mean measurements in the Trisomy 21 and Control samples at the age range of 3-5 years were 58.8 mm. and 54.8 mm. respectively. At this same age range of 3-5 years, the IoR-IoL mean measurements were 53.4 mm. and 60.4 mm. in the Trisomy 21 and Control groups, respectively. In Figure 31 A and B these measurements are depicted graphically.

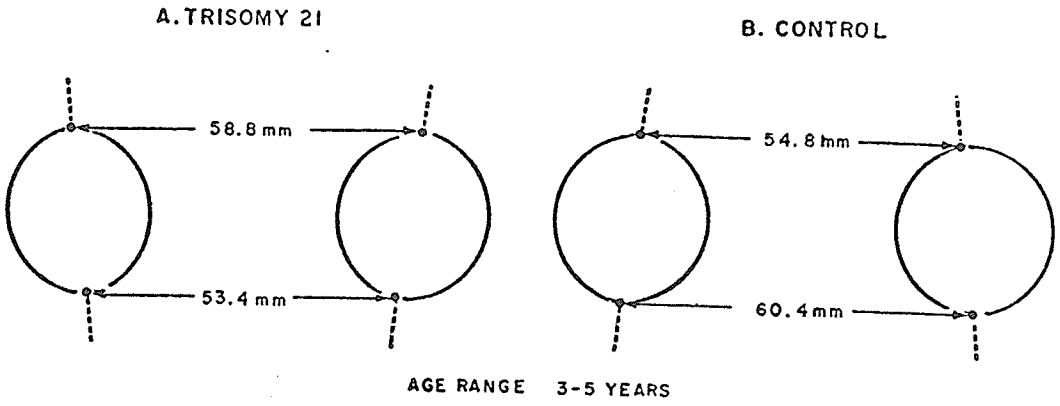


Figure 31. Slant of the orbits at the age range of 3-5 years. A. Trisomy 21, and B. Control subjects.

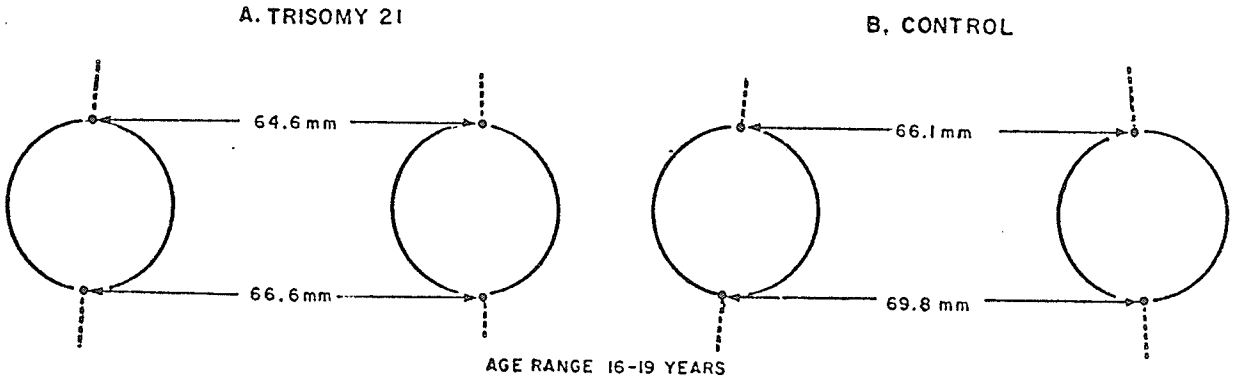


Figure 32. Slant of the orbits at the age range of 16-19 years in A. Trisomy 21, and B. Control subjects.

It can be seen from Figure 31A that in the Trisomy 21 individuals the most superior point on the superior orbital margin is located laterally in relation to the most inferior point on the inferior orbital margin, giving a lateral slant to the orbits. The Control individual, shown in Figure 31B, has the most superior point on the superior orbital margin located medially, in relation to the most inferior point on the inferior orbital margin, giving the opposite slant to that seen in the Trisomy 21 sample.

Observation of the mean measurements of the same landmarks, when seen at the age range of 16-19 years, showed a definite change in the slant of the orbits in the Trisomy 21 individuals, but the same orbital slant was maintained in the Control individual, as shown in the Figure 32 A and B. Figure 32A shows that in the Controls the most superior point on the superior orbital outline is still located medially, in relation to the most inferior landmark on the inferior orbital margin. Figure 32B shows that in the Trisomy 21 sample, at the age range of 16-19 years, the most superior point on the orbital margin is no longer located lateral to the most inferior point on the inferior orbital margin, as was seen in the age range of 3-5 years; rather the most superior point on the superior orbital outline is located medial to or in line with the most inferior point on the inferior orbital outline.

The mean computer polygonal plot for the changes

seen in the orbital margin at the age ranges of 3-5 years, 9-11 years, and 16-19 years has been shown in Figures 33 and 34. In Figure 33, the polygonal plot of the changes seen in the nasal cavity landmarks at the above age ranges has been shown for purposes of orientation. The tables pertaining to the means and standard errors of all the orbital measurements has been presented in the Appendix in Tables XXIII to XXXIII.

The total mean increment in the RoR-RoL measurement in the Control was 11.3 mm., while the mean increment in the IoR-IoL measurement was 9.4 mm. In the Trisomy 21 individuals, however, the total increment in the RoR-RoL measurement was 5.1 mm., while the IoR-IoL measurement showed an increment of 13.2 mm.

In summary, these changes suggest that greater accommodative changes take place at the inferior orbital margins to change the lateral slant of the orbits in the Trisomy 21 individuals. These changes in the IoR-IoL measurement along with the decreased changes in the RoR-RoL measurement of the Trisomy 21 group would also contribute towards changing the often quoted oval shape of the orbits (Benda, 1946; Frostad, 1969) to a more circular shape as seen in the Control group. These changes in the shape of the orbits have also to be viewed with the changes seen in the lateral orbital margins.

Bilateral-orbital width

The changes that have occurred at the inferior orbital margins to contribute to the changes seen in the orbital

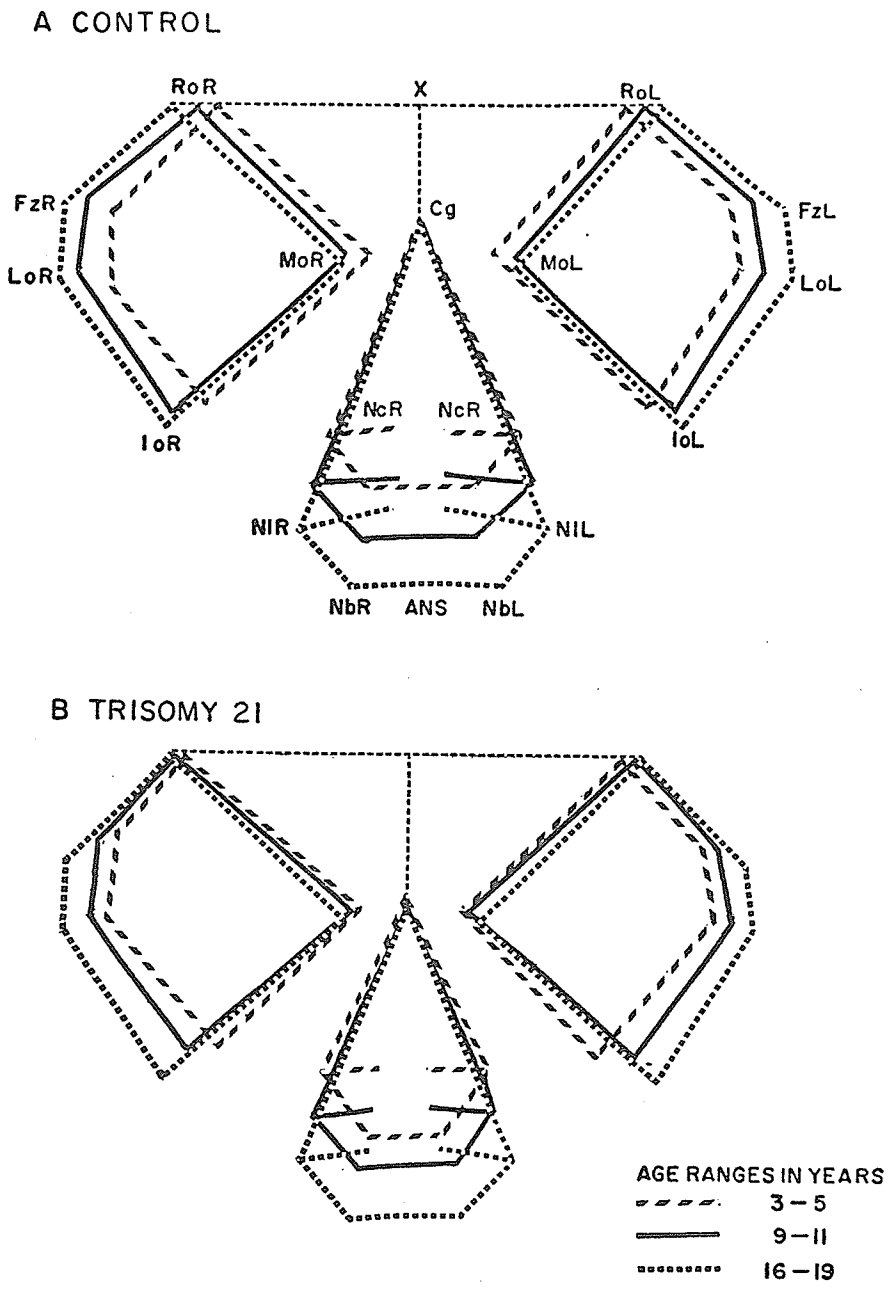


Figure 33. Computer polygonal plot to show changes in the orbits and nasal cavity between the age range of 3-5, 9-11, and 16-19 years. Note: Minimal changes at the roof of the orbits (RoR and RoL) in the Trisomy 21 group as opposed to the changes seen in the Control group. Also note minimal changes in Trisomy 21 in nasal cavity height.

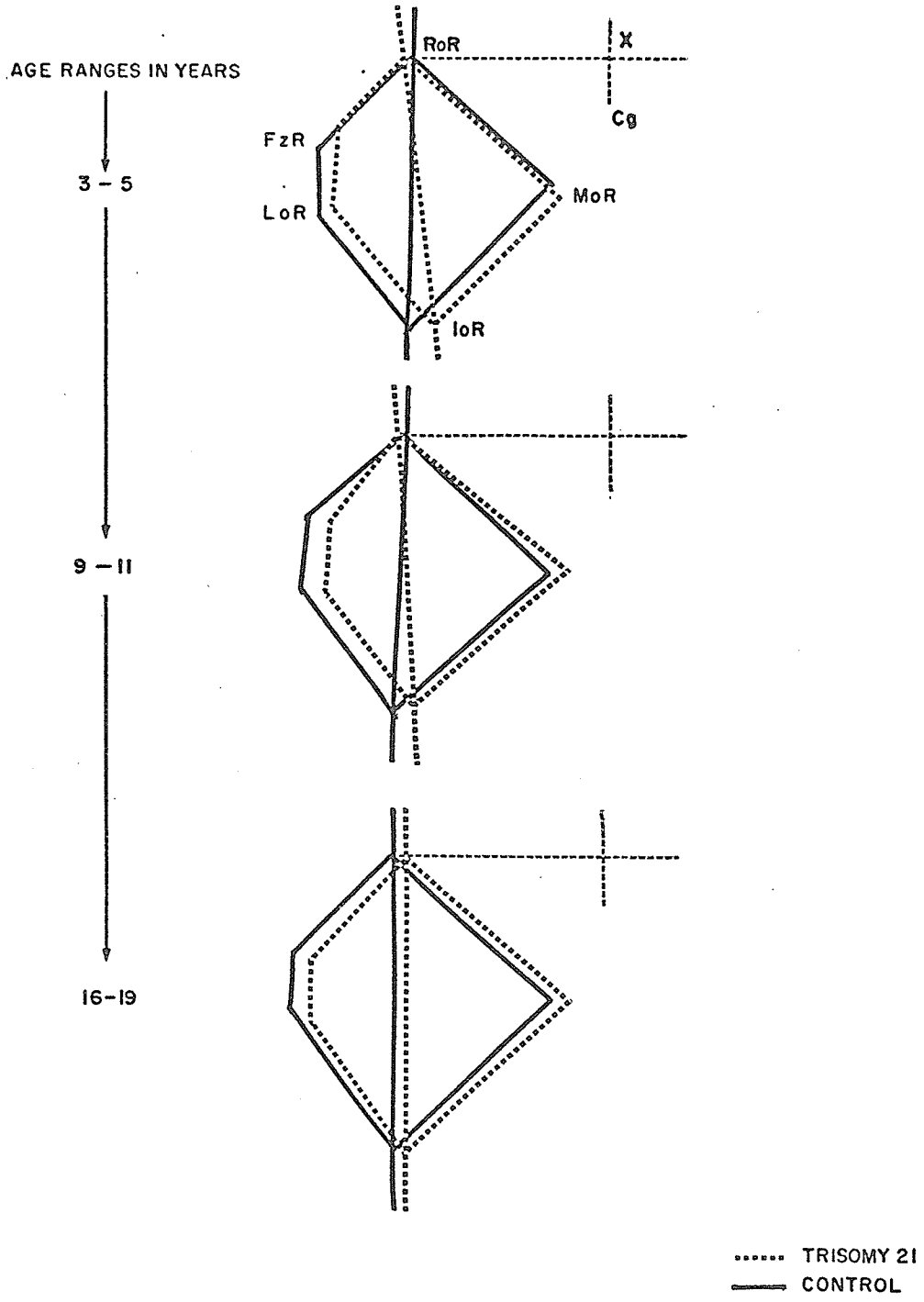


Figure 34. Computer polygonal plot to show changes in the slant of the right orbit in the Trisomy 21 and the Control from the age range of 3-5 years to the age range of 16-19 years.

outlines in the Trisomy, as compared to the Control group, have already been noted. To further substantiate these changes, the two measurements showing the changes at the lateral orbital margins were measured. One of these measurements was the bilatero-orbital width, which was represented by the distance LoR-LoL. The second measurement was the bifronto-zygomatic suture width, represented by the linear measurement, FzR-FzL, which will be described later.

The changes in the bilatero-orbital width (LoR-LoL) showed that a between group effect was significant at the 1% level with the Trisomy 21 group being smaller. The Control group mean was 94.4 mm. while the Trisomy 21 mean was 91.1 mm. A main sex effect which was significant at the 1% level showed the males to be larger than the females. No group x sex effects were significant.

Among the age ranges, a significant difference at the 1% level was detected (Figure 35). The largest increases were found to occur between the age ranges of 3-5 to 6-8 years and between 9-11 to 12-15 years. Diminished incremental growth was seen between the age ranges of 6-8 years to 9-11 years and between the age ranges of 12-15 years to 16-19 years. No changes were seen after the age range of 16-19 years. Since no group x age interactions were significant, it can be said that the development of this dimension was parallel in the two groups. Therefore, the illustration of the main effect of age was considered representative of both groups for this variable.

Examination of the total increment in this measurement, in the Trisomy 21 and Control groups, between the age range of

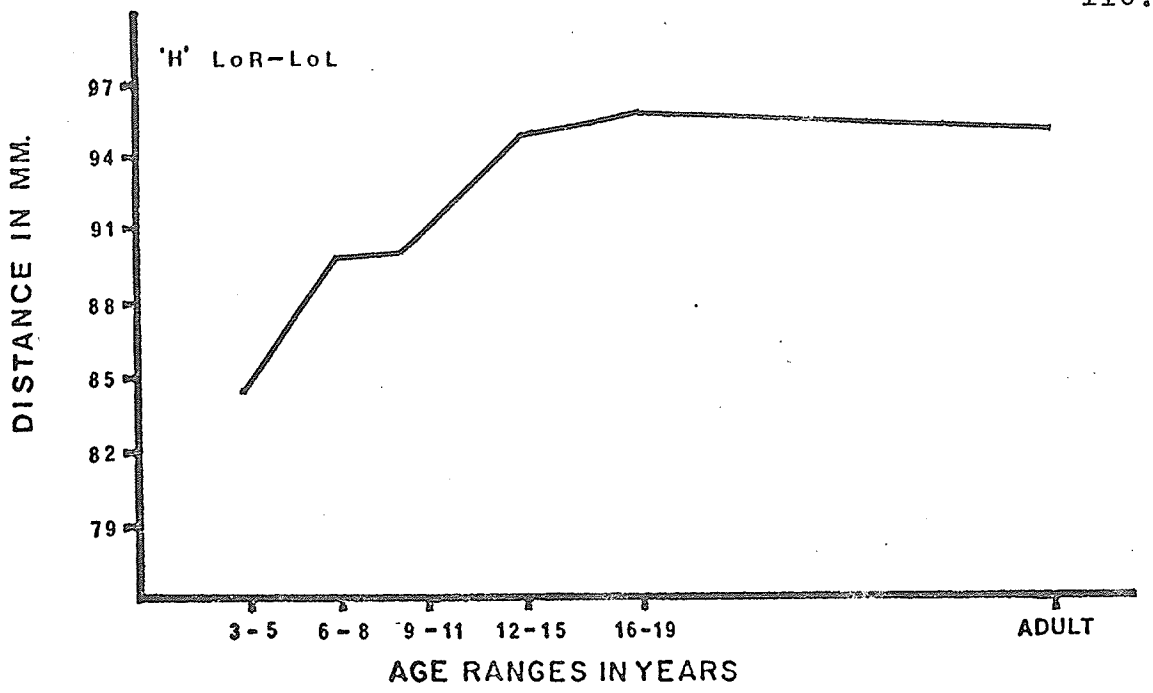


Figure 35. Main effect of age on the linear distance LoR-LoL.

3-5 years to adulthood, showed that in the Trisomy 21 a total increment of 11.2 mm. occurred, while in the Control group the total increment was 12.3 mm.

Bifronto-zygomatic suture width

The changes observed in the bifronto-zygomatic suture width, represented by the linear distance, FzR-FzL, were similar to those observed in the bilatero-orbital width. A between group effect significant at the 1% level showed the Trisomy 21 group to be smaller than the Control group. The Control group mean was 92.2 mm. while the Trisomy 21 group mean was 89.0 mm.

A sex effect, significant at the 1% level, showed the males to be larger than the females, but a sex x age interaction, significant at the 1% level (Figure 36), indicated that the

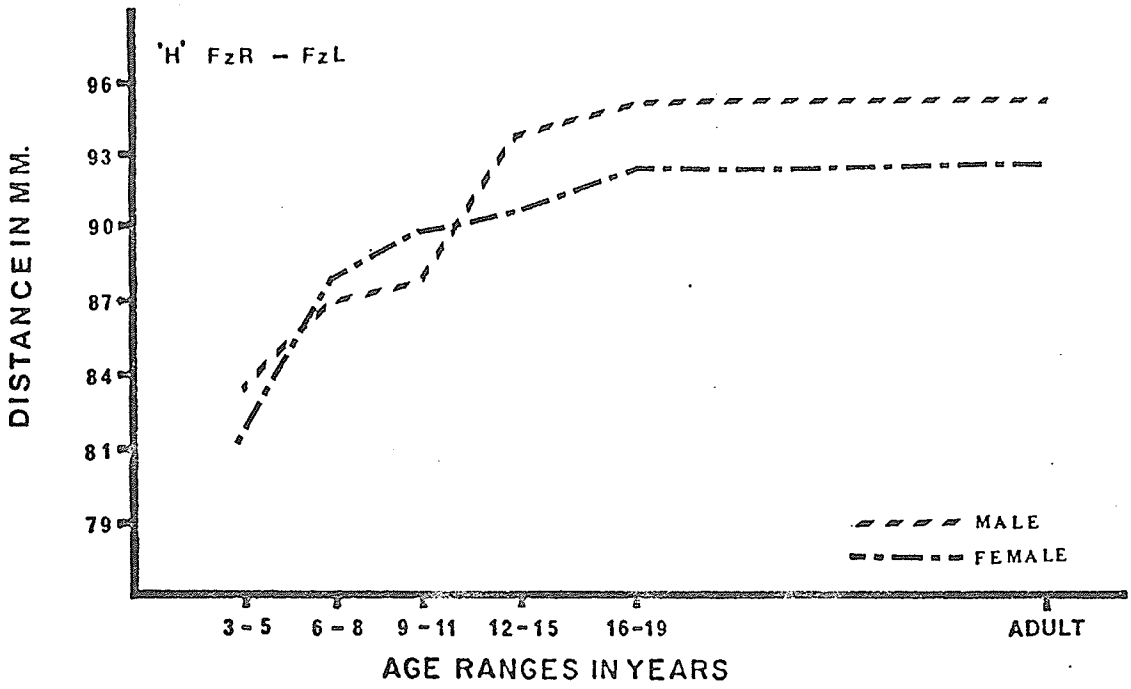


Figure 36. Effect of age on the linear distance FzR-FzL for the males and the females of both groups.

female measurements may tend to exceed the male measurements from the age range of 6-8 years to 9-11 years. However, the males showed a larger growth increment between the age ranges of 9-11 years to 12-15 years. The male lead at this age range is well known. Parallel growth increments were observed in the males and females after the age range of 12-15 years, with no increment occurring after the age range of 16-19 years.

Among the age ranges a significant effect was detected at the 1% level (Figure 37). The largest growth increments in this measurement were found to occur between the age ranges of 3-5 to 6-8 years and between the age ranges of 12-15 years to 16-19 years. Diminished incremental growth was seen between the age ranges of 6-8 years to 9-11 years, and between

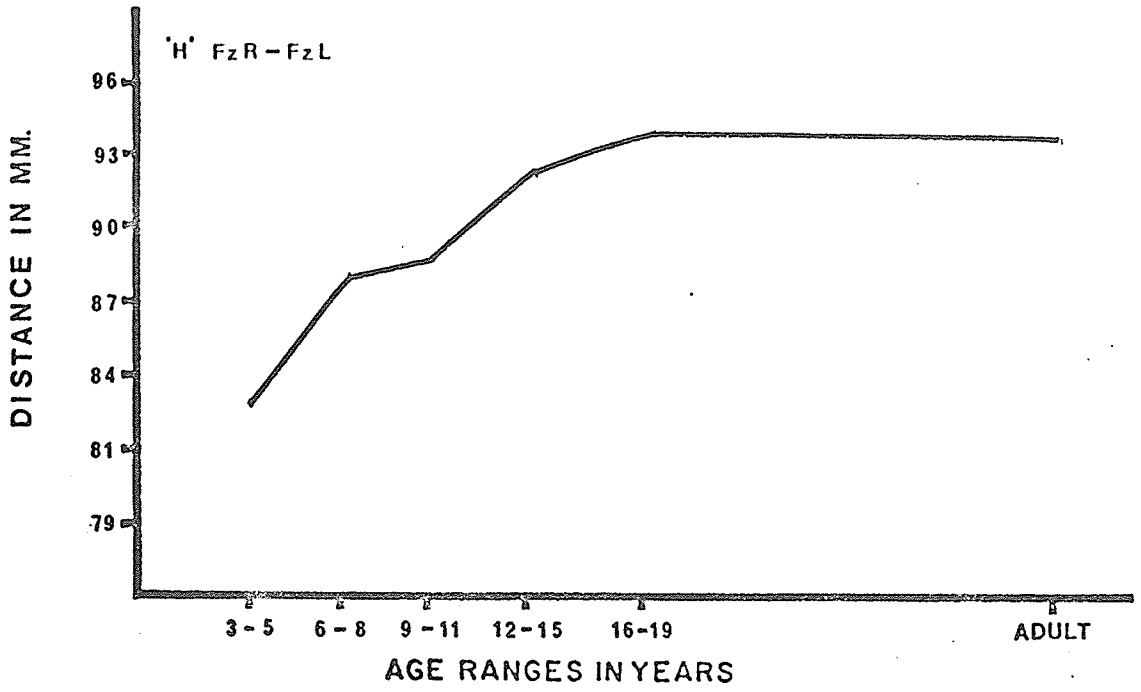


Figure 37. Main effect of age on the linear distance FzR-FzL.

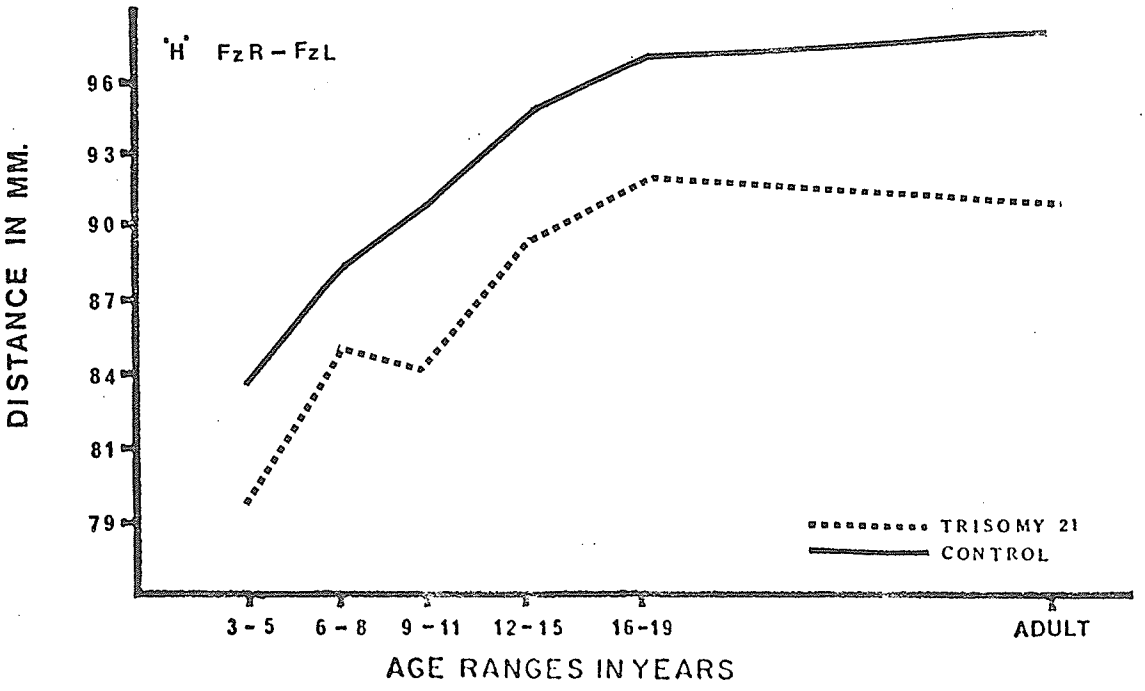


Figure 38. Effect of age on the linear distance FzR-FzL for the Trisomy 21 and Control groups.

the age ranges of 12-15 years to 16-19 years. No significant changes were present after the age range of 16-19 years. No interactions were significant as illustrated by the similar growth patterns which occurred between the Trisomy and Control groups shown in Figure 38.

Examination of the difference between minimal and maximal values for this measurement in the Trisomy and Control groups indicated that the increment was 13.7 mm. in the Controls and 12.5 mm. in the Trisomy 21 group.

Width of the orbits

The width of the right and left orbits were investigated by taking the linear measurements MoR-LoR and MoL-LoL respectively. Significant differences at the 1% level could only be found among the age ranges and between the sexes. No significant differences could be found between the Trisomy 21 and Control groups. The mean measurements for the right and left orbital widths of the Control group were 36.8 mm. and 36.7 mm. respectively, while in the Trisomy 21 group the mean measurement was 37.0 mm. for both the right and left orbits.

An age effect significant at the 1% level showed that the widths of the right orbit (Figure 39) and left orbit (Figure 41) increased from the age ranges of 3-5 years to 6-8 years. A decreasing rate of growth was seen from the age range of 9-11 years to 16-19 years. No appreciable changes were seen after the age range of 16-19 years. No group x age

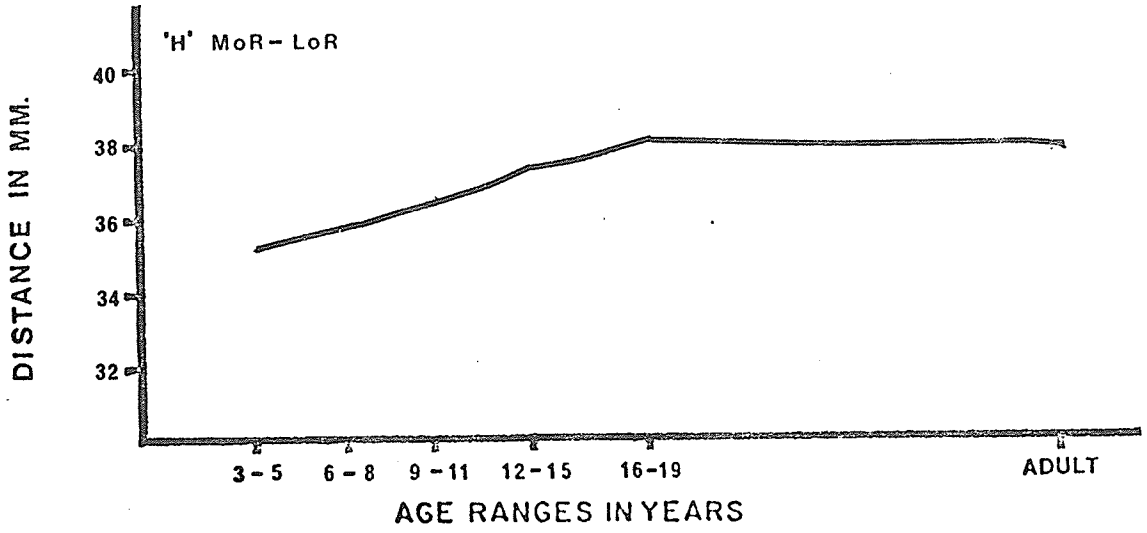


Figure 39. Main effect of age on the width of the right orbit as represented by the linear distance MoR-LoR.

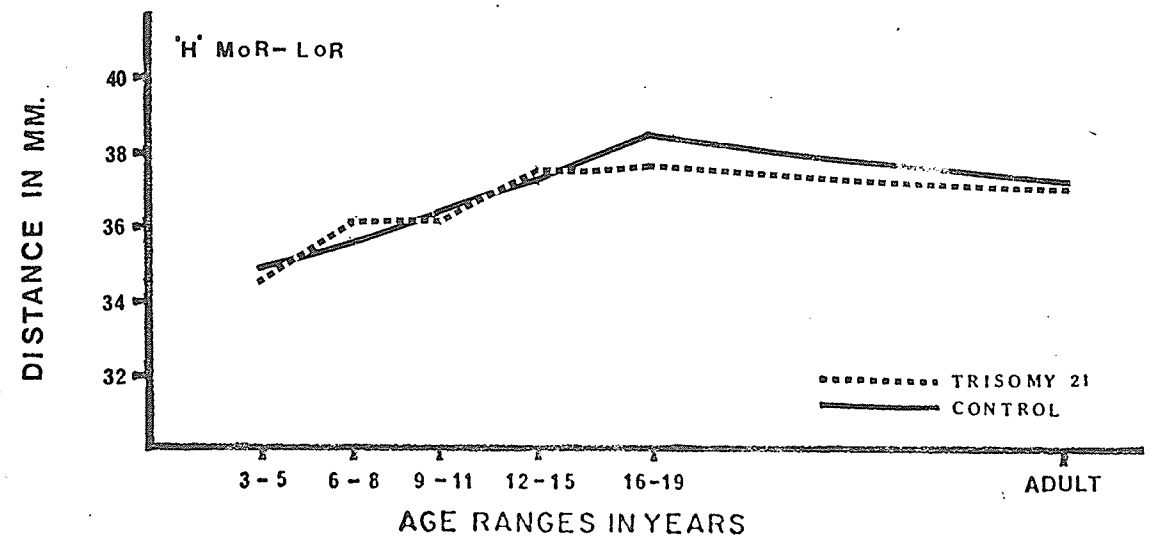


Figure 40. Effect of age on the width of the right orbit as represented by the linear distance MoR-LoR in the Trisomy 21 and Control groups.

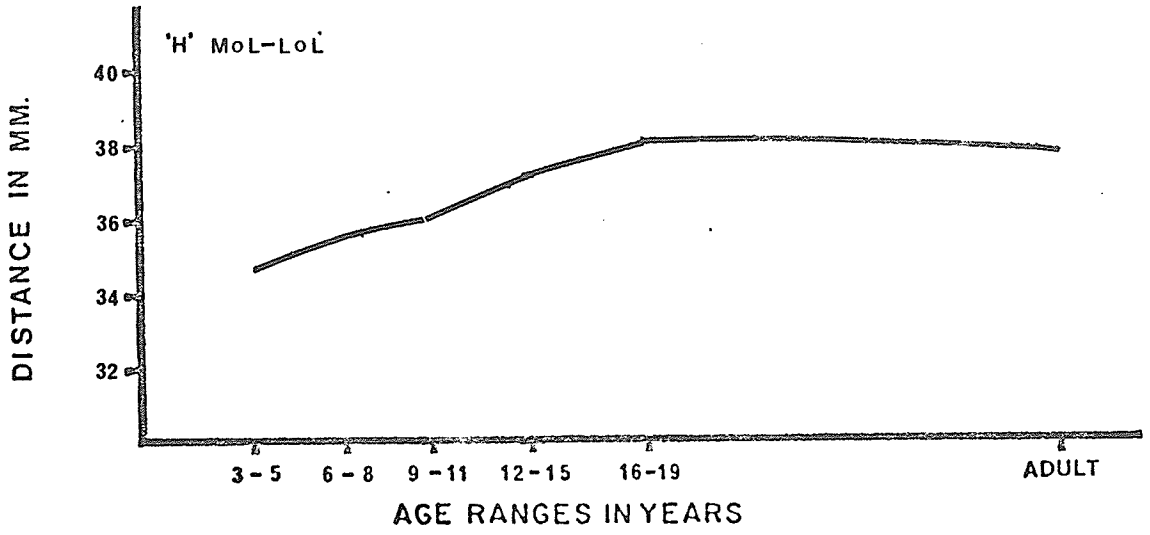


Figure 41. Main effect of age on the width of the left orbit as represented by the linear distance MoL-LoL.

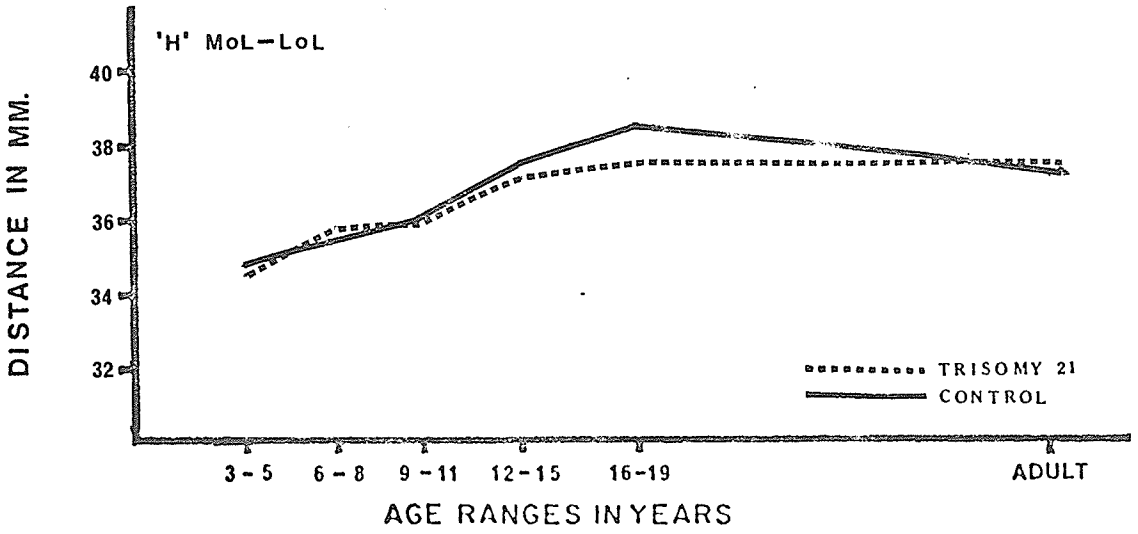


Figure 42. Effect of age on the width of the left orbit as represented by the linear distance MoL-LoL for the Trisomy 21 and Control groups.

effect was significant and the similar development of the right and left orbital widths in the two groups is indicated in Figures 40 and 42, respectively.

A sex effect significant at the 1% level indicated the males to have significantly larger orbits than females. However, no group x sex effects were significant. The mean measurements for the Control males and females for the right and left orbits were 37.3 mm. and 36.2 mm., respectively. In the Trisomy 21 group the mean measurement of the right and left orbits in the males was 37.6 mm. and the mean measurement of the right and left orbits in the females was 36.3 mm.

It would seem, therefore, that the width of each orbit in the Trisomy 21 sample is comparable to that of the Control sample, and is not affected as much as the width between the two orbits, MoR-MoL, which has already been discussed in Figure 25. It is interesting to note that the main bony component between the medial walls of the orbits is the cartilagenous labyrinth of the ethmoid bone.

Height of the orbits

The height of the orbits were measured by the vertical projection distances, RoR-IoR, for the right orbit and RoL-IoL, for the left orbit. These two measurements were significant at the 1% level only among the age ranges and between sexes. Examination of the mean measurements indicated that the height of the right orbit in the Control was 42.4 mm. and 41.9 mm. in the Trisomy 21 individuals and the same measurement

for the left orbit indicated the means for the Controls to be 41.9 mm. and 41.7 mm. for the Trisomy 21 group.

The effect of age significant at the 1% level is indicated in Figures 43 and 45 for the right and left orbits respectively. It can be seen that an increase in orbital height is seen to occur until the age range of 12-15 years and no appreciable increase in orbital height is seen thereafter. No group x age effect was significant and almost parallel development in the two groups is indicated in Figures 44 and 46.

A sex effect significant at the 1% level indicated the males to have significantly larger orbits than the females. However, no group x sex effects were significant. The mean measurements for the right orbit in the Control and Trisomy males were 43.0 mm. and 42.1 mm., respectively and in the females they were 41.8 mm. and 41.6 mm., respectively.

The mean measurements for the left orbital height in the males were 42.5 mm. and 42.2 mm. in the Control and Trisomy 21 groups, and 41.4 mm. and 41.1 mm. for the females in the Control and Trisomy 21 groups.

C. LOWER FACE

Bicondylar width

The bicondylar width was represented by the linear measurement, CdR-CdL, and showed significant differences at the 1% level when comparing groups, sexes, and age ranges. A sex x age effect was also significant at the 5% level.

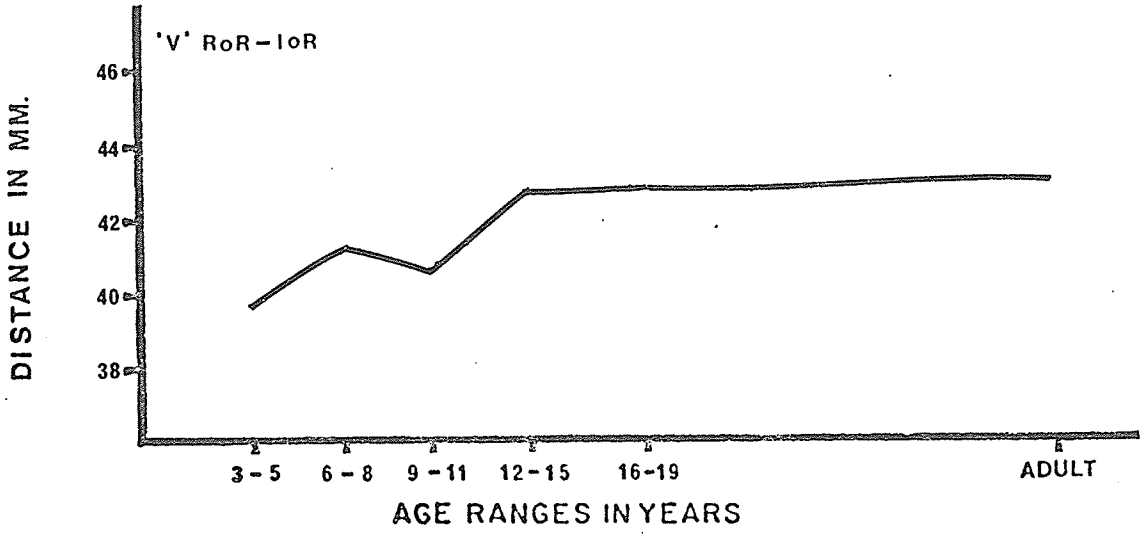


Figure 43. Main effect of age on the height of the right orbit, as represented by the linear distance RoR-IoR.

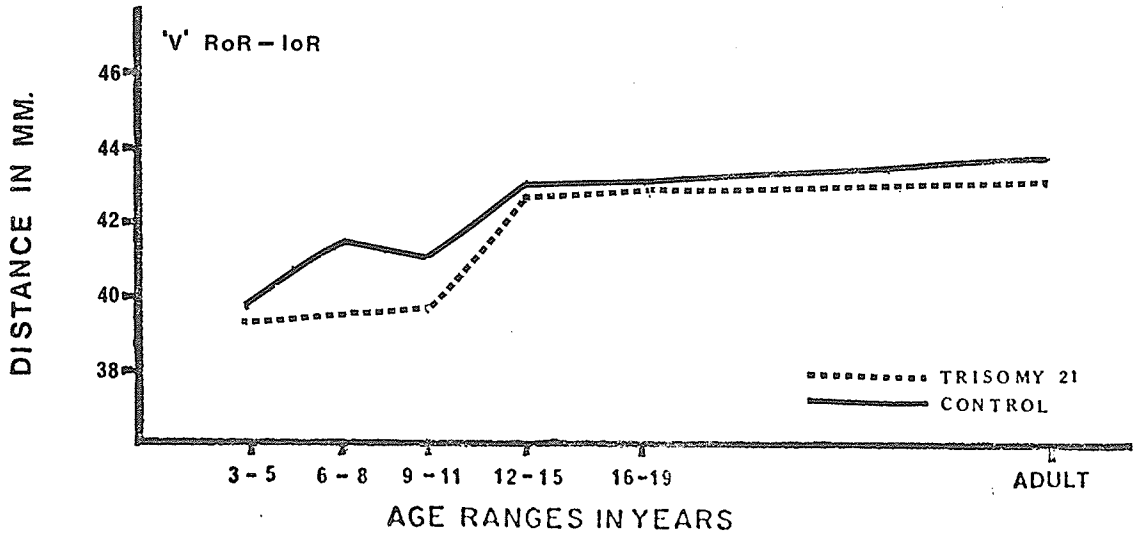


Figure 44. Effect of age on the height of the right orbit as represented by the linear distance RoR-IoR for the Trisomy 21 and Control groups.

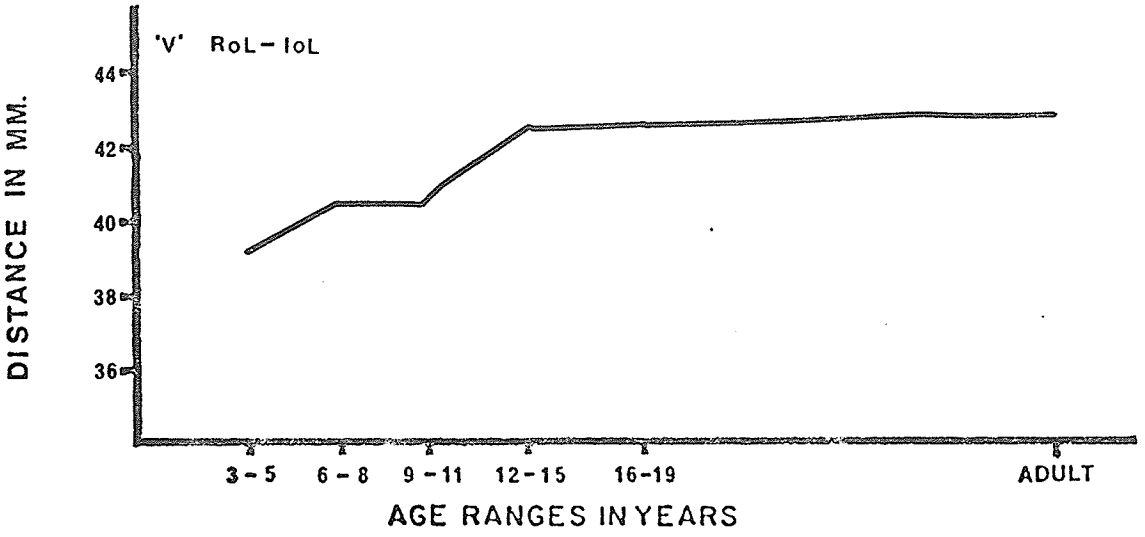


Figure 45. Main effect of age on the height of the left orbit as represented by the linear distance RoL-IoL.

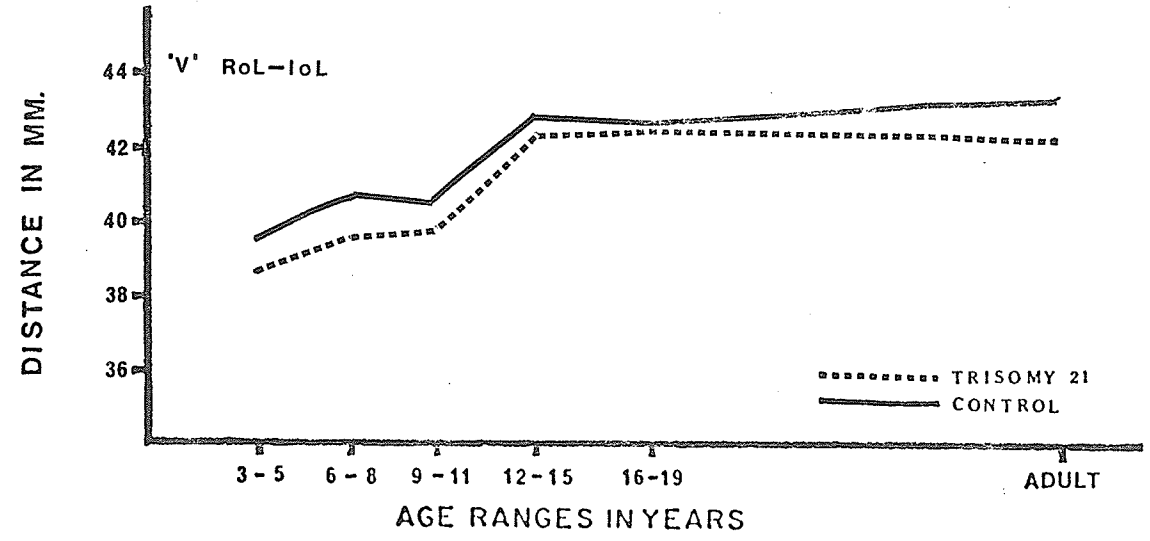


Figure 46. Effect of age on the height of the left orbit as represented by the linear distance RoL-IoL for the Trisomy 21 and Control groups.

The Trisomy 21 group had a smaller bicondylar width than the Control, with the mean measurement of 113.6 mm. and the mean for the Control group was 116.4 mm.

The main effect of age illustrated in Figure 47 showed that increments in this measurement occurred at a decreasing rate, until the age range of 16-19 years. After this age range no significant increase in this measurement occurred. No group x age effects were significant, indicating that parallel development was occurring in the two groups.

The males were significantly larger than the females. The means for the Control males was 118.6 mm., for the Control females was 111.9 mm., for the Trisomy males was 114.3 mm., and for the Trisomy females was 110.2 mm. A sex x age effect shown in Figure 48 illustrates that the males and females maintain a similar developmental pattern until the age range of 9-11 years, and thereafter, the males continue to increase in the bicondylar width up until the age range of 16-19 years, with very little increment in this measurement after this age range. The increment in the females after the age range of 9-11 years is, however, much lower up to the age range of 16-19 years and no significant increases are seen thereafter.

Bigonial width

The width of the lower face was assessed by the measurement between the right and left gonial landmarks. A between group effect significant at the 1% level showed

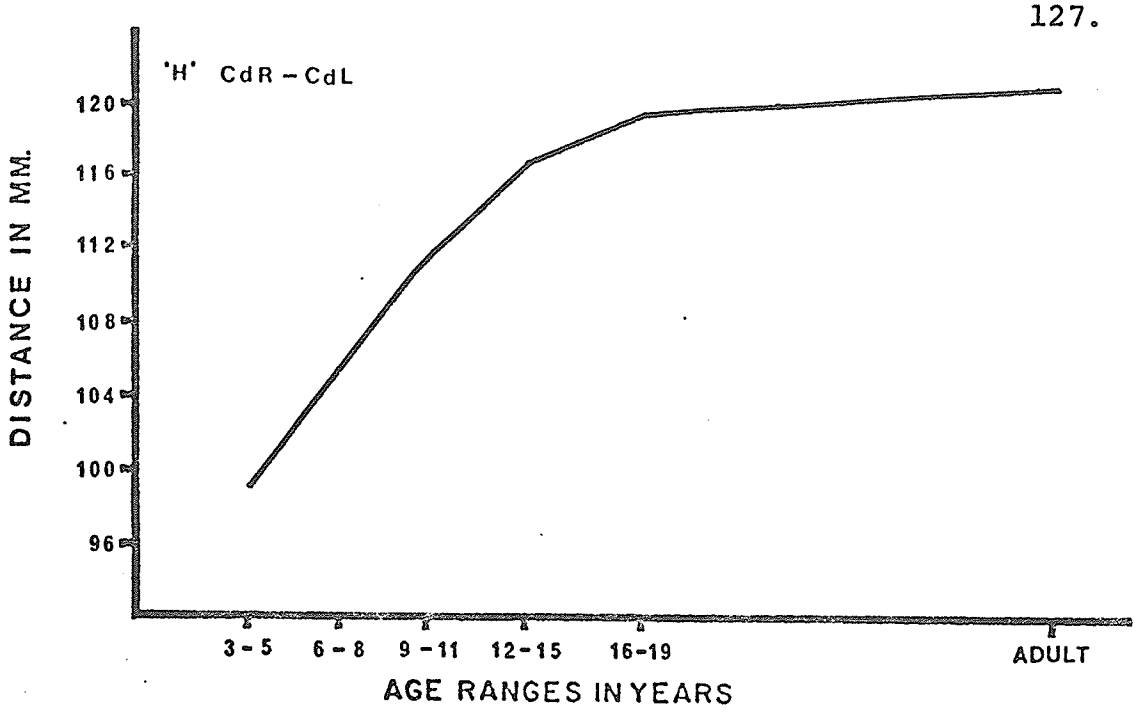


Figure 47. Main effect of age on the linear distance CdR-CdL.

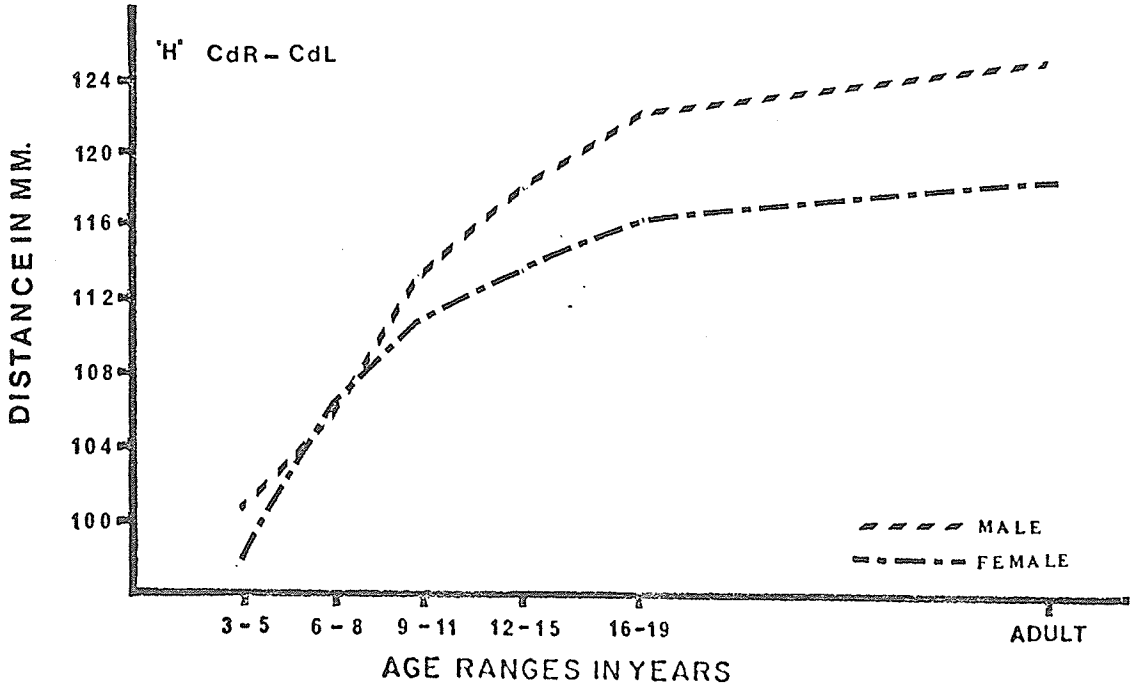


Figure 48. Effect of age on the linear distance CdR-CdL for the males and females of both groups.

the Trisomy group to be smaller than the Control group. The mean width for the Trisomy group was 88.8 mm. and that for the Control group was 94.8 mm.

Among the age ranges, a significant difference at the 1% level was observed (Figure 49). A nearly linear increment took place from the age range of 3-5 years to 12-15 years. After the age range of 12-15 years, little further change was noted except for a small increase from the age range of 12-15 years to 16-19 years. No group x age effects were significant and the parallel developmental changes for both groups until the age range of 12-15 years are illustrated in Figure 51.

A significant sex x age interaction, significant at the 1% level (Figure 50), indicated that the males and females showed similar increases in this measurement from the age range of 3-5 years to 9-11 years. After the age range of 9-11 years, the males showed larger growth increments than the females until the age range of 16-19 years. After the age range of 16-19 years, no appreciable changes in this width were seen.

Summary of the Skeletal Analysis

Most of the linear measurements investigated in this study indicated that the Trisomy 21 group was significantly smaller than the normal group. However, there were some areas of the craniofacial complex in the Trisomy 21 group

which seemed to be more severely affected than others.

In order to localize the areas in which the craniofacial complex was most affected, the ratio of the mean width attained by the Trisomy 21 group over the mean width of the Control group was calculated for each of the 21 variables used in the skeletal analysis and has been expressed as the percentage width attained by the Trisomy 21 group for each of these variables in Table VIII.

From Table VIII it is evident that some areas of the craniofacial complex were more severely affected than others. The possible implications of these findings will be discussed in the following chapter keeping in mind the statistical differences which were found for each variable in the Trisomy 21 and Control groups. These statistical differences for each variable have already been described when the findings for each variable were reported.

II. ASYMMETRIES IN THE CRANIOFACIAL COMPLEX

The horizontal asymmetries of the craniofacial skeleton were measured from similar bilateral landmarks to the constructed midline X-Cg. These landmarks were located in the cranial vault, upper face and lower face. Thirty linear variables represented the distance of 14 bilateral

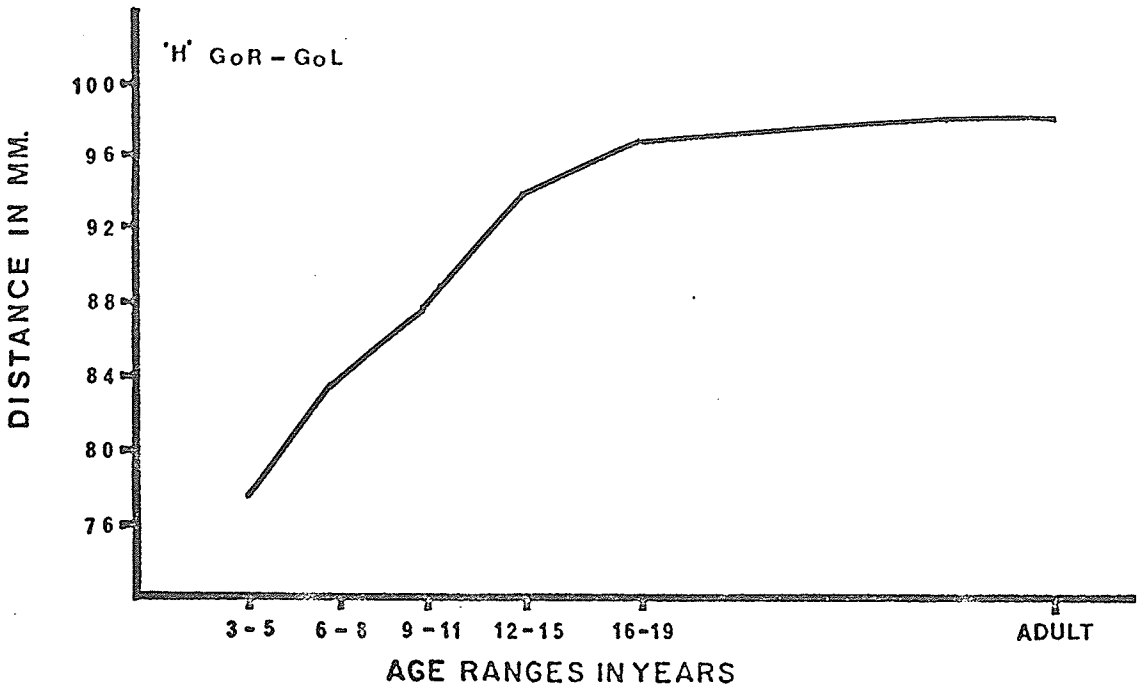


Figure 49. Main effect of age on the linear distance GoR-GoL.

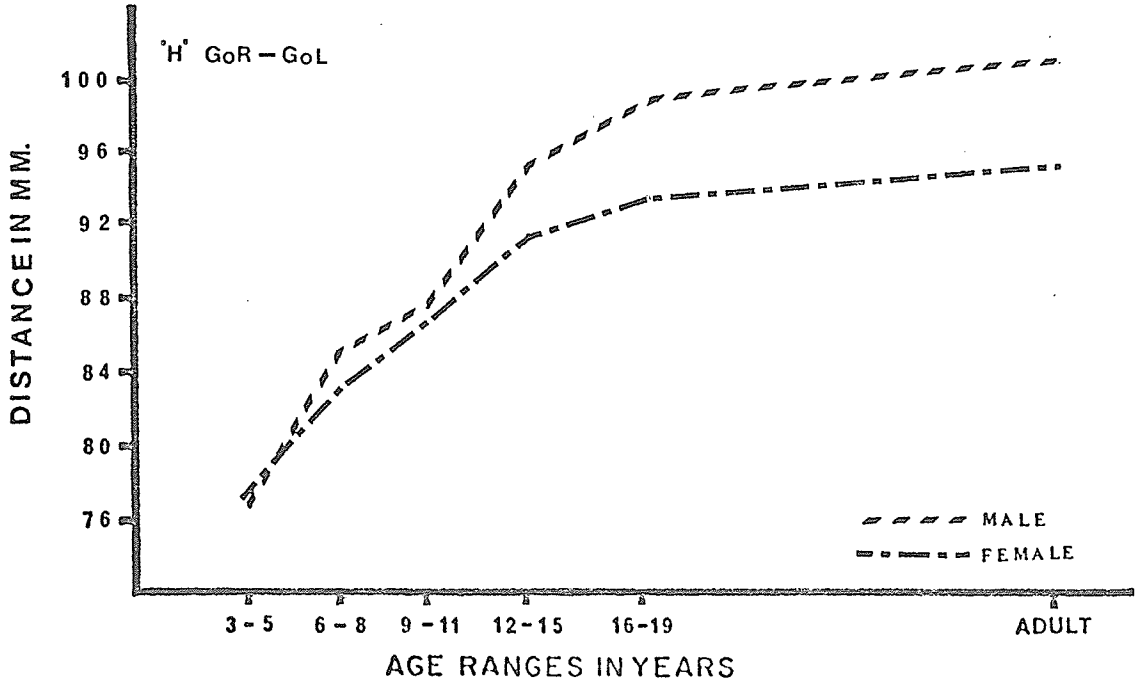


Figure 50. Effect of age on the linear distance GoR-GoL for the males and females of both groups.

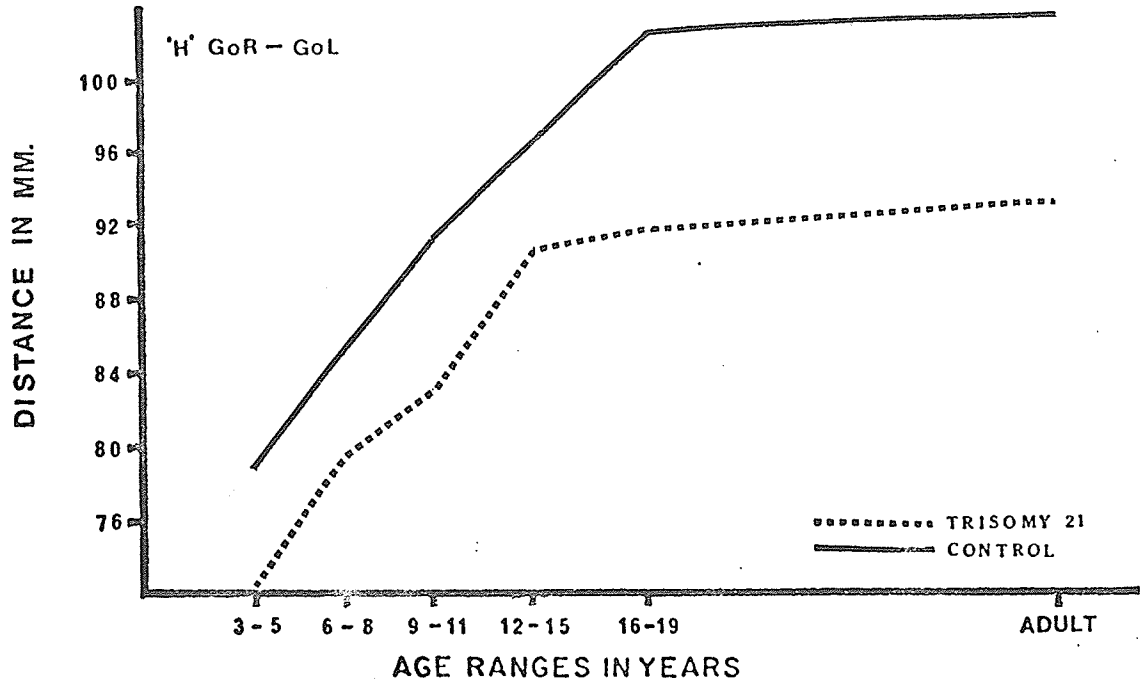


Figure 51. Effect of age on the linear distance GoR-GoL for the Trisomy 21 and Control groups.

(right and left) landmarks from the midline, and in addition the width of the right and left orbits were compared. These linear variables have been shown in Figure 11 in the Methods and Materials.

Levels of significance revealed by the mixed analysis of variance have been shown previously in Table VII, at the beginning of this chapter. The main effect of side, and the second order interaction of group x side, age x side, and third order interaction of group x age x side were selected for study in order to show which side was larger and whether this was true of both groups, and also observe whether any

TABLE VIII

PERCENTAGE OF WIDTH ATTAINED BY THE TRISOMY 21 GROUP, USING THE MEAN MEASUREMENTS OF THE CONTROL AND TRISOMY 21 GROUPS FOR 21 VARIABLES

VARIABLE	TRISOMY 21 Mean Width mm.	CONTROL Mean Width mm.	PER CENT TRISOMY 21 TO CONTROL
"H" MoR-MoL	17.1	20.9	81.8
"V" Cg-ANS	39.0	45.5	83.5
"H" MxR-MxL	51.6	61.2	84.3
"H" NbR-NbL	14.5	16.1	90.0
"H" NlR-NlL	28.1	30.8	91.2
"H" GoR-GoL	88.8	94.8	93.6
"H" IoR-IoL	64.2	67.4	95.2
"H" MsR-MsL	105.7	110.9	95.3
"H" FzR-FzL	89.0	92.9	95.8
"H" LoR-LoL	91.1	94.4	96.5
"H" ZyR-ZyL	123.5	126.8	97.3
"H" TeR-TeL	147.6	151.3	97.5
"H" CdR-CdL	113.6	116.4	97.5
"V" RoR-IoR	41.9	42.4	98.8
"V" RoL-IoL	41.7	41.9	99.5
"H" MoR-LoR	37.0	36.8	100.5
"H" MoL-LoL	37.0	36.7	100.8
"H" RoR-RoL	63.4	62.2	101.9
"H" MoR-RoR	23.4	21.2	110.3
"H" MoL-RoL	22.9	20.1	113.9
"H" NcR-NcL	8.9	6.2	143.5

changes in asymmetry occurred with age. Table IX gives the means and standard errors for the main effect of side for all variables considered in this part of the study, and Table X gives the means and standard errors for all the variables as observed for the second order interaction of group x side.

No significant asymmetries could be detected in the right and left sides of the maxilla, the width of the right orbit and left orbit, and the distance separating the right inferior nasal concha and the left inferior nasal concha from the midline.

A main side effect significant at the 1% level indicated that the five landmarks located on the orbital margin and the landmarks on the left nasal cavity outline, representing the most lateral point of the nasal cavity and the nasal base, were further away from the midline than similar bilateral structures on the right side.

Since no interactions involving side were significant, this conclusion, left versus right, is applicable to both the Trisomy 21 and Control groups, both sexes, and at all ages.

The measurements representing asymmetries of the cranium (TeR and TeL and MsR and MsL to X-Cg), the zygomatic arches (ZyR and ZyL to X-Cg), the condyles (CdR and CdL to X-Cg), and the right and left gonial landmarks (GoR and GoL to X-Cg) showed significant effects at the 1% level between sides and group x side, age x side and group x age x side.

A between side effect, in the five areas listed

TABLE IX

MEANS AND STANDARD ERRORS FOR THE MAIN EFFECT OF SIDE FOR THE ASYMMETRIES IN THE CRANIOFACIAL COMPLEX (in millimeters)

Asymmetry of Landmark from X-Cg plane	Right	Left	SE
A. CRANIUM			
TeR and TeL	72.85	75.00	0.26
MsR and MsL	52.04	54.46	0.25
B. UPPER FACE			
ZyR and ZyL	60.28	61.34	0.16
MxR and MxL	27.87	28.02	0.13
NlR and NlL	13.95	14.40	0.11
NbR and NbL	6.95	7.77	0.12
NcR and NcL	3.57	3.75	0.12
RoR and RoL	30.89	31.22	0.10
FzR and FzL	44.43	44.78	0.07
LoR and LoL	45.05	46.21	0.08
IoR and IoL	31.46	32.71	0.14
MoR and MoL	8.53	9.83	0.07
MoR-LoR and MoL-LoL	36.54	36.41	0.08
C. LOWER FACE			
CdR and CdL	55.32	56.65	0.19
GoR and GoL	43.82	45.05	0.23

TABLE X

MEANS AND STANDARD ERRORS FOR THE EFFECT OF SIDE FOR THE ASYMMETRIES IN THE TRISOMY 21 AND CONTROL GROUPS (in millimeters)

Asymmetry of Landmark from X-Cg plane	TRISOMY 21 Right Mean	TRISOMY 21 Left Mean	TRISOMY 21 SE	CONTROL Right Mean	CONTROL Left Mean	CONTROL SE
A. CRANIUM						
TeR and TeL	70.87	74.43	0.38	74.83	75.56	0.37
MsR and MsL	49.28	53.22	0.37	54.21	55.69	0.35
B. UPPER FACE						
ZyR and ZyL	58.30	60.09	0.23	62.26	62.58	0.22
MxR and MxL	25.45	25.62	0.18	30.29	30.42	0.17
NlR and NlL	13.08	13.36	0.15	14.82	15.44	0.15
NbR and NbL	6.59	7.08	0.18	7.31	8.46	0.17
NcR and NcL	4.24	4.22	0.17	2.90	3.28	0.17
RoR and RoL	31.17	31.60	0.15	30.61	30.85	0.14
FzR and FzL	43.02	43.42	0.10	45.82	46.14	0.10
LoR and LoL	43.98	44.95	0.12	46.13	47.47	0.11
IoR and IoL	30.29	31.54	0.20	32.64	33.88	0.19
MoR and MoL	7.53	8.72	0.10	9.53	10.94	0.09
MoR-LoR and MoL-LoL	36.45	36.26	0.11	36.63	36.55	0.10
C. LOWER FACE						
CdR and CdL	53.61	55.67	0.27	57.04	57.62	0.26
GoR and GoL	41.52	43.02	0.33	46.13	47.09	0.32

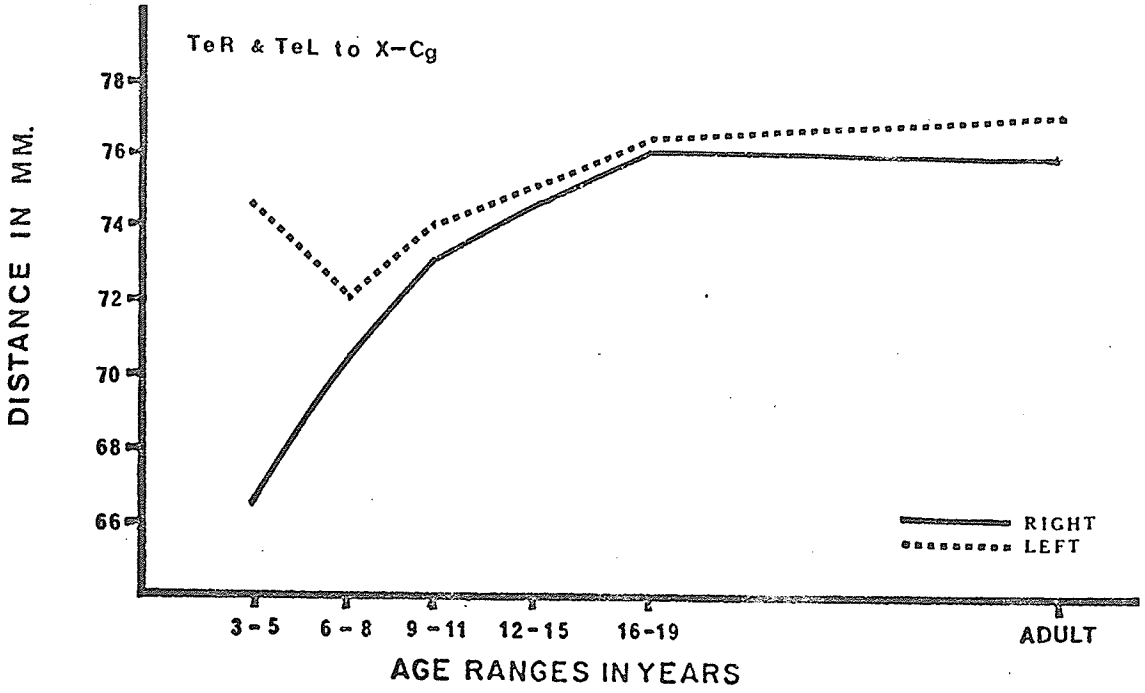


Figure 52. Effect of side x age for the asymmetry of the linear distances TeR and TeL to X-Cg.

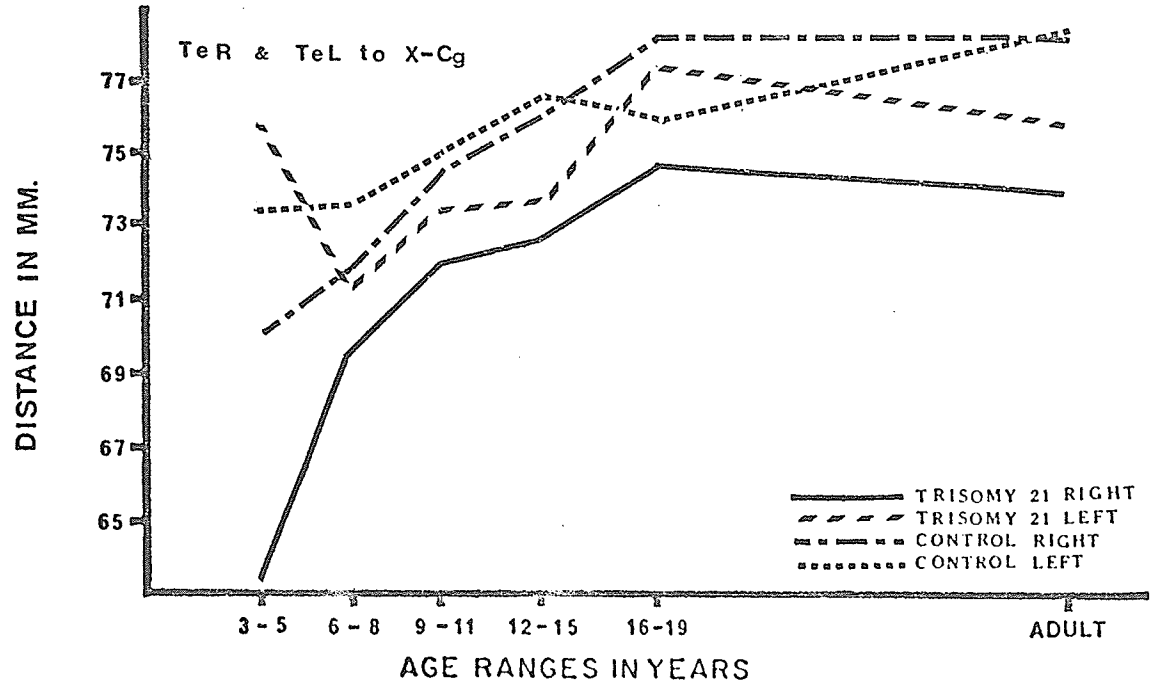


Figure 53. Effect of side x age for the asymmetry of the linear distances TeR and TeL in the Trisomy 21 and Control groups.

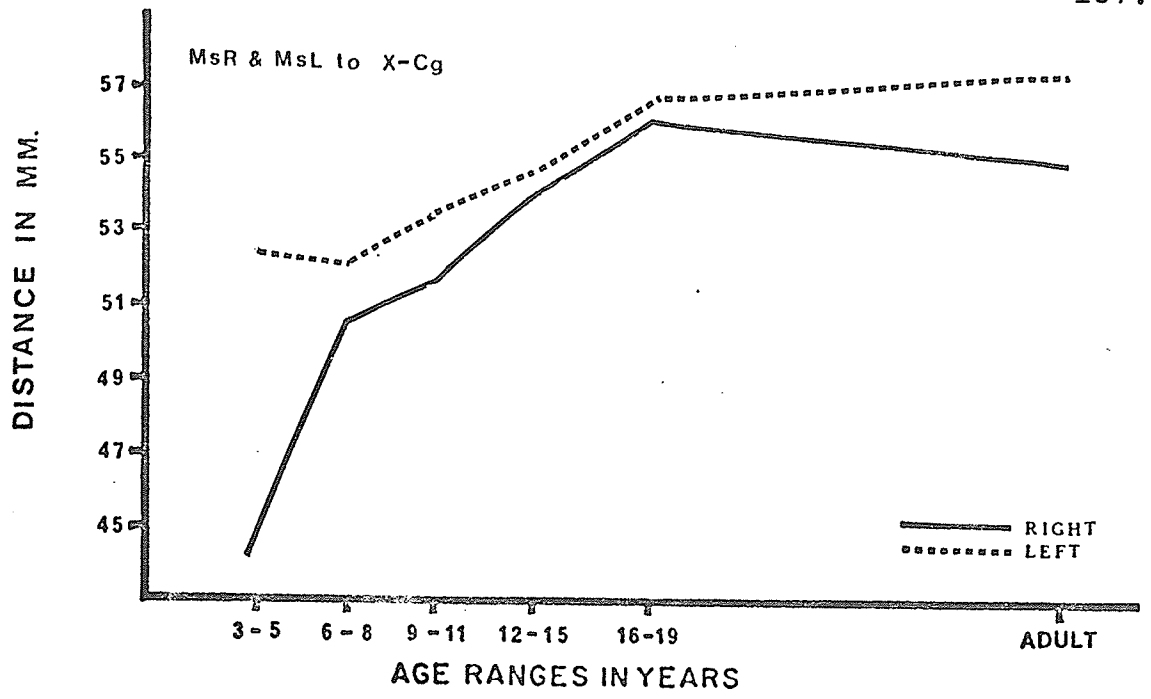


Figure 54. Effect of side x age for the asymmetry of the linear distances MsR and MsL to X-Cg.

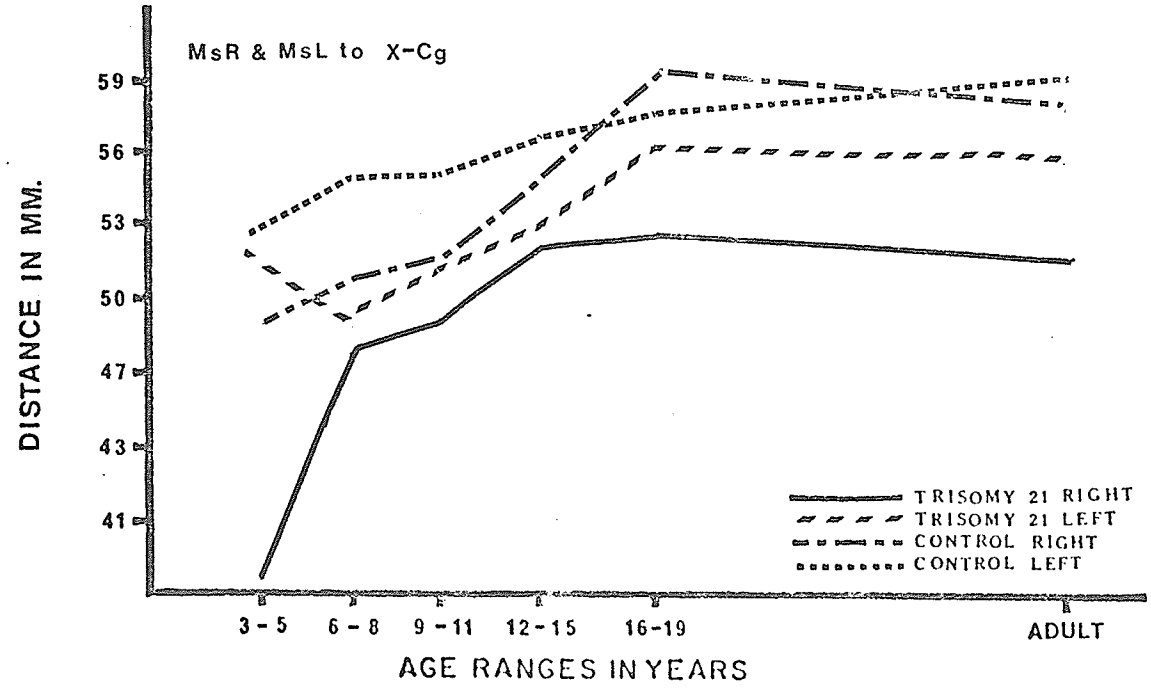


Figure 55. Effect of side x age for the asymmetry of the linear distances MsR and MsL to X-Cg in the Trisomy 21 and Control groups.

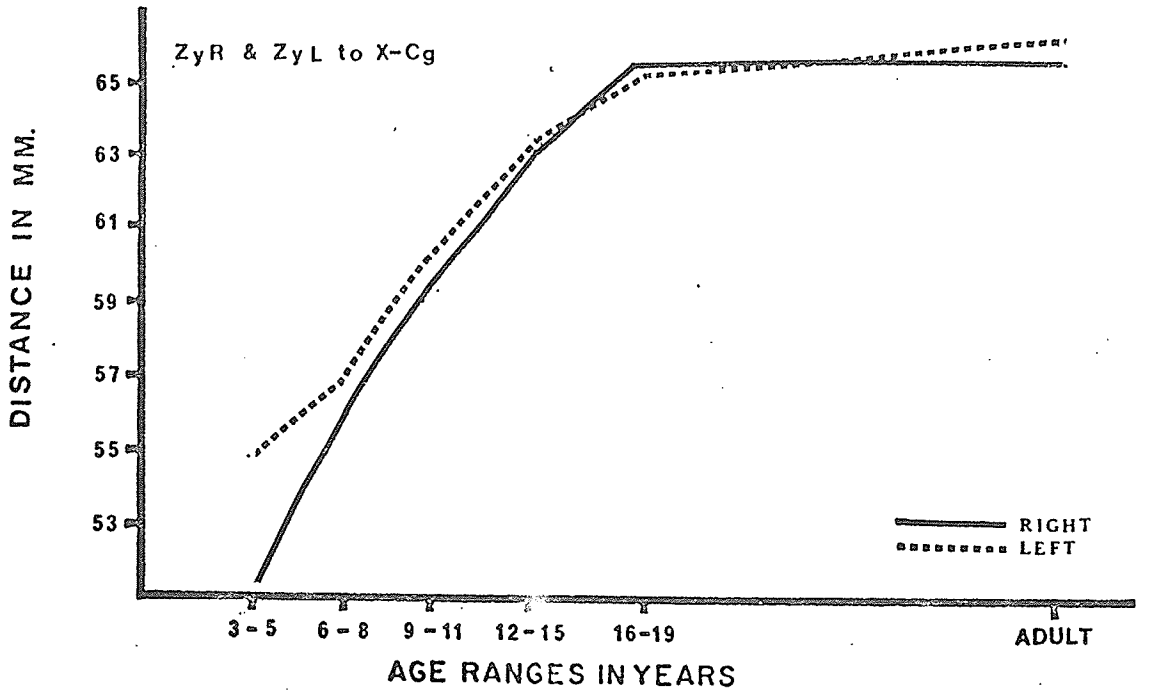


Figure 56. Effect of age x side for the asymmetry of the linear distances ZyR and ZyL to X-Cg.

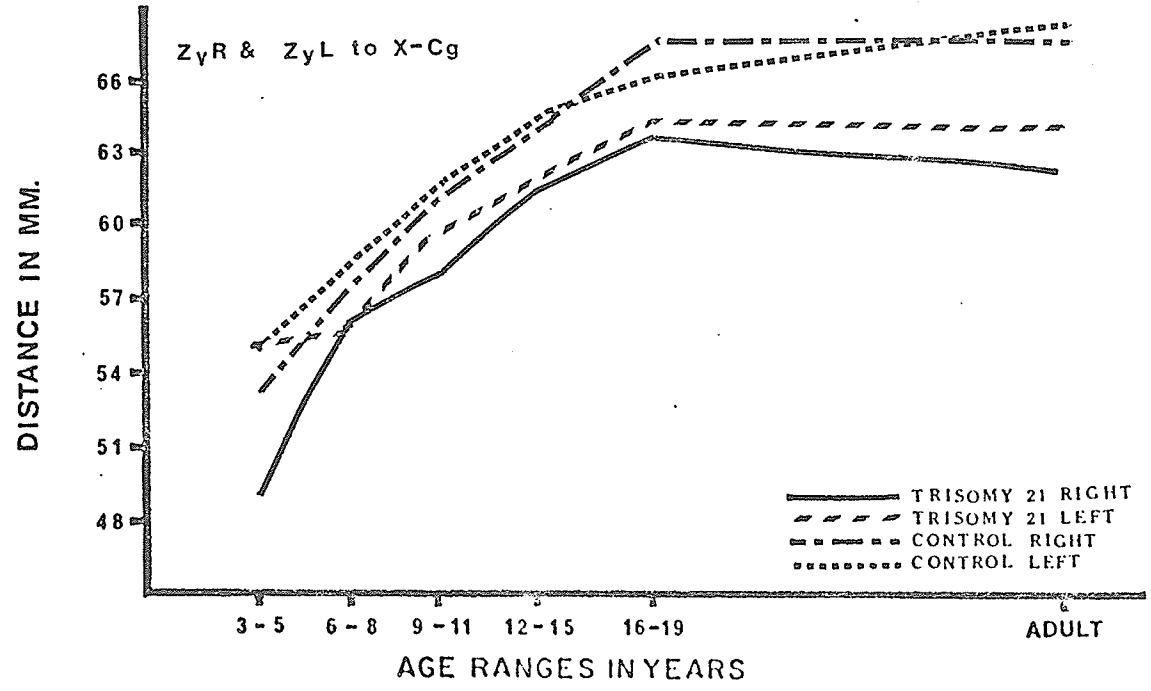


Figure 57. Effect of age x side for the asymmetries of the linear distances ZyR and ZyL to X-Cg for the Trisomy 21 and Control groups.

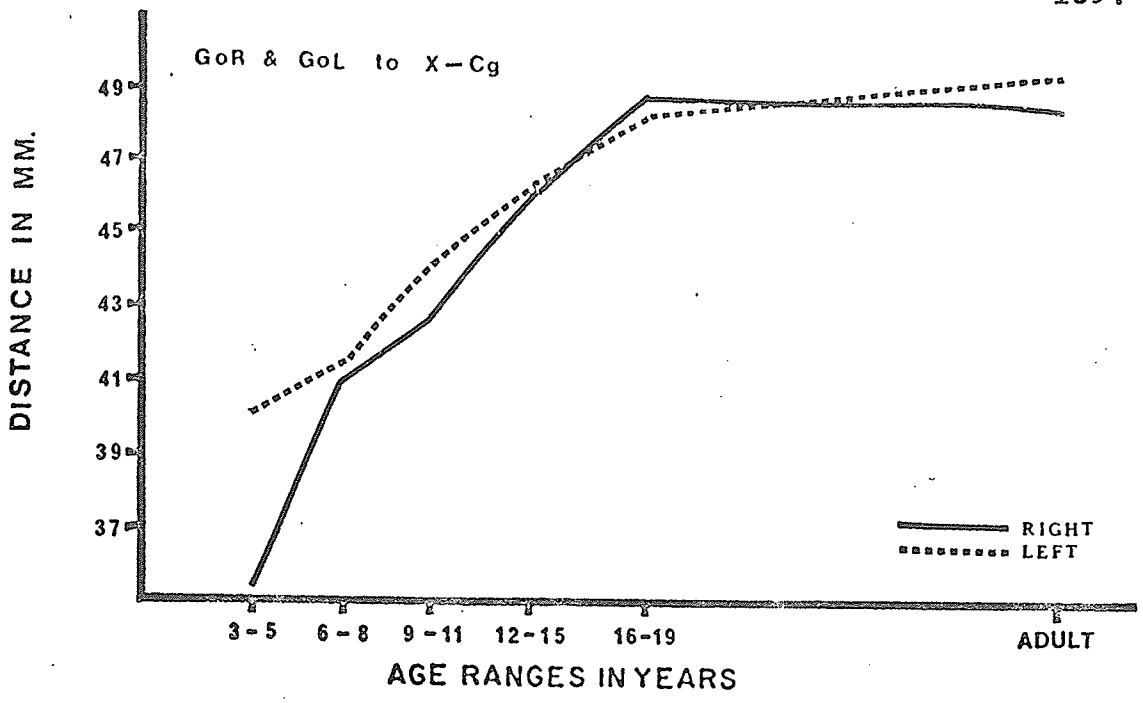


Figure 58. Effect of side x age for the asymmetry of the linear distances CdR and CdL to X-Cg.

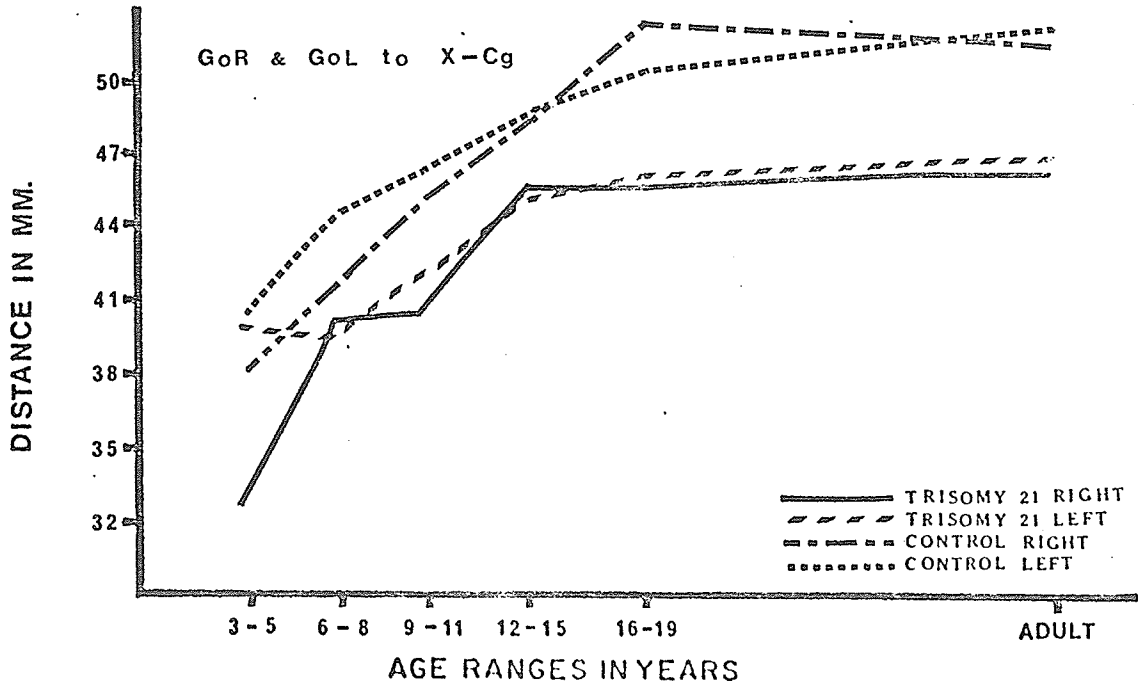


Figure 59. Effect of age x side for the asymmetry of the linear distances CdR and CdL to X-Cg in the Trisomy 21 and Control groups.

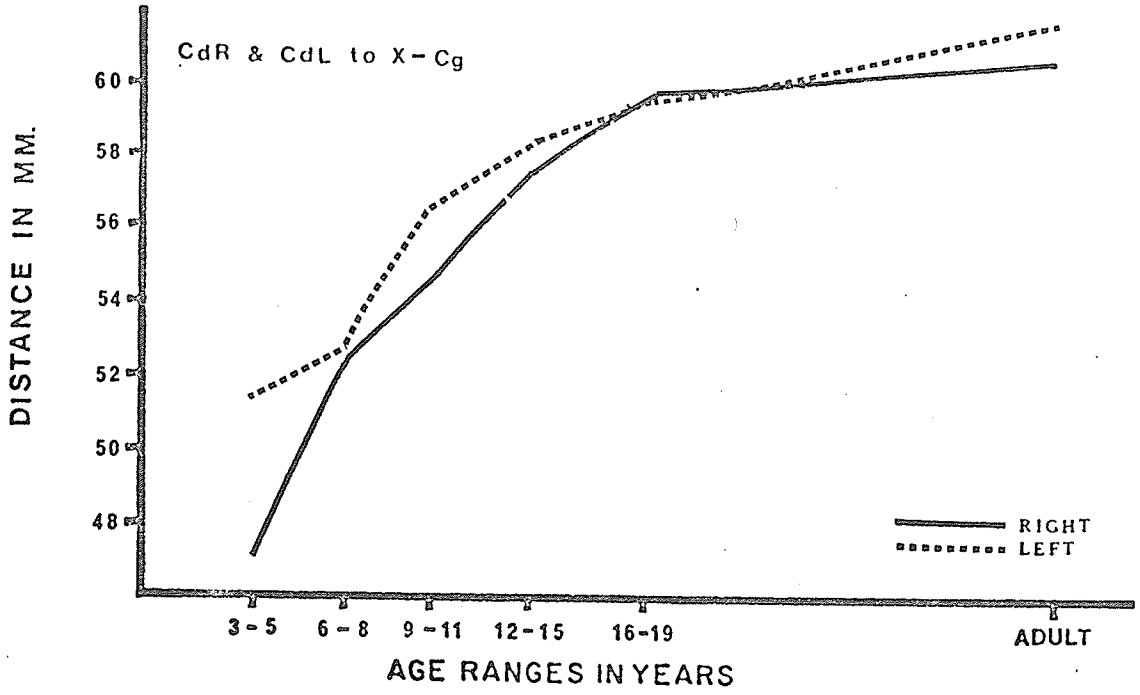


Figure 60. Effect of age x side for the asymmetry of the linear distances GoR and GoL to X-Cg.

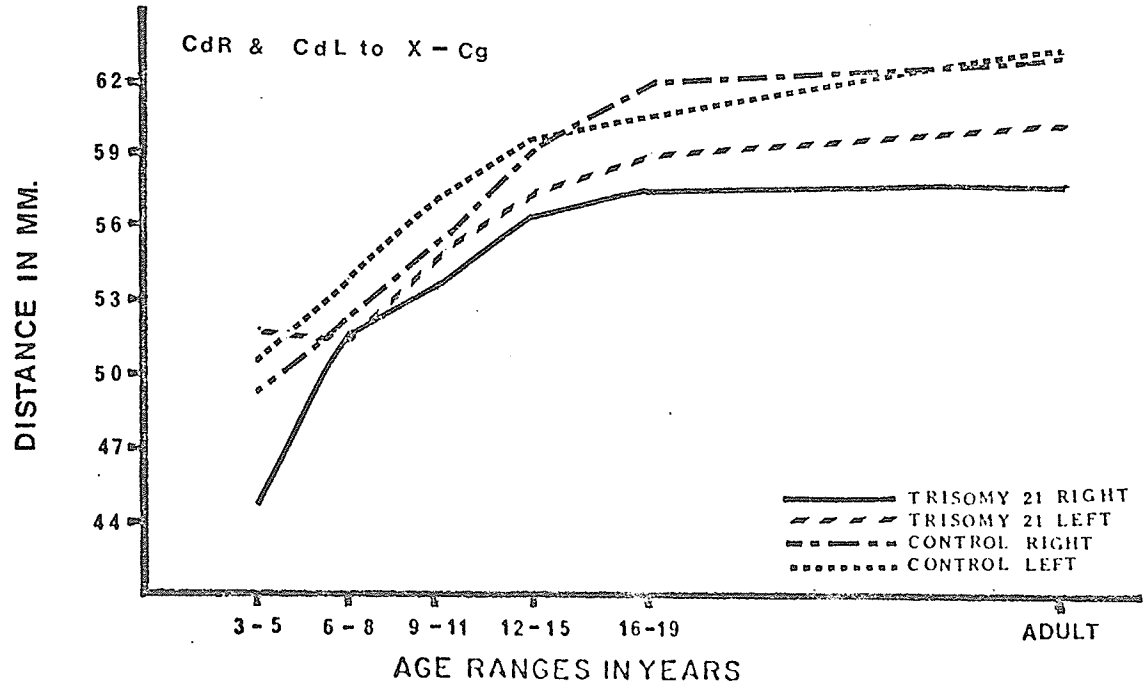


Figure 61. Effect of age x side for the asymmetry of the linear distances GoR and GoL to X-Cg in the Trisomy 21 and Control groups.

above, indicated that the left side was larger than the right side, and an age x side effect indicated that at the age range of 3-5 years, the left side was more prominent than the right side. However, there was a tendency for this asymmetry to reduce with age (Figures 52,54,56,58,60).

A significant group x side effect indicated that in the Controls, differences between the right and left sides in the above five areas were less than that of the Trisomy 21 sample (Table X).

A group x side x age effect indicated that the dominance of the left side over the right side was not true at all ages in both groups for these five areas. The graphs for the effect of side x age and age x group x side for the linear distances of TeR and TeL to X-Cg, MsR and MsL to X-Cg, ZyR and ZyL to X-Cg, CdR and CdL to X-Cg, and GoR and GoL to X-Cg are presented in Figures 52 to 61, and the means and standard errors for these five measurements are presented in the Appendix in Tables XL to XLIV.

III. ASSESSMENT OF THE DISTANCE BETWEEN THE ORBITAL CAVITIES, THE PUPILS AND THE EYES

Two soft tissue measurements and two skeletal measurements were utilized to assess the presence of hypo or hypertelorism between the orbital cavities, the eyes, and the pupils in the Trisomy 21 and Control groups.

The presence of hypo or hypertelorism in these three areas was obtained by taking the ratio of the distance between these structures over the skeletal bizygomatic width.

These three ratios were obtained for each individual in the Trisomy 21 and Control sample. The ratios were subjected to a statistical test of variance, as described previously for the skeletal analysis.

In addition to these three ratios, the Canthal index was utilized to denote whether the Trisomy 21 individual was hypo or hyperteloric, with respect to the separation of his eyes.

Distance between the orbital cavities

The assessment of the hypo or hypertelorism of the orbital cavities was done by taking the ratio of the inter-

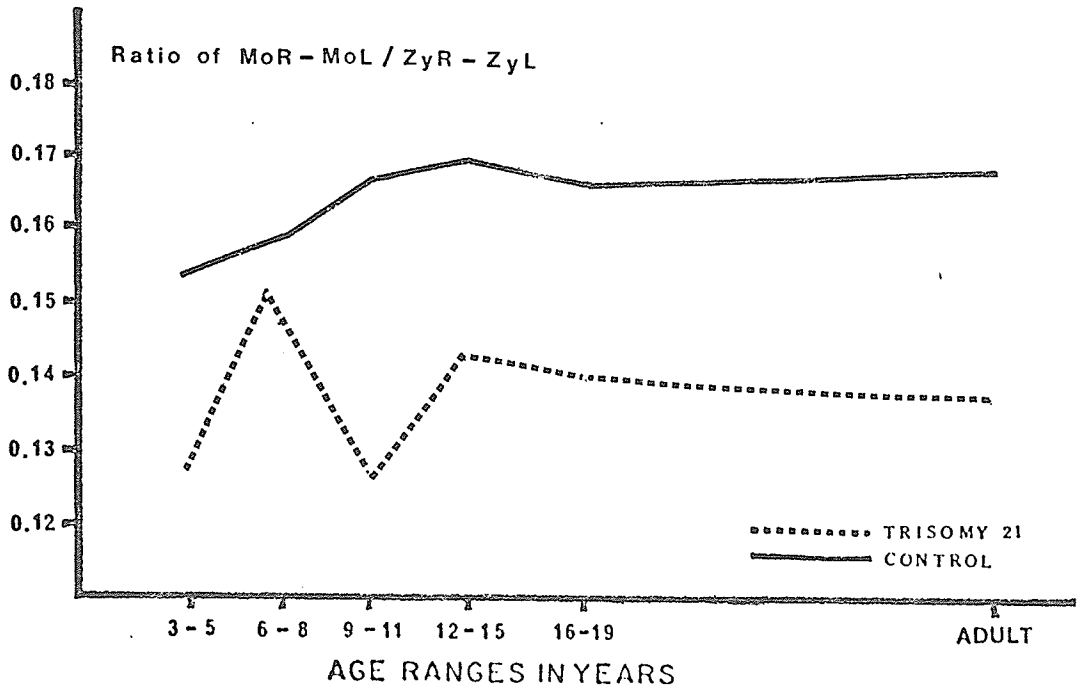


Figure 62. Effect of age on the ratio MoR-MoL/ZyR-ZyL for the assessment of the separation between the bony orbits in the Trisomy 21 and Control groups.

orbital width, MoR-MoL, over the bizygomatic width, represented by the linear measurement ZyR-ZyL. The main effects of age, group, and sex were significant at the 1% level and a group x age interaction was significant at the 5% level.

The mean ratio for the Trisomy 21 was 0.137, while the mean ratio for the Control was 0.165 (Table XI). The highly significant group x age effect (Figure 62) indicated that the Trisomy 21 individual showed a smaller ratio than the Control at all ages, which shows that the orbital cavities are situated closer together in the Trisomy 21 individual, in relation to the width of his face, at all ages. Hence, this finding shows the evidence of orbital hypotelorism in Trisomy 21 individuals.

Distance between the pupils

The assessment of the presence of pupillary hypo or hypertelorism in the Trisomy 21 group, as compared to the Control group, was obtained by taking the ratio between the inter-pupillary width, PR-PL over the width of the face, ZyR-ZyL.

A between group effect significant at the 1% level indicated that this ratio was significantly lower in the Trisomy 21 group than in the Control sample. This finding, therefore, shows that the pupils in the Trisomy 21 group are closer together than in the Control group, or that the Trisomy 21 group shows pupillary hypotelorism. Table XI indicates

the mean and standard errors for this ratio in the Trisomy 21 and Control groups.

Distance between the eyes

The presence of hypo or hypertelorism of the eyes in the Trisomy 21 group, as compared to the Control group was assessed by taking the ratio between the inter-endocanthal width, IER-IEL, over the width of the face, ZyR-ZyL.

A between group effect significant at the 1% level indicated that this ratio was significantly larger in the Trisomy 21 than in the Control. This finding, therefore, shows that the endocanthions are more widely separated in the Trisomy 21 group than in the Controls. Table XI shows the mean and standard errors for this ratio in the Trisomy 21 and Control groups.

In addition to the ratio of the inter-endocanthal width to bizygomatic width described above, the Canthal index was utilized to determine the degree of hypertelorism of the eyes. The Canthal index described in the Methods and Materials is obtained as follows:

$$\text{Canthal index} = \frac{\text{Inter-endocanthal distance}}{\text{Inter-ectocanthal distance}} \times 100$$

According to this index, a score of 38 is considered to be the upper limits of normality, while a score above 42 is considered to represent the condition known as hypertelorism. The range from the score of 38 to 42 is considered

TABLE XI

MAIN EFFECT OF GROUP FOR THE RATIOS OF THE DISTANCE BETWEEN THE ORBITAL CAVITIES, THE EYES AND THE PUPILS IN RELATION TO THE WIDTH OF THE FACE

RATIO	TRISOMY 21 MEAN	TRISOMY 21 SE	CONTROL MEAN	CONTROL SE
1. ORBITAL CAVITIES				
MoR-MoL/ZyR-ZyL	0.137	0.002	0.165	0.001
2. PUPILS				
PR-PL/Zyr-ZyL	0.426	0.003	0.440	0.003
3. EYES				
IER-IEL/Zyr-ZyL	0.258	0.002	0.242	0.002

TABLE XII

RESULTS OF THE CANTHAL INDEX IN THE 6 AGE RANGES OF THE TRISOMY 21 AND CONTROL GROUPS (Group x Age)

AGE RANGE IN YEARS	TRISOMY 21 MEAN	TRISOMY 21 SE	CONTROL MEAN	CONTROL SE
3-5	39.9	1.5	36.5	0.9
6-8	42.4	1.5	36.5	0.9
9-11	38.8	1.1	36.1	0.9
12-15	38.0	0.7	36.2	0.7
16-19	38.7	0.8	35.0	0.9
Adult	35.7	0.7	34.0	1.1

to be an intermediate condition called "Euryopia".

The results of the Canthal index at each age range for the Trisomy 21 and Control groups are indicated in Table XII. Using the same terminology for the interpretation of the Canthal index as described above, the Trisomy 21 group may be considered to be euryopic from the age range of 3-5 years to 6-8 years and after these age ranges, their scores were at the upper limits of normality.

Comparison of the scores obtained by the Trisomy 21 group with those obtained by the Control sample indicate that this score is always higher than the Control group at all age ranges.

IV. DIFFERENCES OBSERVED IN THE PRESENCE OF PATENT METOPIC SUTURES

Patent metopic sutures or partially patent metopic sutures were observed in 61.6% of the Trisomy 21 individuals, while the Control group showed only 5.7% of the metopic sutures to be patent. Table XIII shows that out of 121 Trisomy 21 individuals, 39 males and 35 females were affected. In the Control groups, out of a total of 139 individuals, only three males and five females showed patent metopic sutures. No apparent difference seems to exist between the sexes in the Trisomy 21 or Control groups.

Within the Trisomy 21 or Control population, no difference seems to exist at different age ranges. However, it is interesting to note that in the Control group, patent metopic sutures were only seen up until the age range of

TABLE XIII

PATENT METOPIC SUTURES PRESENT IN TRISOMY 21
AND CONTROL INDIVIDUALS

AGE RANGES IN YEARS	TRISOMY 21				CONTROL			
	NO.	PER CENT AFFECTED	MALES	FEMALES	NO.	PER CENT AFFECTED	MALES	FEMALES
3-5	7	42.8	2	1	20	5.0	1	0
6-8	7	42.8	1	2	21	0.0	0	0
9-11	13	76.9	5	5	22	13.6	0	3
12-15	30	70.0	13	8	32	12.5	2	2
16-19	28	50.0	7	7	14	0.0	0	0
Adult	36	69.4	11	14	30	0.0	0	0
TOTAL	121	61.1	39	35	139	5.7	3	5

12-15 years, while in the Trisomy 21 group, patent metopic sutures could be observed in over 50% of the individuals, even in the 16-19 and adult age ranges. The patent metopic suture, as seen in a P.A. radiograph, is shown in Figure 67 on page 181.

V. DIFFERENCES OBSERVED IN THE PRESENCE OF SUTURAL BONES

Table XIV shows the percentage of Trisomy 21 and Control individuals who were observed to be showing the presence of wormian bones in the cranial sutures. Out of a total number of 77 Trisomy 21 individuals, 27 males and 21 females showed the presence of wormian bones. In the Controls, out of a total of 104 individuals, three males and one female showed the presence of wormian bones in the cranial sutures. On a percentage basis, 62.3% of the Trisomy 21 individuals showed the presence of wormian bones, while only 3.8% of the Control individuals showed the presence of wormian bones. No apparent difference appears to exist between the sexes in both the Trisomy 21 and Control males and females. In the Trisomy 21 group, a higher percentage of individuals were affected in the age range of 9-11 years and above. It is conceivable that the Trisomy 21 individuals in the younger age ranges, who do not show the presence of wormian bones in the cranial sutures, may show the presence of wormian bones at an older age. The sutural bones, as seen on the P.A. radiograph can be seen in Figure 67 on page 181.

TABLE XIV

SUTURAL BONES (WORMIAN) PRESENT IN TRISOMY 21 AND CONTROL INDIVIDUALS

	TRISOMY 21				CONTROL			
AGE RANGES IN YEARS	NO.	PER CENT AFFECTED	MALES	FEMALES	NO.	PER CENT AFFECTED	MALES	FEMALES
3-5	6	33.3	1	1	14	0.0	0	0
6-8	6	50.0	0	3	18	0.0	0	0
9-11	7	71.4	2	3	14	0.0	0	0
12-15	23	60.8	9	5	18	11.1	2	0
16-19	18	61.1	8	3	12	0.0	0	0
Adult	17	76.4	7	6	28	7.1	1	1
TOTAL	77	62.3	27	21	104	3.8	3	1

CHAPTER V

DISCUSSION

I. SKELETAL ANALYSIS

Most of the past investigations on Down's syndrome have utilized lateral cephalometric radiographs to make objective measurements of the craniofacial complex in these individuals. These studies, using lateral cephalometric radiographs, have shown the differences in craniofacial growth in the Trisomy 21 and Control groups, mainly in the antero-posterior and vertical dimensions.

The changes in the width of the craniofacial complex in the Trisomy 21 group as compared to that seen in the Control group have not been reported in literature by means of objective measurements. In previous studies using postero-anterior radiographs, the information reported has either been on a subjective basis, or the investigators selected only certain age ranges for study and in most cases the specific karyotype of the sample was not determined before the investigation.

This study, by the use of measurements made on postero-anterior radiographs of the cytogenetically confirmed Trisomy 21 sample, ranging in age from three to fifty-six years, indicated that the overall width of

the craniofacial complex was smaller in the Trisomy 21 group than the Control group.

It was shown in the Results, in Table VIII, that most of the areas measured in the craniofacial complex in the Trisomy 21 group were smaller than that found in the Control group. It was also evident from the Results that some areas of the craniofacial complex were more affected than others and that these areas did not show the same pattern of development in the Trisomy 21 and Control groups. In Figure 63 is represented the mean computer polygonal plot for the Trisomy 21 and Control samples.

The areas in the craniofacial complex of the Trisomy 21 groups, which were most affected and reached only 80 to 85 per cent of the width attained by the Control group were the inter-orbital width (MoR-MoL), the height of the nasal cavity (Cg-ANS), and the width of the maxilla (MxR-MxL). All these three areas showed significant differences as regards their pattern of development in the Trisomy 21 group, as compared with the Control sample, as indicated by the significant group x age interactions shown on page 85 in Table VI.

It was observed that the inter-orbital width (MoR-MoL) was significantly smaller in the Trisomy 21 group than in the Control group at the age range of 3-5 years (Figure 25). However, the rate of increase in

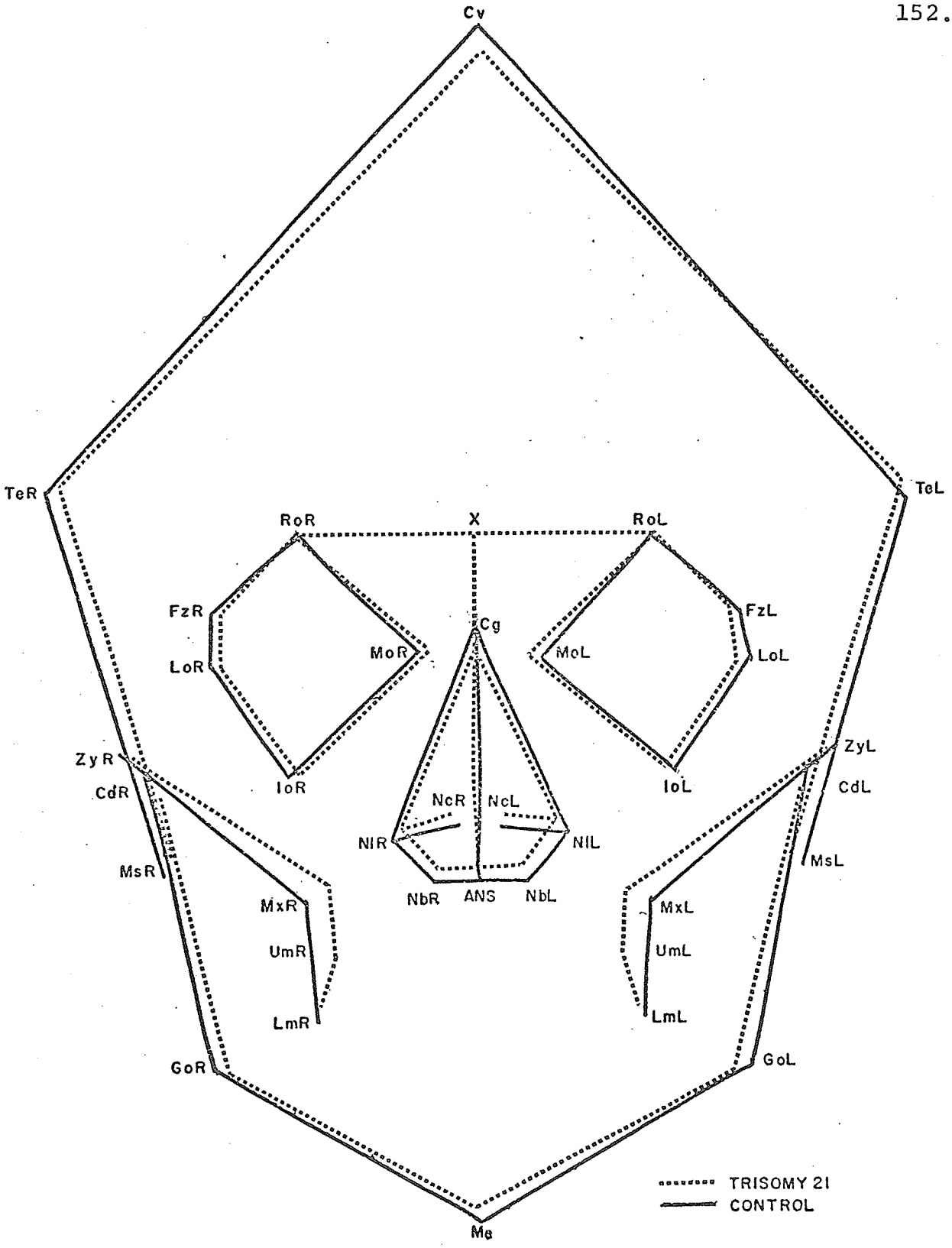


Figure 63. Computer polygonal plot for the Trisomy 21 and Control samples.

this measurement was slower in the Trisomy 21 group than in the Control sample, leading to a much smaller inter-orbital width in the Trisomy 21 group as compared with the Control group, in the age range of 12-15 years and above. This measurement is partly dependent on the growth of the cartilagenous ethmoid bone and the formation of the ethmoid air cells (Ford, 1958).

The height of the nasal cavity (Cg-ANS) is partly dependent on the growth of the cartilagenous nasal septum (Scott, 1953a). This measurement was small in the Trisomy 21 group at the age range of 3-5 years, but the rate of increase in this measurement in the Trisomy 21 group was slower than that seen in the Control group, and the height of the nasal cavity was only 83.5% of that seen in the Control group (Table VIII and Figure 23).

The width of the maxilla (MxR-MxL) was considerably smaller in the Trisomy 21 individuals at all age ranges when compared with the Control individuals (Figure 16). The width of the maxillary bones reached only 84.3% of the width attained by the Control sample. Although the maxillary bones are membranous in their origin, a possible answer to their diminutive size may lie in the fact that the downward and forward growth of the maxilla is dependent on the growth of the cartilagenous nasal septum.

Supporting the above statement, Wexler and Sarnat (1961) showed that interference with growth of the nasal septum created a midfacial underdevelopment and an anterior crossbite in animals. Also, Bjork, in 1964, with the use of metallic implants in humans, has suggested that the growth activity in the palatal suture is associated with the downward growth of the maxilla. Enlow (1968) also indicates that the soft tissue, which is responsible for pacing sutural separation in the face, is the enlarging nasal septum. Enlow states that, because this structure is composed largely of cartilage during earlier growth stages, it is capable of growth and interstitial expansion in the presence of pressure involved in moving the facial bones away from the cranial base. It has already been noted that the nasal cavity height, which is associated with the growth of the nasal septum, is markedly affected in the Trisomy 21 individuals.

Another possible explanation for lack of growth of the maxilla may be the relationship of the palatine tuberosity to the notch between the pterygoid plates. Scott (1954a) points out that the relationship of the palatine tuberosity is interesting because, by this interlocking mechanism, the growth between the greater wings and the body of the sphenoid bone during fetal life is correlated with growth at the midpalatal suture. After the union between the parts

of the sphenoid, the pterygoid plates can no longer undergo a process of bodily separation, and this will limit to a considerable extent the amount of growth that can occur between the palatine bones at the midpalatal suture.

Davies and Davies (1962) state that the body, the lesser wings, and the base of the greater wings of the sphenoid develop in cartilage, while the major part of the greater wings develop in membrane. At birth the sphenoid bone consists of three pieces, a central portion consisting of the body, the lesser wings, and the two lateral pieces, each consisting of the greater wings and the pterygoid processes. In the first year after birth, these three pieces unite.

Lowe, in 1949, had noted that the apices of the orbital cavities in the Trisomy 21 individuals were very close to their medial walls, which suggests that the cartilagenous body of the sphenoid is small.

It is conceivable, therefore, that if the cartilagenous body of the sphenoid is more seriously affected in its growth than the major part of the greater wings, then the diminutive size of the body of the sphenoid would limit the growth of the maxilla, as the right and left pterygoid processes would now be closer together, because of the small body of the sphenoid.

The effect of this abnormal karyotype seems to be mainly directed against the growth of cartilage, as indicated

by the above three measurements. These three measurements are representative of the areas of the craniofacial complex that are largely influenced by the growth of cartilage, and they were considerably more affected than the bones that develop in membrane, as the remaining measurements were over 90% of the measurement reached by the Control group (Table VIII). To further elaborate on this statement, the measurements made in each area of the craniofacial skeleton will be discussed under the headings of the Cranium, Upper face, and Lower face.

A. CRANIUM

The two cranial measurements were the width of the cranial vault (TeR-TeL), and the width between the mastoid processes (MsR-MsL). These two measurements were smaller in the Trisomy 21 group but were not as seriously affected as the nasal cavity height, the inter-orbital width, and the maxillary width. The mean measurements of these two variables in the Trisomy 21 group were over 95% of the width attained by the Control group (Table VIII).

According to Scott (1958), the growth of the brain does not seem to affect the growth of the cranial base, but both brain growth and the cranial base growth contribute to the form of the cranial vault. He cites the example of the achondroplastic dwarf, where the cartilagenous cranial base is underdeveloped; he notes that the brain tends to provide the necessary room by a rounding out or brachycephali-

zation of the cranial vault.

The brachycephalic appearance of the cranial vault of Trisomy 21 individuals has been well substantiated by Kisling (1966). Gosman and Vineland (1951) also found the head breadth to be less affected than the head length in the Trisomy 21 individuals.

The findings of this study also tend to substantiate the point that the head breadth in the Trisomy 21 group was slightly smaller than that of the Control group, and the mean width of the cranial vault was 97.5% of the mean cranial width of the Control sample. It would, therefore, seem that the bones of the cranial vault which develop in membrane are comparatively less affected than the cartilagenous areas of the cranial base.

Whether the membrane bones are forced to adapt to an essentially normal sized brain or not cannot be determined from this study. However, the subjective findings of Frostad, Cleall, and Melosky (1971), and Spitzer, Rabinowitch, and Wybar (1961) as regards the thinness of the cranial bones and the increased digital markings, seen in Trisomy 21 individuals, tends to suggest that the growth of the bones that develop in membrane is also affected.

The postnatal changes taking place in the width of the cranial vault were found to be occurring in the same direction as that of the Control, as no statistically significant group x age effects could be detected, implying, therefore, that parallel developmental changes were occurring

in both the cranial width and the bimastoid width measurements. However, both these widths were smaller in the Trisomy 21 sample and the means and standard errors of these measurements are presented in Tables XV and XVI in the Appendix.

B. UPPER FACE

Face width

The width of the face was represented by the linear distance, ZyR-ZyL. The Trisomy 21 sample again attained 97.3% of the mean width attained by the Control sample (Table VIII). This width is measured between the zygomatic processes of the squamous temporal bone, which are membranous in origin and seem to be less affected than the cartilagenous areas described previously. The size difference was seen in the Trisomy 21 group at the age range of 3-5 years, and growth from this age to the adult stage appeared to be occurring at equal rates within the two groups, as no group x age interactions were significant. The mean values for this measurement have been presented in Table XVII in the Appendix.

Width of the maxilla

The possible reasons for the decreased maxillary width in the Trisomy 21 group have already been discussed at the beginning of this chapter. It can also be noted that the maxilla was one of the most affected areas in the cranio-facial complex of the Trisomy 21 group and this can be seen in Figure 63.

Nasal Cavity

The fact that the nasal cavity height is smaller in the Trisomy 21 group has also been discussed previously. Further support to the above can be added by the measurements of Ghiz (1968), who showed that the upper facial height was smaller in the Trisomy 21 group, while the lower facial height was larger than normal in the Trisomy 21 individuals. It is realized that the measurements of Ghiz for upper facial height were made on lateral cephalometric radiographs, from the point nasion to the anterior nasal spine (ANS), and this measurement could be affected by the absence or diminutive size of the nasal bones seen in the Trisomy 21 individuals (Frostad, 1969). The findings of this study, however, tend to confirm the findings of Ghiz (1968) as they were taken from the landmark Cg (Crista galli), located on the anterior cranial base to the point ANS.

Several investigators have frequently mentioned in the literature that the Trisomy 21 individuals exhibit an open mouth posture and a protrusive tongue position at earlier ages (Figure 64), and this abnormal tongue position and open mouth posture seems to be no longer present at later ages (Figure 65). Also, conflicting reports exist in the literature as regards the size of the tongue in Trisomy 21 individuals. In view of the decreased nasal cavity height and small size of the maxilla, it would be interesting to observe by means of cinefluorographic studies whether there

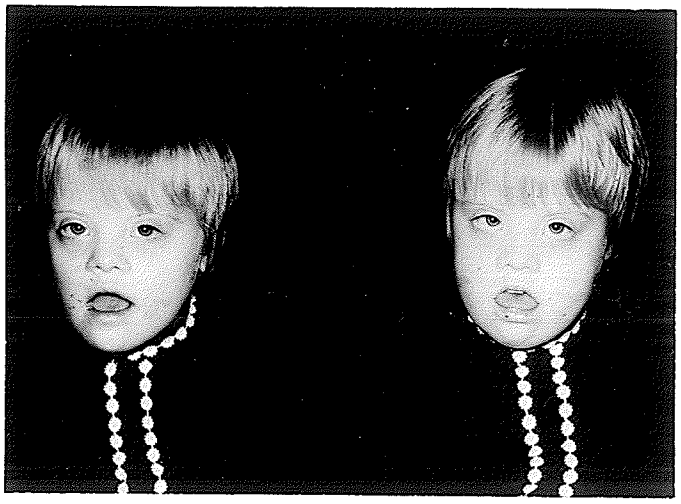


Figure 64. Open mouth posture present in young Trisomy 21 individuals.

Figure 65. Adult Trisomy 21 individuals showing absence of open mouth posture.

are any deviations from the normal in the tongue posture and pharyngeal areas of the Trisomy 21 individuals. Longitudinal studies would also perhaps explain whether the open mouth posture, which is not usually seen at older ages, is related to a maturational process, or whether it is a gene dosage effect.

The fourth and fifth smallest measurements (Table VIII) in the Trisomy 21 sample were associated with the width of the nasal base (NbR-NbL) and the width of the nose (NlR-NlL). The mean measurements in the Trisomy 21 sample were 90.0% for the nasal base width and 91.2% for the width of the nose, as compared with the same measurement of the Control sample.

It can be observed that these measurements were approximately 5% larger than the width of the maxilla (MxR-MxL) seen in Table VIII. This suggests that in proportion to the width of the maxilla, the width of the nasal cavity was larger in the Trisomy 21 sample than the width of the nasal cavity in the Control sample. This finding is interesting, because it implies that some accommodative changes do occur in response to the function of respiration in the Trisomy 21 individual. Or this finding might suggest that increases in the width of the maxilla and that of the nasal cavity occur independently of one another.

Scott (1967) has stated that the changes in the lower part of the nasal cavity occur more in response to functional demands. These changes are believed to occur until adulthood.

The findings of this study showed that the lower part of the nasal cavity did increase in width until the age range of 16-19 years (Figure 18).

Examination of the nasal cavity width (N1R-N1L) did show that this measurement was significantly smaller in the Trisomy 21 group than the nasal cavity width of the Control sample. No statistically significant differences could be shown for the changes occurring in this measurement with age in the two groups. However, examination of the mean measurements at the various age ranges in the Control and Trisomy 21 groups, did tend to indicate an increase in the width of the nasal cavity in the Trisomy 21 group until late adulthood, while no increase in this measurement was observed in the Control group after the age range of 16-19 years (Figure 19). This difference, although slight, may tend to indicate that the increased nasal cavity width changes occurring until late adulthood in the Trisomy 21 individuals, may be an accommodative phenomenon which occurs in response to the function of respiration as the nasal cavity height in these individuals is reduced.

Another interesting finding was the increased width between the inferior nasal conchae (NcR-NcL) in the Trisomy 21 group. The mean width in the Trisomy 21 sample was 143.5% of the distance between the inferior nasal conchae seen in the Control sample (Table VIII). This increased width between the inferior nasal conchae, when viewed with the smaller nasal cavity width (N1R-N1L), seen in the Trisomy 21 sample,

again, tends to indicate that the width of the inferior nasal conchae, which develop from the cartilagenous nasal capsule, are considerably affected in their growth.

To again see to what degree the inferior nasal conchae were affected in their width, the difference between the width of the nasal cavity (NlR-NlL) and the width between the inferior nasal conchae (NcR-NcL) was first obtained.

The mean width of both the right and left inferior nasal conchae in the Trisomy 21 group was 19.2 mm. and in the Control sample was 24.6 mm. These measurements, expressed in the terms of the percentage width attained by the Trisomy 21 individuals, indicated that the Trisomy 21 sample showed the width of the right and left inferior nasal conchae to be 78% of the mean width of the inferior nasal conchae seen in the Control sample.

Each inferior nasal concha is believed to develop from one ossification center, which appears at about the fifth month of intra-uterine life in the lower incurved border of the cartilagenous nasal capsule (Davies and Davies, 1962). Since these bones reach only 78% of the mean width reached by the Control sample, this is in keeping with the observation that bones that develop from cartilage are more seriously affected in the Trisomy 21 individuals.

Orbits

Width and height of the orbits. The findings of this

study as shown in the Results, indicated that in both the Trisomy 21 and Control groups, an increase in the height of the orbits (RoR-IoR and RoL-IoL) occurred until the age range of 12-15 years (Figures 43, 45), while the changes occurring in the width of the right and left orbits, MoR-LoR and MoL-LoL respectively, occurred until the age range of 16-19 years (Figures 39, 41). No statistically significant differences could be detected for the orbital height and orbital width in the Trisomy 21 and Control groups as shown in Table VI on page 85. Furthermore, the orbital height and width measurements were one of the least affected measurements (Table VIII).

The fact that the orbits are least affected in their height and width may be interpreted by the explanation given by Enlow (1968), who states that the main underlying force that contributes to the displacement of the flat bones of the cranium is the growth of the soft tissue brain.

Similarly, the main underlying force that would contribute to the growth of the orbital cavities is the growth of the eyeball and its extrinsic musculature, which, in the Trisomy 21 individuals is probably not as much affected in its size. Therefore, the bones of the orbital cavity move ahead of the growing eyeball, and corresponding additions of bone at the various sutures between the bones of the orbital cavity passively function to maintain the bones in continuous contact and to enlarge.

In support of the above, Scott (1967) states that the

growth at the sutures between the bones of the medial wall of the orbit are regulated by the growth of the cartilage of the nasal septum and especially the eyeball. He states that the eyeball achieves 90% of its adult size by the age of seven years.

The findings of this study also showed that the orbits increased in their width at the expense of the changes occurring at the lateral orbital margins. The measurements representing the changes at the lateral orbital margins were the bilatero-orbital width (LoR-LoL) and the fronto-zygomatic suture width (FzR-FzL). These two measurements showed larger increments than the inter-orbital width (MoR-MoL), thereby increasing the width of each orbit. It mentioned previously in the Results that the increase in the bilatero-orbital width from the age range of 3-5 years to adulthood in the Trisomy 21 group was 11.2 mm., and in the Control group, this increment was 12.3 mm. The amount of increase in the bifronto-zygomatic suture width was similar to that found in the bilatero-orbital width. The total increment was 13.7 mm. in the Control group and 12.5 mm. in the Trisomy 21 group. However, the total increment in the inter-orbital width showed that the Trisomy 21 individuals only increased by 3.9 mm., while the increment in the Control sample was 4.2 mm.

Some of these changes may be explained by the changes that are found to occur in the malar region, as described by Enlow (1968). He states that the malar complex undergoes

growth movement in a progressive posterior direction. This posterior positioning occurs so as to maintain a constant position of the malar region relative to the maxillary arch, the orbit, the temporal area, and the cranial base. He explains that progressive resorption occurs at the anterior face of the zygoma and the forward margin of the lateral orbital rim so as to bring about the posterior repositioning of the malar bone. Enlow also states that the medial wall of the orbit is appositional in nature.

It was also interesting to note that the lateral orbital margin is formed by the zygomatic bone which is membranous in origin, and in the Trisomy 21 group these widths, namely, the bifronto-zygomatic suture width and the bilatero-orbital width, which represent changes at the lateral orbital margin reached approximately 95.8% and 96.5% of the mean width of the Control sample (Table VIII).

In the Results, it was shown that the width of each orbit was not as seriously affected as the width between the orbits, which gave the appearance of orbital hypotelorism to the Trisomy 21 individuals. The findings of this study also showed that there were no significant differences in the Trisomy 21 and Control groups, as regards the height of the orbits. Table VIII indicated that the mean orbital height in the Trisomy 21 group was 98.8% and 99.5% of the mean height of the right and left orbits attained by the Control group. The mean orbital width attained by the Trisomy 21 group for the right and left orbits was 100.5%

and 100.8% of the mean width of right and left orbits, as seen in the Control sample.

Some reasons as to why the orbital height was smaller than the orbital width in the Trisomy 21 group can be given by the findings of Frostad (1969) and Kisling (1966). Both these investigators, from measurements on lateral cephalometric radiographs, found the anterior opening of the orbit to be inclined downward in the Trisomy 21 sample, as compared to the Control sample. This downward inclination of the orbits would make the height of the orbits appear slightly smaller on the postero-anterior radiograph. Frostad (1969) also stated that this downward angulation of the anterior orbital opening tended to change to a more forward facing angulation in the Trisomy 21 individuals at older age ranges. Examination of the means for the orbital height in the Trisomy 21 groups at the various age ranges did show that the orbital height was smaller at the younger age ranges but approached the orbital height of the Control in the older age groups (Figures 44, 46).

Height of orbital roof from the anterior cranial base point Crista galli (Cg). Although the distance X-Cg, measuring the height of the orbits from the anterior cranial base, was not considered in this study, the computer polygonal plot (Figure 63) did show that the landmark Cg, which represents the base of crista galli, was lower than the most superior point on the orbital margin (RoR and RoL).

The base of crista galli is located on the cribriform plate of the ethmoid and it does seem to indicate that the most superior point on the roof of the orbit is located superiorly relative to a point located on the anterior cranial base.

Frostad, Cleall and Melosky (1971), from their measurements made on lateral cephalometric radiographs, have also shown that the roof of the orbit, relative to the Sella Nasion plane, was located superiorly in the Trisomy 21 group. Kisling (1966) also showed this to be present in adult Down's syndrome individuals.

Position of the Roof of the orbit relative to medio-orbitale. Benda (1946, 1969) reported from subjective observations that the orbits in Down's syndrome were egg shaped. Frostad (1969) also, from subjective observations, felt that the most superior point on the superior orbital margin was located further laterally. The objective findings of this study showed that the most superior point on the orbital margin is located further laterally in Trisomy 21 individuals, as shown by the measurement, MoR-RoR and MoL-RoL, as was reported in the Results (Figures 27, 28).

These measurements for the right and left orbits were larger in the Trisomy 21 group and were 110.3% and 113.9%, respectively, of the mean measurements of the right and left orbits of the Control group (Table VIII).

Some explanation as to why this may occur may be

given by Arey (1965) and Moss (1955). Arey (1965) states that in the prenatal development of the human embryo, anterior to the parachordal plate, are found two trabecular cartilages which form part of the sphenoid bone. Anteriorly these trabecular cartilages are fused with the cartilagenous nasal septum and ethmoid bone.

The optic capsules are believed to arise as separate entities, although in most vertebrates below mammals, cartilage has been incorporated in the optic capsules. In man, however, the optic capsules lie adjoining the trabecular cartilage but develop in the membranous connective tissue. Arey (1965) states that at the 7th week, chondrification begins in the areas where the sphenoid is destined to form and spreads anteriorly into the nasal capsule. At this time, however, the connective tissue around the optic capsules, in which membranous bones appear, do not show the presence of the ossification centers. It would seem, therefore, that if there was a deficiency in the development of cartilage in the nasal capsule area, then the eyeball which is developing at this time would be moved superiorly and laterally as the brain is developing superior to it. At about the third month, when the ossification of the frontal bone begins (Davies and Davies, 1962), due to a change in the positional relationship of the eyeball, the most superior point on the roof of the orbit would be placed superiorly and laterally.

Furthermore, the most inferior point on the orbital

outline would be found closer to the midline, due to the lack of growth of the nasal cavity height and inter-orbital breadth, as shown in this study. Moss (1955) also states that postnatally, in normal individuals, there is an upward growth of the roof of the orbit relative to the S.N. plane.

Changes in the shape and the slant of the orbits.

In the Results, it was shown that the most superior points on the orbital roofs were found to be further apart in the Trisomy 21 group until the age range of 12-15 years (Figure 26), while the most inferior points on the orbital margins were located closer together in the Trisomy 21 group at the age range of 3-5 years (Figure 29). It was also shown in Figure 31 that the orbits in the Trisomy 21 group had a lateral slant at the age range of 3-5 years and this lateral slant of the orbits has been shown in the photograph in Figure 66A which also shows that the orbits have an oval shape at the younger age ranges.

This lateral slant, seen at the younger ages, was observed to change to a medial slant with age, as the total increment in the distance, RoR-RoL, separating the most superior points on the orbital outlines in the Trisomy 21 group was only 4.5 mm., and the increment in the distance, IoR-IoL, separating the most inferior points on the orbital outlines was 12.4 mm. These changes would not only give a

A.

B.

C.

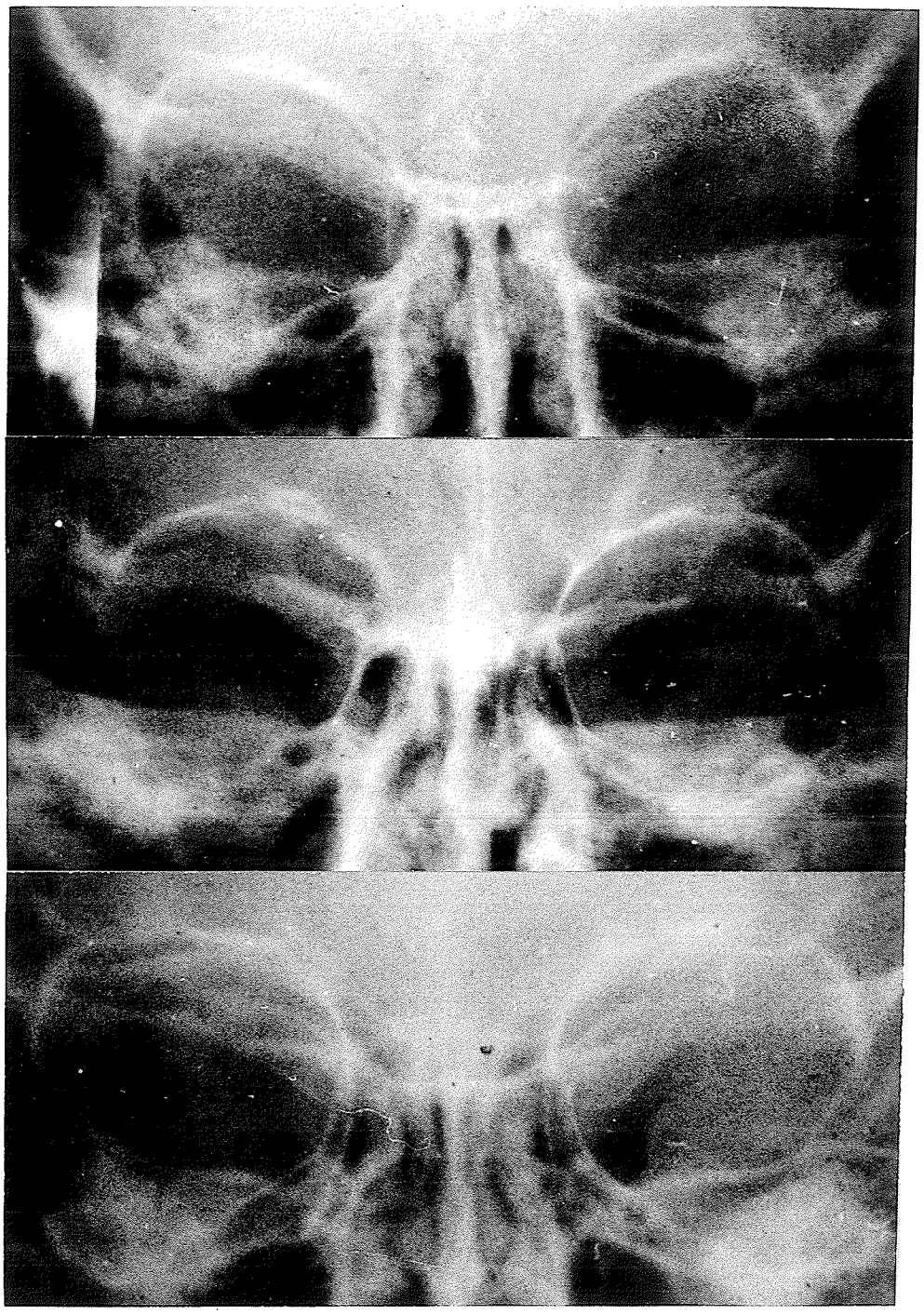


Figure 66. The orbital outlines and slant of the orbits in A. Trisomy 21 at younger ages, B. Trisomy 21 at older ages, C. Normal.

medial slant but also contribute to changing the oval shape of the orbital outline to a circular shape in the Trisomy 21 individuals at a later age (Figure 66B). This circular shape of the orbits found in the Trisomy 21 group at a later age is similar to the circular shape of the orbits that is seen in the Control group from the age range of 3-5 years to adulthood (Figure 66C). These changes in the Trisomy 21 and Control groups have been shown diagrammatically and are also given by the computer polygonal plot in Figures 31, 32, 33 and 34 in the Results. Furthermore, since the increments seen at the lateral orbital margins were fairly large and similar to that seen in the Control group, they would also contribute to change the shape of the oval orbital outline of the Trisomy 21 group to a more circular outline as seen in the Control group.

The possible answers as to why the medial slant and the circular shape of the orbital outline is maintained in the Control group, is that the total increment found at the roofs of the orbits is 8.5 mm. and the increment at the inferior orbital margin is 10.5 mm. Since these changes are approximately equal, the slant of the orbits does not change in the Control group and the circular shape is maintained.

As regards changes in the orbital roof, Enlow (1968) has implied that, in normal individuals, the roof of the orbit drifts laterally due to the formation of the supraorbital ridge which grows anteriorly, while the infero-lateral margin moves posteriorly due to this area being resorptive in nature. Enlow also states that the frontal bone in the region just superior to the orbital rim is seen to drift forward and its cortical thickness increases. The intervening diploe becomes progressively replaced by the frontal sinus.

Frostad, Cleall, and Melosky (1971) have noted that in Trisomy 21 individuals the thickness of the frontal bone across the frontal sinus area was found to be smaller than in the Controls. Furthermore, they state that the supraorbital ridges were formed in some Trisomy 21 individuals despite the lack of frontal sinus formation in 85% of the Trisomy 21 sample.

The findings of this study show that there is a lack of separation between the roofs of the orbits in the Trisomy 21 group, as compared to the Control group. This has been previously explained and shown in Figures 26 and 33. It would seem, therefore, that the formation of the supraorbital ridge is somehow linked with the functional activity of the frontalis muscle, but the lack of lateral drift of the orbital roofs is probably associated

with the lateral extension of the frontal sinus in this region. As the frontal sinuses are missing in a high percentage of Trisomy 21 individuals, no lateral extension of the frontal sinus in the region of the orbital roofs occurs, and therefore, the roofs of the orbits do not drift laterally with age in the Trisomy 21 individuals.

It has already been mentioned that in the Trisomy 21 group the changes taking place at the lateral orbital margins were similar to those seen in the Controls, as no group x age interactions were significant. Furthermore, compensatory changes were taking place at the inferior orbital margins, as shown by the significant group x age interactions. These changes contributed to the change in the shape of the orbit from an oval outline as seen at younger ages to a more circular outline in the older age groups of the Trisomy 21 individuals.

C. LOWER FACE

The measurements in the lower face indicated that in the Trisomy 21 individuals, the bigonial width and bicondylar width was smaller than the Controls. The bicondylar width was 97.5% of the mean bicondylar width in the Control group, and the bigonial width was 93.6% of the mean bigonial width of the Control sample (Table VIII).

Since no significant group x age interactions

occurred, the growth of the mandible in these two areas was considered to occur in a parallel manner in the Trisomy 21 and Control groups.

The smallness in width of the mandible was present at the age range of 3-5 years and this smallness persisted throughout the older age ranges.

D. SEXUAL DIAMORPHISM

Significant sex x age interactions were found to occur in seven facial measurements, as shown in the Results. These seven measurements were the bizygomatic width (Figure 15), the bimaxillary width (Figure 17), the height of the nasal cavity (Figure 24), the bi-inferior orbital width (Figure 30), the bifronto-zygomatic suture width (Figure 36), the bicondylar width (Figure 48), and the bigonial width (Figure 50).

In all these seven measurements, the males tended to increase more than the females after the age range of 9-11 years. Woods (1950), from serial data, found that the bigonial and bizygomatic width tended to increase more in males than in the females after the thirteenth year. These changes can be attributed to the difference in the onset of adolescence, as suggested by Woods (1950).

Since no group x sex or group x sex x age interactions were significant, it can be said that the males and females in the Trisomy 21 and Control groups showed similar developmental changes in these measurements.

II. ASYMMETRIES IN THE CRANIOFACIAL SKELETON

Since most of the measurements of asymmetry in the craniofacial skeleton showed a predominance of left side versus right, it would appear that there is a genetic tendency for this to occur.

The fact, that the measurements representing asymmetries of the temporal bones (TeR and TeL to X-Cg), mastoid processes (MsR and MsL to X-Cg), zygomatic arches (ZyR and ZyL to X-Cg), condyles (CdR and CdL to X-Cg), and right and left gonial region (GoR and GoL to X-Cg), did not show significant differences of left side dominance versus right side in both groups through the six age ranges, is interesting, because these areas are under the influence of relatively powerful muscles. The muscles concerned are the temporals, the sternocleidomastoids, the masseters, and the lateral pterygoid muscles.

Sicher (1970) and several other authors have stated that the outer table of the cranial vault grows in response to its cranial superstructures. Washburn (1947) and Ryll (1972) have shown that the removal of certain muscles will affect the size and shape of the skeletal unit to which they are attached.

Research, however, is lacking on the functional activity of muscles at different ages, and also how the functional activity of the muscles differs from one side to the other has not been determined by any research

investigator. Any attempts to try and explain the findings in asymmetry on the basis of muscle physiology alone would be premature. There is no doubt that there are several other factors such as habit patterns, unilateral chewing, sleeping position, etc. which would contribute to these asymmetries.

The largest asymmetries were found to occur in the cranial region of the Trisomy 21 group, as shown in Table X and Figure 63.

III. DISTANCE BETWEEN THE ORBITS, THE PUPILS AND THE EYES

The findings of this study showed that the width, MoR-MoL, which measures the distance between the orbits was diminished in the Trisomy 21 individuals (Figure 25). These findings point to a definite hypotelorism of the bony orbits in the Trisomy 21 group. Gerald and Silverman (1965), who only measured the width between the orbits in 46 clinically diagnosed Down's syndrome individuals, came to the same conclusion.

A more accurate appreciation of hypotelorism of the orbits should be done by considering the inter-orbital width (MoR-MoL), in relation to the width of the face or cranium, as the latter measurements are also smaller in Trisomy 21 individuals. The hypotelorism of the bony orbits in relation to the width of the face was confirmed in Trisomy 21 individuals (Figure 62).

Conflicting reports occur in literature as regards the separation of the pupils in Down's syndrome. The findings of this study showed that the inter-pupillary width

in the Trisomy 21 group was smaller, not only by itself, but also in relation to the width of the face. Therefore, it can be said that the Trisomy 21 individuals show evidence of pupillary hypotelorism (Table XI). Kisling (1966) and Lowe (1949) also found the pupils closer together in adult Down's syndrome individuals but they did not compare their measurements to the width of the face or the cranium.

The findings of orbital hypotelorism, in association with pupillary hypotelorism are interesting, because it would be logical to think that if the orbits are closer together, then the eyeballs which are contained within the orbital cavities should also be closer together. The pupils are landmarks on the eyeballs and they do show evidence of pupillary hypotelorism.

Contrary to hypotelorism of the bony orbits and the pupils, the distance between the endocanthions (IER-IEL) in the Trisomy 21 group was larger than the Control group; not only by itself but also in relation to the width of the face (Table XI). Therefore, as mentioned in the results, the Trisomy 21 individuals are hyperteloric when one talks of the inter-endocanthal distance or the separation between the eyes. This is denoted as occular hypertelorism in this study.

The pupillary hypotelorism associated with the occular hypertelorism is interesting, as this may tend to explain the fact that the often quoted convergent strabismus seen in these individuals may be a subjective appearance,

as the Trisomy 21 individual's pupils are abnormally close together, but the endocanthions are further apart.

By the use of the Canthal index (Table XII), it was shown that in the Trisomy 21 sample, the ocular hypertelorism was greater in the younger age ranges. This is probably related to the presence of the epicanthic folds, which cover the medial corners of the eyes. These epicanthic folds are believed to disappear by about the first decade of life (Benda, 1969; Solomons et al., 1964; Eissler and Longenecker, 1962). After the age range of 6-8 years, the ocular hypertelorism was still found to be present in the Trisomy 21 individuals. This can probably be related to the findings of Frostad (1969), who showed that the nasal bones were angled more acutely to the S.N. plane in the Trisomy 21 group, and at the age range of 9-11 years, an increase in this angulation occurred, which would also help in the disappearance of the epicanthic folds. Frostad (1969) also showed that the nasal bones were not only smaller but also more acutely angled to the cranial base at all age ranges in the Trisomy 21 individuals. This acute angulation of the nasal bones would cause the persistence of the flat nasal bridge and contribute to the effect of occular hypertelorism in the Trisomy 21 individuals.

IV. PRESENCE OF PATENT METOPIC SUTURES

The metopic suture showed a general tendency to be patent in Trisomy 21 individuals. The metopic suture was

patent in 61.1% of the Trisomy 21 group and in 5.7% of the Controls (Table XIII). These findings are slightly higher than those reported by Roche (1961b). This suture was found to be patent even in the adult age range of 20-56 years (Figures 67, 68).

The possible explanation for the presence of a high incidence of patent metopic sutures in the Trisomy 21 individuals may be that the rate of growth of the bones that develop in membrane is slow in relation to the rate of the growth of the soft tissue contents, and growth activity is still taking place at the patent metopic suture.

Some support for the above explanation may lie in the findings of Ghiz (1968) and several other investigators, who have reported that there is a retardation of the growth centers of the craniofacial skeleton in the Trisomy 21 individuals. In addition, Frostad, Cleall, and Melosky (1971) reported that the bones of the cranial vault showed increased digital markings, while Roche (1960) reported the cranial bones to be thinner and also found a delayed closure of the anterior fontanelle in these individuals.

It is interesting to note that Bolk (1917) theorized, from a phylogenetic point of view, that metopism occurred in individuals with a more prominent forehead, a less pronounced development of the masticatory musculature, and a slightly retarded dentition. Bolk felt that this was related to the position of the temporal muscle and its functional activity in man. It is well known that the

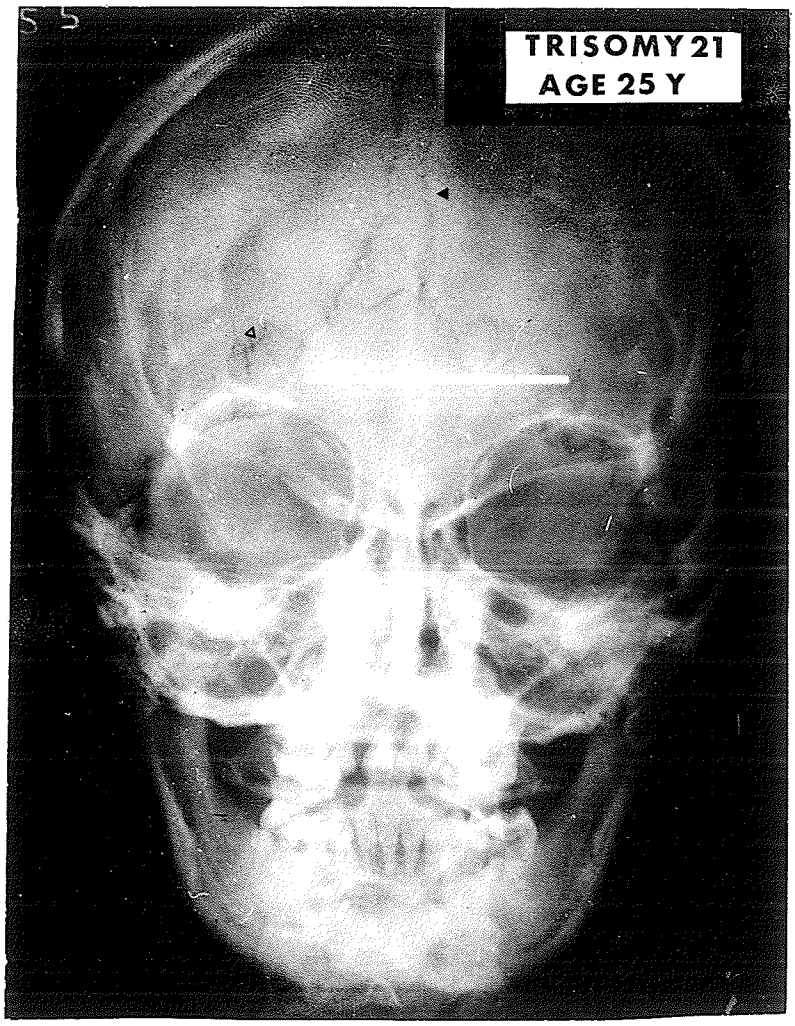


Figure 67. A P.A. radiograph of an adult Trisomy 21 individual showing a patent metopic suture and sutural bones.

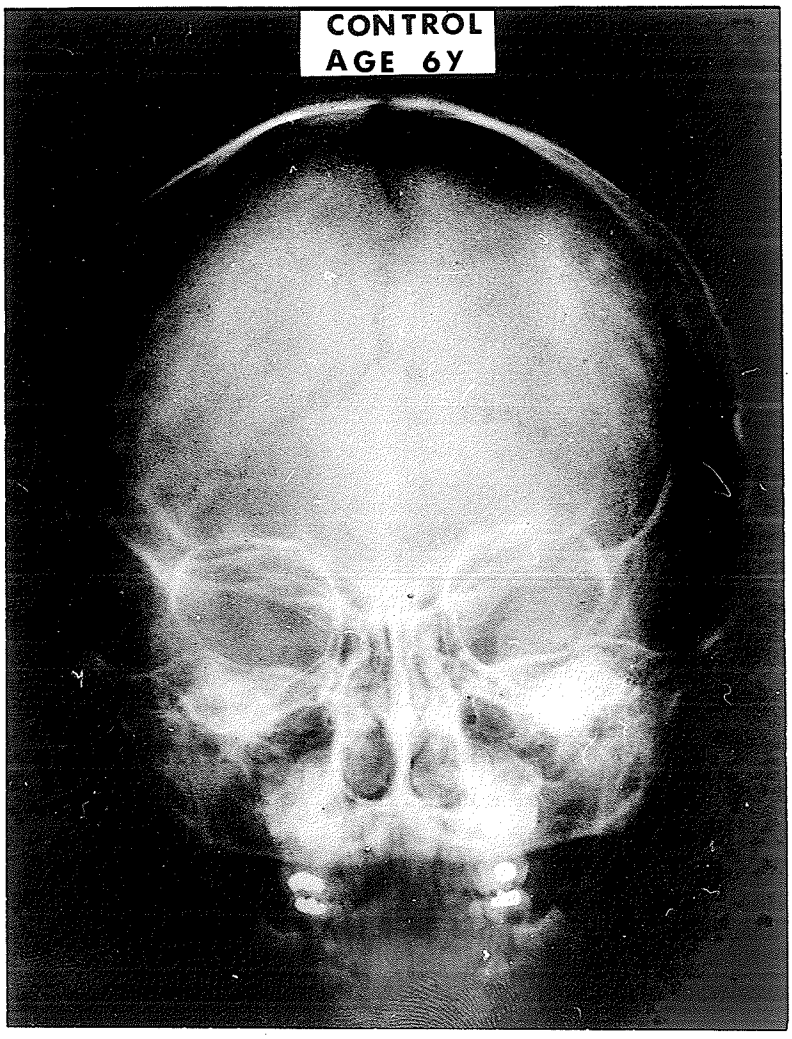


Figure 68. P.A. radiograph of a Control individual showing no patent metopic suture even at a young age and no wormian bones can be identified in the lambdoid suture.

dentition in Trisomy 21 individuals is retarded in its eruption and teeth are frequently found to be missing (Jensen, 1972). These individuals also show muscular hypotonia (Penrose and Smith, 1966; McIntire and Menolascino, 1965; Hall, 1966). Frostad (1969) has also shown that the glabella region was located higher in the Trisomy 21 group, giving a more rounded appearance to the forehead. All these three factors, according to Bolk would be most conducive for the metopic suture to persist.

V. PRESENCE OF SUTURAL BONES

The percentage of Trisomy 21 individuals showing the presence of sutural bones was found to be 62.3%, as opposed to 3.8% in the Control individuals (Table XIV). Most of these sutural bones were observed to occur in the lambdoid suture (Figures 67, 68).

The number of sutural bones that could be identified on the postero-anterior cephalometric radiograph exceeded five in number in some Trisomy 21 individuals. There was a large variation in the size of the sutural bones. No particular tendency for them to be occurring symmetrically was observed, as had been stated by Davies and Davies (1962), although the symmetrical occurrence of the sutural bones was seen in some cases.

Pritchard, Scott, and Girgis (1956) have noted the presence of large celled cartilage with a scanty matrix

interspersed with trabeculae of woven bone at or near sutural edges in the cranium. They state that Sisten (1933) believed that the presence of cartilage in the lambdoid sutures of infants may be associated with recumbency and the consequent shearing stresses between the bones in the cranial vault. Pritchard, Scott, and Girgis (1956) also state that it is well known that fibrous tissues may become cartilagenous when subject to such stresses.

In the Trisomy 21 individuals, there was a general tendency for the sutures to close late, although only the figures for the number of individuals showing patent metopic sutures have been reported in this study (Table XIII).

Benda (1941) and Roche (1961b) have also stated that the sutures close late in the Trisomy 21 individuals. Perhaps the high incidence of sutural bones found in the Trisomy 21 sample may be related to the possibility that shearing stresses could be acting on the fibrous connective tissues of the cranial sutures for a longer time, as these sutures remain open for a long time.

One cannot disregard the possibility that one of the effects of this abnormal genotype may be the formation of additional wormian bones. However, animal experiments designed to create tension in sutures would be able to give a possible answer as to why these sutural bones occur.

CHAPTER VI

SUMMARY AND CONCLUSIONS

The purpose of this cross sectional, cephalometric study, was to determine the phenotype and to evaluate the pattern of change in the width of the craniofacial complex of a group of individuals confirmed by cytogenetic analysis as having a Trisomy 21 karyotype.

The sample consisted of 127 Trisomy 21 individuals and 137 Control subjects, who ranged in age from three to fifty-six years and were divided according to sex and subgrouped into six age ranges. Linear horizontal and vertical projection distances were obtained from postero-anterior radiographs and direct measurements were made on the subject's face. The assessment of the significant differences between the Trisomy 21 group and the Control group were determined by obtaining ratios between the various measurements and by means of a factorial analysis of variance.

The findings of this study warrant the following conclusions:

1. Almost all the linear measurements of the Trisomy 21 group were significantly smaller than the Control group at all ages. Therefore, the overall size of the craniofacial complex of the Trisomy 21 group was smaller than that of the Control group. This smallness in size of

the craniofacial complex was evident at the age of three years and growth occurred after this age at a comparable rate and direction to that found in the Control group.

2. There were some areas in the craniofacial complex of the Trisomy 21 individuals that were more affected than others. The areas most affected in the Trisomy 21 group were the inter-orbital width, the nasal cavity height and the width of the maxilla. Growth retardation, as a result of interference with development and maturation in these areas, was present at the age range of 3-5 years and increases in these measurements occurred at a comparatively decreasing rate as compared to that seen in the Control group.
3. The females were smaller than the males in both the Trisomy 21 and Control groups. Differences were found between the sexes in the Trisomy 21 group; however, these differences also occurred in the Control group.
4. On the postero-anterior radiographs of the Trisomy 21 group, the most superior point on the orbital roof was located further laterally from the most medial point on the orbital outline within each orbit.
5. In the Trisomy 21 group, at the younger age ranges, the most superior points on the orbital

roofs were located laterally in relation with the most inferior points on the orbital outlines, giving a lateral slant to the orbits. However, as their ages advanced, the most superior points on the orbital outlines were located medial to the most inferior points on the orbital outlines, so that the orbits appeared to have a medial slant similar to that seen in the Control group at all age ranges. This change in the slant of the orbits of the Trisomy 21 group may be due to a diminished increase in the supraorbital width accompanied by the compensatory and normal changes occurring at the inferior and lateral orbital margins respectively.

6. In most areas of the craniofacial complex studied in both the Trisomy 21 and Control groups, asymmetries were evident. However, the asymmetries in the temporal region of the Trisomy 21 group were most prominent.
7. The incidence of patent metopic sutures was 61.1% and 5.7% in the Trisomy 21 and Control groups respectively. In the former group, patent metopic sutures often persisted in adulthood.
8. The percentage of Trisomy 21 individuals showing sutural bones in the cranial sutures was 62.2% as opposed to only 3.8% in the Control sample.
9. The Trisomy 21 group showed evidence of orbital

and pupillary hypotelorism when the distances between the bony orbits and the pupils respectively, were considered in relation with the width of the face. In contrast to the orbital and pupillary hypotelorism, the distance separating the endocanthions or the eyes was greater in the Trisomy 21 group not only by itself, but also in relation to the width of the face. These findings, therefore, gave the Trisomy 21 individuals a greater separation between the eyes or it may be said that the Trisomy 21 group showed evidence of occular hypotelorism as compared to the Control group.

BIBLIOGRAPHY

Adams, J.W. 1940. Correction of error in cephalometric roentgenograms. Angle Orthodont. 10:3-13.

Aita, J.A. 1969. Congenital facial anomalies with neurologic defects. A clinical atlas. Springfield, Illinois: Charles C. Thomas.

Allen, G., et al. 1961. Mongolism. Lancet, 1:775.

Arey, L.B. 1965. Developmental Anatomy. Philadelphia: W.B. Saunders Company.

Becker, G., and Chebib, F. 1969. Simplified computational programming for mixed analysis-of-variance designs with equal and unequal subclass numbers. Psychological Reports, 25:767-772.

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

Benda, C.E. 1941. Observation on the malformation of the head in mongoloid deficiency. J. Pediat. 19:800-816.

Benda, C.E. 1946. Mongolism and Cretinism. New York: Grune and Stratton.

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

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

Berg, J.M., Crome, L., and France, N.E. 1960. Congenital cardiac malformations in mongolism. Brit. Heart J. 22:331-346.

Bjork, A. 1955. The cranial base development. Amer. J. Orthodont. 41:198-225.

Bjork, A. 1964. Sutural growth of the upper face studied by the implant method. Europ. Orthodont. Soc. Trans. :49-65

Bolk, L. 1917. On metopism. Amer. J. Anat. 22:27-47.

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

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

Broadway, E.S., Healy, M.J.H., and Poyton, H.G. 1962. Accuracy of tracings from lateral skull radiographs. Brit. Soc. Study Orthodont. Trans. 9-12.

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

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

Caffey, J., and Ross, S. 1956. Mongolism (mongoloid deficiency) during early infancy - some newly recognized diagnostic changes in pelvic bones. Pediatrics, 17: 642-651.

Caffey, J., and Ross, S. 1958. Pelvic bones in infantile mongoloidism. Amer. J. Roentgenol. 80:458-467.

Campbell, J. 1950. The mylohyoid line in the assessment of facial asymmetry. D. Record, 70:204-208.

Chebib, F.S., and Burdick, J.H. 1973. Estimation of measurement error. J. Gen. Psychology, In Press.

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

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

Clemens, C. 1949. Mongolism and Cretinism. New York: Grune and Stratton.

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

Cohen, M.M., and Winer, R.A. 1965. Dental and facial characteristics in Down's syndrome. J. Dent. Res. Suppl. 44:197-208.

Colby, W.B., 1972. Cephalometric analysis of the Northern Foxe Basin Eskimo: a cross sectional study. Master's Thesis, University of Manitoba.

Cummins, H. 1936. Dermatoglyphic stigmata in mongoloid imbeciles. Anat. Rec. 64, Suppl. 1.

Cummins, H. 1939. Dermatoglyphic stigmata in mongoloid imbeciles. Anat. Rec. 73:407-415.

Davies, D.W., and Davies, F. 1962. Gray's Anatomy - Descriptive and Applied. Toronto: Longmans Green and Co. Ltd.

Dorland's Illustrated Medical Dictionary. 1965. Philadelphia: W.B. Saunders Company.

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

Downs, W.B. 1948. Variations in facial relationships, their significance in treatment and prognosis. Amer. J. Orthodont. 34:812-840.

Draper, G., Dupertuis, G.W., and Caughey, J.L. 1944. Human Constitution in Clinical Medicine. New York: Paul B. Hoeber.

Eissler, R., and Longenecker, L.P. 1962. The common eye findings in mongolism. Amer. J. Ophthal. 54:398-406.

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

Esen, F.M. 1957. Congenital heart malformations in mongolism with special reference to ostium atrioventriculare commune. Arch. Pediat. 74:243-277.

Fischer, B. 1954. Asymmetries of the dentofacial complex. Angle Orthodont. 24:179-192.

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

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

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

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

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

Gaard, R.A. 1961. Occular hypertelorism of Grieg: A congenital craniofacial deformity. Amer. J. Orthodont. 47:205-219.

Gerald, B.E., and Silverman, F.N. 1965. Normal and abnormal inter-orbital distances, with special reference to Mongolism. Amer. J. of Roentgenol. 95:154-161.

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

Gibson, D., and Pozsonyi, J. 1965. Morphological and behavioral consequences of chromosome subtype in Mongolism. Amer. J. Ment. Defic. 69:801-804.

Goldberg, S. 1929. Biometrics of identical twins from the dental viewpoint. J. Dent. Res. 9:363-409.

Gorlin, R.J. 1963. Chromosomal abnormalities and oral anomalies. J. Dent. Res. (Supplement, Part 1), 42: 1297-1306.

Gorlin, R.J., and Pindborg, J.J. 1964. Syndrome of the Head and Neck. New York: McGraw-Hill Book Co.

Gosman, S.D., and Vineland, N.J. 1951. Facial development in Mongolism. Amer. J. Orthodont. 37:332-349.

Grant, J.C.B., and Basmajian, J.V. 1965. Grant's Method of Anatomy - Dry regions, descriptive and deductive. 7th Ed. Baltimore: The Williams and Wilkins Co.

Greig, D.M. 1927. Skulls of Mongolian imbeciles. Edinb. Med. J. 34:253-274 and 321-339.

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

Hall, B. 1964. Mongolism in newborns. Acta Pediat. Suppl. 154:1-95.

Hall, B. 1966. Mongolism in newborns. Clin. Pediat. 5:4-12.

Hall, B. 1970. Somatic deviations in newborn and older mongoloid children. A follow up investigation. Acta Pediat. Scand. 59:199-204.

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

Harvold, E. 1954. Cleft lip and palate. Amer. J. Orthodont. 40:493-506.

Hatton, M.E., and Grainger, R.M. 1958. Reliability of measurements from cephalograms at the Burlington Research Center. J. Dent. Res. 37:853-859.

Higley, L.B. 1936. Head positioner for scientific radiographic and photographic purposes. Int. J. Orthodont. and O. Surg. 22:699-706.

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

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

Kanner, L. 1935. Child Psychiatry. Springfield: Charles C. Thomas.

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

Kerwood, L.A., Lang-Brown, H., and Penrose, L.S. 1954. The inter-pupillary distance in mentally defective patients. Hum. Biol. 26:313-323.

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

Korkhaus, G. 1957. Disturbance in development of the upper jaw and middle face. Amer. J. Orthodont. 43:848-868.

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

Last, R.J. 1966. Anatomy, Regional and Applied. 3rd Ed. London: J. and A. Churchill Ltd.

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

Lejeune, J. 1964. 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.

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

Lowe, R.F. 1949. The eyes in mongolism. Brit. J. Ophthal. 33:131-174.

Margolis, H.I. 1940. Standardization in x-ray cephalographics. Amer. J. Orthodont. and Oral Surg. 26:725-740.

Margolis, H.I. 1947. A basic facial pattern and its application to clinical orthodontics. Amer. J. Orthdont. and Oral Surg. 33:631-642.

Marshall, D. 1969. Interpretation of the postero-anterior skull radiograph - assembly of disarticulated bones. Dent. Radiography and Photography, 42:27-35.

McGonagle, R.R. 1960. An evaluation of the accuracy of cephalometric tracings. Angle Orthodont. 30:134-140.

McIntire, M.D., Menolascino, F.J., and Wiley, J. 1965. Mongolism - some clinical aspects. Amer. J. Ment. Defic. 69:794-804.

Meredith, H.V., and Higley, L.B. 1951. Relationships between dental arch widths and widths of the face and head. Amer. J. Orthodont. 37:193-204.

Meredith, H.V. 1954. Growth in bizygomatic face breadth during childhood. Growth, 18:111-134.

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

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

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

Mulick, J.F. 1965. An investigation of craniofacial asymmetry using the serial twin study method. Amer. J. Orthodont. 51:112-129.

Oster, J. 1951. Some problems concerning mongolism in the newborns. Acta Paediat. 40:338-348.

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

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

Paris Conference (1971). Standardization in Human Cytogenetics Birth Defects, Original Article Series. VII:1-44, 1972. The National Foundation, New York. In press.

Peck, H., and Peck, S. 1970. A concept of facial esthetics. Angle Orthodont. 40:284-317.

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

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

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

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

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

Roche, A.F. 1966. Cranium in mongolism. Acta Neurol. Scand. 42:62-78.

Roche, A.F., Seward, F.S., and Sunderland, S. 1961a. Growth changes in the mongoloid head. Acta Paediat. 50:133-140.

Roche, A.F., Seward, F.S., and Sunderland, S. 1961b. Non-metrical observations on cranial roentgenograms in mongolism. Amer. J. Roentgenol. 85:659-662.

Roche, A.F., and Sunderland, S. 1960. Postmortem observations on mongoloid crania. J. Neuropath. Exp. Neurol. 19:554-558.

Rowe, R.D., and Uchida, I.A. 1961. Cardiac malformation in mongolism. A prospective study of 184 mongoloid children. Amer. J. Med. 31:726-735.

Rowe, R.D. 1962. Cardiac malformations in mongolism. Amer. Heart J. 64:567-569.

Ryll, J.U. 1972. Bone alterations after unilateral masseterectomy or molar extractions. A quantitative microscopic assessment. Master's Thesis, University of Manitoba.

Salzmann, J.A. 1966. Practice of Orthodontics. Vol. 1, Philadelphia: J.B. Lippincott Co.

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

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

Sassouni, V., and Forrest, E.J. 1971. Orthodontics in Dental Practice. St. Louis: The C.V. Mosby Co.

Savara, B.S. 1965. A method for measuring facial bone growth in three dimensions. Human Biol. 37:245-255.

Scott, J.H. 1953a. The cartilage of the nasal septum. Brit. Dent. J. 95:37-43.

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

Scott, J.H. 1957. Growth in width of the facial skeleton. Amer. J. Orthodont. 43:366-371.

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

Scott, J.H. 1958. The cranial base. Amer. J. Orthodont. 16:319-348.

Scott J.H. 1959. Further studies on the growth of the human face. Proc. Roy. Soc. Med. 52:263-268.

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

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

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

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

Shuttleworth, G.E. 1909. Mongolian imbecility. Brit. Med. J. 2:661-665.

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

Sisten, A.E. 1933. Zur Entwicklung der Nahte des Schadeldaches. Z. ges. Anat., Z. Anat. Entw. Gesch. 101:121-152, as quoted in: Pritchard, J.J., Scott, J.H., and Girgis, F.G., 1956.

Snedecor, G.W. 1946. Statistical Methods. Ames: Iowa State College Press.

Solomons, G., Zellweger, H., Jahnke, P.G., and Opitz, E. 1965. Amer. J. Dis. Child. 110:46-50.

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

Spitzer, R., and Quilliam, R.L. 1958. Observations on congenital anomalies in teeth and skull in two groups of mental defectives. A comparative study. Brit. J. Radiol. 31:596-604.

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

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

Subtelney, J.D. 1955. Width of the nasopharynx and related anatomic structures in normal and unoperated cleft palate children. Amer. J. Orthodont. 41:889-909.

Symons, N.B.B. 1952. The development of the human mandibular joint. J. Anat. Lond. 86:326-332, as quoted in: Pritchard, J.J., Scott, J.H., and Girgis, F.G., 1956.

Thelander, H.E., and Pryor, H.B. 1966. Abnormal patterns of growth and development in mongolism. Clinical Pediat. 5:493-501.

Thompson, J.R. 1943. Asymmetry of the face. J. Amer. Dent. Assoc. 30:1859-1871.

Thurow, R.C. 1951. Cephalometric methods in research and private practice. Angle Orthodont. 21:104-116.

Tildesley, M.L. 1932. A critical analysis of investigations into facial growth changes. Int. J. Orthodont., Oral Surg., and Radiol. 18:1131-1169.

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

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

Warkany, J. 1960. Etiology of mongolism. J. Pediat. 56: 412-419.

Washburn, S.L. 1947. The relation of the temporal muscle to the form of the skull. Anat. Rec. 99:239-248.

Wei, S.H.Y. 1970. Craniofacial width dimensions. Angle Orthodont. 40:141-147.

Weingart, M.A. 1948. A simplified cephalometric head positioner. Amer. J. Orthodont. 34:362-366.

Wexler, M.R., and Sarnat, B.G. 1961. Rabbit snout growth. Arch. Otolaryng. 74:305-313.

Weygandt, W. 1927. Uber mongoloids degeneration. Med. Klin. 23:747-750, as quoted in: Kisling, E., 1966.

Wilson, S.A.K. 1940. Neurology. Vol. 2. London: Edward Arnold and Co.

Woods, G.A.,Jr. 1950. Changes in width dimensions between certain teeth and facial points during human growth. Amer. J. Orthodont. 36:676-700.

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

Wylie, W.L., and Elsasser, W.A. 1948. Undistorted vertical projection of the head from lateral and postero-anterior roentgenograms. Amer. J. Roentgenol. 60:414-417.

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

A P P E N D I X

TABLE XV

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE TeR-TeL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	143.03	2.68	134.69	3.10	145.56	1.90	141.30	2.03
6-8	140.59	3.10	140.53	2.68	145.17	1.90	145.60	1.62
9-11	143.84	1.90	146.03	2.19	152.49	1.70	146.48	1.62
12-15	149.08	1.20	143.74	1.55	154.84	1.34	151.38	1.43
16-19	153.91	1.30	149.72	1.55	155.79	1.70	152.53	1.70
20-56	150.25	1.23	146.39	1.23	159.51	1.49	154.00	1.34

TABLE XVI

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE MsR-MsL
(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	93.90	2.62	89.57	3.03	101.82	1.86	100.47	1.98
6-8	101.37	3.03	96.89	2.62	105.58	1.86	105.80	1.58
9-11	102.16	1.86	101.59	2.14	108.16	1.66	106.12	1.66
12-15	107.45	1.17	103.13	1.58	115.37	1.31	108.50	1.40
16-19	111.58	1.27	107.09	1.51	120.37	1.66	113.07	1.66
20-56	110.79	1.20	104.54	1.20	121.00	1.40	112.54	1.31

TABLE XVII

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE ZyR-ZyL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	108.86	2.57	99.08	2.96	109.62	1.81	107.35	1.94
6-8	111.35	2.96	110.74	2.57	115.66	1.81	116.54	1.55
9-11	117.03	1.81	117.11	2.09	124.86	1.62	121.56	1.55
12-15	126.38	1.18	120.75	1.48	132.03	1.28	127.61	1.37
16-19	133.05	1.24	122.40	1.48	136.94	1.62	130.95	1.62
20-56	130.86	1.18	123.14	1.18	142.12	1.37	132.87	1.28

TABLE XVIII

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE MxR-MxL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	50.87	1.81	46.28	2.09	54.80	1.28	54.44	1.37
6-8	50.34	2.09	52.47	1.81	58.16	1.28	59.40	1.09
9-11	52.31	1.28	50.28	1.48	62.58	1.14	60.84	1.09
12-15	54.52	0.83	50.88	1.04	63.93	0.90	61.38	0.97
16-19	55.01	0.88	49.68	1.04	65.59	1.14	62.15	1.14
20-56	52.06	0.83	47.86	0.83	65.69	0.97	59.53	0.90

TABLE XIX

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE N1R-N1L

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	22.54	1.31	22.76	1.51	25.09	0.87	24.78	0.99
6-8	23.65	1.51	23.95	1.31	26.59	0.93	27.61	0.79
9-11	24.88	0.93	24.85	1.07	30.08	0.83	29.06	0.79
12-15	28.35	0.60	27.30	0.76	31.85	0.66	32.55	0.70
16-19	30.21	0.64	28.13	0.76	34.16	0.83	33.64	0.83
20-56	31.10	0.62	29.56	0.60	34.70	0.70	33.00	0.66

TABLE XX

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE NbR-NbL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	11.47	1.71	9.69	1.98	12.35	1.14	12.83	1.29
6-8	13.96	1.98	13.01	1.71	13.91	1.29	13.10	1.03
9-11	12.64	1.21	11.92	1.40	15.37	1.08	14.28	1.08
12-15	14.54	0.79	16.82	0.99	15.88	0.86	17.63	0.92
16-19	14.77	0.83	14.90	1.03	18.32	1.08	20.26	1.08
20-56	15.68	0.81	14.68	0.79	17.78	0.92	17.53	0.86

TABLE XXI

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE NcR-NcL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	7.29	0.93	6.28	1.08	7.00	0.62	5.08	0.70
6-8	8.31	1.08	8.84	0.93	5.78	0.66	5.73	0.56
9-11	7.11	0.66	8.50	0.83	5.92	0.59	6.35	0.56
12-15	8.99	0.42	8.55	0.54	5.91	0.47	6.81	0.50
16-19	9.16	0.45	9.60	0.54	5.85	0.59	7.00	0.59
20-56	9.23	0.45	9.62	0.43	6.75	0.50	6.04	0.47

TABLE XXII

MEANS AND STANDARD ERRORS FOR THE VERTICAL PROJECTION DISTANCE Cg-ANS

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	32.80	1.82	31.82	2.10	36.11	1.21	35.19	1.37
6-8	31.29	2.10	33.09	1.82	39.48	1.28	39.69	1.10
9-11	37.33	1.28	33.80	1.48	42.18	1.15	43.50	1.10
12-15	39.49	0.83	37.18	1.05	47.72	0.91	45.28	0.97
16-19	44.01	0.88	37.49	1.05	51.63	1.15	48.38	1.15
20-56	41.86	0.86	40.46	0.83	54.80	0.97	50.10	0.91

TABLE XXIII

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE MoR-MoL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	13.68	1.13	13.05	1.31	16.29	0.75	17.09	0.86
6-8	16.15	1.31	16.38	1.13	17.83	0.80	18.96	0.68
9-11	14.50	0.80	15.29	1.01	20.47	0.72	20.73	0.68
12-15	17.69	0.51	17.37	0.65	22.85	0.57	21.01	0.61
16-19	18.87	0.55	17.29	0.65	22.26	0.75	22.13	0.72
20-56	18.00	0.52	16.70	0.52	22.66	0.61	23.42	0.57

TABLE XXIV

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE RoR-RoL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	59.81	2.63	57.41	3.03	55.80	1.75	53.62	1.99
6-8	63.81	3.03	63.13	2.63	57.44	1.86	58.76	1.58
9-11	59.88	1.86	65.86	2.15	60.74	1.66	60.39	1.58
12-15	64.30	1.17	64.55	1.52	65.07	1.31	61.67	1.40
16-19	64.92	1.27	63.01	1.52	67.63	1.66	64.59	1.66
20-56	63.21	1.21	63.35	1.21	67.04	1.40	64.75	1.31

TABLE XXV

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE MoR-RoR

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	24.18	1.39	22.77	1.60	21.16	0.93	18.09	1.05
6-8	24.17	1.60	24.23	1.39	20.60	0.98	20.63	0.84
9-11	22.80	0.98	25.66	1.24	20.71	0.88	20.37	0.84
12-15	23.14	0.62	23.94	0.80	21.77	0.69	20.53	0.74
16-19	23.27	0.67	23.12	0.80	23.29	0.93	21.86	0.88
20-56	22.98	0.64	23.50	0.64	23.15	0.74	20.62	0.69

TABLE XXVI

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE MoL-RoL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	21.95	1.37	21.59	1.58	18.53	0.91	18.44	1.03
6-8	23.48	1.58	22.52	1.37	19.01	0.97	19.16	0.83
9-11	22.58	0.97	24.53	1.22	19.56	0.87	19.29	0.83
12-15	23.47	0.61	23.23	0.79	20.45	0.68	20.14	0.73
16-19	22.78	0.66	22.60	0.79	22.02	0.87	20.60	0.87
20-56	22.24	0.63	23.16	0.63	21.23	0.73	20.71	0.68

TABLE XXVII

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE IoR-IoL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	56.92	1.97	48.67	2.28	60.58	1.40	60.12	1.49
6-8	61.40	2.28	61.45	1.97	61.95	1.40	63.37	1.19
9-11	59.86	1.40	61.01	2.28	66.19	1.32	65.93	1.19
12-15	65.47	0.88	63.07	1.14	72.55	0.99	66.94	1.09
16-19	68.05	0.96	64.40	1.19	71.18	1.25	68.36	1.32
20-56	67.69	0.93	63.96	0.93	70.64	1.05	70.42	0.99

TABLE XXVIII

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE FzR-FzL (in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	81.36	1.79	76.54	2.07	84.51	1.27	82.94	1.35
6-8	84.03	2.07	85.61	2.07	88.23	1.27	88.13	1.08
9-11	83.65	1.27	84.11	2.07	90.81	1.13	90.71	1.13
12-15	90.51	0.82	87.90	1.03	96.38	0.89	93.05	0.99
16-19	93.70	0.87	88.77	1.08	98.12	1.13	95.51	1.13
20-56	92.52	0.84	88.75	0.82	99.15	0.99	96.07	0.89

TABLE XXIX

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE LoR-LoL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	84.90	1.91	78.44	2.21	86.78	1.28	84.43	1.45
6-8	89.07	2.21	88.06	1.91	90.48	1.35	89.21	1.21
9-11	86.62	1.35	86.70	1.91	93.03	1.21	92.37	1.21
12-15	93.16	0.88	90.48	1.10	97.50	0.96	95.32	1.02
16-19	95.57	0.93	90.02	1.10	100.11	1.21	97.44	1.28
20-56	93.66	0.88	90.58	0.88	100.16	1.02	96.34	0.96

TABLE XXX

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE MoR-LoR

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	35.63	0.96	32.86	1.11	35.34	0.64	33.90	0.72
6-8	34.00	1.92	36.45	0.96	36.33	0.58	35.19	0.58
9-11	35.77	0.68	36.57	0.96	36.47	0.61	36.03	0.61
12-15	37.83	0.44	36.99	0.55	37.30	0.48	37.11	0.51
16-19	38.40	0.47	36.09	0.55	38.76	0.64	37.90	0.64
20-56	37.88	0.44	36.56	0.44	38.83	0.51	36.40	0.48

TABLE XXXI

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE MoL-LoL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	35.59	0.90	32.54	1.04	35.16	0.60	33.44	0.68
6-8	36.49	1.04	35.23	0.90	36.35	0.64	35.08	0.57
9-11	36.36	0.64	35.02	0.90	36.09	0.57	35.65	0.57
12-15	37.80	0.41	36.11	0.52	37.35	0.45	37.20	0.48
16-19	38.30	0.44	36.64	0.52	39.12	0.57	37.74	0.60
20-56	37.78	0.41	37.33	0.41	38.68	0.48	36.51	0.45

TABLE XXXII

MEANS AND STANDARD ERRORS FOR THE VERTICAL PROJECTION DISTANCE RoR-IoR

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	39.78	1.30	38.84	1.50	39.77	0.92	39.85	0.98
6-8	38.71	1.50	39.51	1.30	41.57	0.92	41.75	0.78
9-11	39.79	0.92	38.65	1.50	41.72	0.86	40.47	0.78
12-15	42.29	0.58	42.77	0.75	43.90	0.65	42.38	0.72
16-19	43.82	0.63	41.23	0.78	43.66	0.82	42.48	0.86
20-56	42.56	0.61	42.47	0.61	44.94	0.69	42.85	0.65

TABLE XXXIII

MEANS AND STANDARD ERRORS FOR THE VERTICAL PROJECTION DISTANCE RoL-IoL

(in millimeter)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	38.32	1.21	38.42	1.40	39.40	0.86	39.89	0.92
6-8	39.47	1.40	39.26	1.21	40.88	0.86	40.51	0.73
9-11	40.29	0.86	38.55	1.40	41.38	0.77	39.67	0.73
12-15	42.35	0.54	42.16	0.70	43.38	0.61	42.39	0.67
16-19	43.90	0.59	40.59	0.73	43.44	0.77	42.07	0.81
20-56	42.45	0.57	42.08	0.57	44.23	0.65	42.70	0.61

TABLE XXXIV

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE CdR-CdL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	99.81	2.71	92.99	3.13	100.33	1.92	99.77	2.05
6-8	104.21	3.13	102.54	2.71	105.89	1.92	106.57	1.64
9-11	108.82	1.92	108.88	2.22	115.87	1.72	110.58	1.64
12-15	115.75	1.25	110.43	1.57	121.40	1.35	116.47	1.14
16-19	121.49	1.32	111.35	1.57	123.50	1.72	121.82	1.72
20-56	121.12	1.25	113.98	1.25	131.73	1.45	122.00	1.36

TABLE XXXV

MEANS AND STANDARD ERRORS FOR THE HORIZONTAL PROJECTION DISTANCE GoR-GoL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	71.36	2.66	73.18	3.08	78.47	1.88	78.88	2.01
6-8	79.36	3.08	78.71	2.66	86.10	1.88	85.25	1.61
9-11	82.74	1.88	82.56	2.18	91.83	1.69	90.33	1.61
12-15	91.92	1.19	87.53	1.54	99.32	1.33	94.45	1.42
16-19	94.99	1.29	87.41	1.54	106.27	1.69	100.33	1.69
20-56	95.26	1.22	89.40	1.22	107.33	1.42	100.06	1.33

TABLE XXXVI

STANDARD DEVIATION OF THE MEASUREMENT ERROR AND THE MAXIMUM ERROR ASSOCIATED WITH 95 PER CENT AND 99 PER CENT OF EACH OF THE VARIABLES USED IN THE SKELETAL ANALYSIS

Variable	Standard Deviation of Measurement Error	95 per cent	99 per cent
TeR-TeL	0.282	0.558	0.802
MsR-MsL	0.538	1.122	1.530
ZyR-ZyL	0.648	1.351	1.843
MxR-MxL	0.905	1.887	2.574
NlR-NlL	0.282	0.588	0.802
NbR-NbL	1.288	2.687	3.664
NcR-NcL	0.509	1.061	1.448
Cg-ANS	0.479	0.999	1.362
MoR-MoL	0.321	0.613	1.100
RoR-RoL	0.200	0.417	0.569
MoR-RoR	0.347	0.780	1.640
MoL-RoL	0.331	0.690	0.941
IoR-IoL	0.624	1.301	1.775
FzR-FzL	0.509	1.061	1.448
LoR-LoL	1.063	2.217	3.024
MoR-LoR	0.748	1.560	2.128
MoL-LoL	0.806	1.681	2.293
RoR-IoR	0.734	1.531	2.088
RoL-IoL	0.905	1.887	2.574
CdR-CdL	1.090	2.273	3.101
GoR-GoL	0.331	0.690	0.941

TABLE XXXVII

MEANS AND STANDARD ERRORS FOR THE SOFT TISSUE INTER-ENDOCANTHAL DISTANCE IER-IEL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	30.45	1.61	29.47	1.86	27.83	1.08	28.31	1.14
6-8	31.43	1.68	35.72	1.61	29.69	1.14	28.72	0.97
9-11	31.19	1.22	30.40	1.32	30.61	1.02	29.61	1.08
12-15	33.07	0.81	30.78	0.93	31.81	0.90	30.51	0.86
16-19	34.29	0.81	31.36	1.02	30.90	1.14	31.47	1.02
20-56	30.59	0.78	30.63	0.76	31.16	1.22	29.10	1.32

TABLE XXXVIII

MEANS AND STANDARD ERRORS FOR THE SOFT TISSUE INTER-PUPILLARY DISTANCE PR-PL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	42.13	2.24	44.30	2.58	50.33	1.49	48.88	1.58
6-8	49.57	2.58	44.55	2.24	50.87	1.58	50.82	1.35
9-11	47.59	1.69	48.45	1.83	53.93	1.41	54.06	1.49
12-15	56.05	1.12	51.69	1.29	57.19	1.24	55.36	1.20
16-19	57.21	1.12	52.15	1.41	60.22	1.58	59.55	1.41
20-56	53.79	1.16	53.06	1.05	59.71	1.69	59.40	1.83

TABLE XXXIX

MEANS AND STANDARD ERRORS FOR THE SOFT TISSUE INTER-ECTOCANTHAL DISTANCE OER-OEL

(in millimeters)

Age Range	TRISOMY 21				CONTROL			
	Male		Female		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
3-5	74.75	2.39	75.63	2.75	77.83	1.59	75.94	1.69
6-8	79.67	2.75	80.25	2.39	80.38	1.69	79.68	1.44
9-11	79.26	1.80	79.35	1.95	83.15	1.51	83.94	1.59
12-15	85.88	1.23	82.73	1.38	86.96	1.32	85.60	1.28
16-19	86.17	1.19	83.79	1.51	91.06	1.69	87.97	1.51
20-56	87.61	1.16	84.66	1.12	90.80	1.80	86.42	1.95

TABLE XL

MEANS AND STANDARD ERRORS FOR THE LINEAR MEASUREMENTS TeR AND TeL TO X-Cg FOR THE ASSESSMENT OF ASYMMETRY IN THE TEMPORAL REGION

(in millimeters)

		TRISOMY 21			CONTROL		
Age Range	Sex	Right Mean	Left Mean	SE	Right Mean	Left Mean	SE
3-5	Male	67.47	75.56	2.12	69.83	75.73	1.50
	Female	68.71	75.98	2.45	70.32	70.98	1.60
6-8	Male	70.06	70.53	2.45	71.90	73.27	1.50
	Female	68.68	71.85	2.12	71.69	73.91	1.28
9-11	Male	70.74	73.10	1.50	75.87	76.62	1.34
	Female	72.90	73.13	1.73	73.01	73.46	1.28
12-15	Male	74.28	74.80	0.95	77.49	77.34	1.06
	Female	71.57	72.17	1.22	74.77	76.61	1.13
16-19	Male	75.40	78.51	1.03	78.06	77.73	1.34
	Female	73.60	76.12	1.22	78.43	74.10	1.34
Adult	Male	75.21	76.84	0.97	79.65	79.86	1.17
	Female	71.78	74.61	0.97	76.89	77.12	1.06

TABLE XLI

MEANS AND STANDARD ERRORS FOR THE LINEAR MEASUREMENTS MsR AND MsL TO X-Cg FOR THE ASSESSMENT OF ASYMMETRY AT THE LEVEL OF THE MASTOID PROCESSES

(in millimeters)

		TRISOMY 21			CONTROL		
Age Range	Sex	Right Mean	Left Mean	SE	Right Mean	Left Mean	SE
3-5	Male	41.14	52.75	2.05	48.22	53.60	1.45
	Female	37.00	52.57	0.23	49.28	51.19	1.55
6-8	Male	50.11	51.26	2.37	50.47	55.11	1.45
	Female	49.12	47.76	2.05	52.08	53.72	1.24
9-11	Male	48.81	53.35	1.45	53.63	54.53	1.30
	Female	50.83	50.76	1.68	51.80	54.32	1.30
12-15	Male	53.36	54.09	0.92	57.58	57.79	1.03
	Female	51.19	51.94	1.24	53.36	55.13	1.10
16-19	Male	54.23	57.36	1.00	60.16	60.21	1.30
	Female	51.63	55.46	1.18	58.39	54.68	1.30
Adult	Male	54.43	56.36	0.94	59.70	61.30	1.10
	Female	49.51	55.03	0.94	55.84	56.71	1.03

TABLE XLII

MEANS AND STANDARD ERRORS FOR THE LINEAR MEASUREMENTS ZyR AND ZyL TO X-Cg FOR THE ASSESSMENT OF ASYMMETRY IN THE REGION OF THE ZYGOMATIC ARCHES

(in millimeters)

		TRISOMY 21			CONTROL		
Age Range	Sex	Right Mean	Left Mean	SE	Right Mean	Left Mean	SE
3-5	Male	51.50	57.35	1.27	53.80	55.82	0.90
	Female	46.18	52.90	1.46	53.57	53.78	0.96
6-8	Male	55.48	55.87	1.46	57.16	55.82	0.90
	Female	55.63	55.11	1.27	57.89	58.65	0.76
9-11	Male	47.01	60.02	0.90	62.32	62.54	0.80
	Female	58.60	58.51	1.03	60.09	61.47	0.76
12-15	Male	62.86	63.51	0.58	66.41	65.61	0.63
	Female	60.39	60.36	0.73	63.25	64.36	0.68
16-19	Male	65.94	67.11	0.61	68.37	68.57	0.80
	Female	60.70	61.70	0.73	66.93	64.02	0.80
Adult	Male	65.12	65.74	0.58	71.19	70.93	0.68
	Female	60.21	62.93	0.58	66.17	66.69	0.63

TABLE XLIII

MEANS AND STANDARD ERRORS FOR THE LINEAR MEASUREMENTS CdR AND CdL TO X-Cg FOR THE ASSESSMENT OF ASYMMETRY IN THE REGION OF THE MANDIBULAR CONDYLES

(in millimeters)

		TRISOMY 21			CONTROL		
Age Range	Sex	Right Mean	Left Mean	SE	Right Mean	Left Mean	SE
3-5	Male	47.02	52.79	1.52	48.26	52.07	1.07
	Female	42.40	50.59	1.79	49.93	49.83	1.15
6-8	Male	52.32	51.89	1.75	52.11	53.78	1.07
	Female	51.33	51.21	1.52	52.77	53.80	0.91
9-11	Male	53.08	55.74	1.07	57.36	58.51	0.96
	Female	54.60	54.28	1.24	54.49	56.08	0.91
12-15	Male	57.45	58.31	0.70	61.24	60.16	0.76
	Female	54.87	55.57	0.88	57.47	59.00	0.81
16-19	Male	59.95	61.54	0.74	61.54	61.96	0.96
	Female	54.86	56.48	0.88	62.85	58.97	0.96
Adult	Male	60.18	60.94	0.70	65.69	66.03	0.81
	Female	55.21	58.78	0.70	60.76	61.24	0.76

TABLE XLIV

MEANS AND STANDARD ERRORS FOR THE LINEAR MEASUREMENTS GoR AND GoL TO X-Cg FOR THE ASSESSMENT OF ASYMMETRY IN THE GONIAL REGION OF THE MANDIBLE

(in millimeters)

		TRISOMY 21			CONTROL		
Age Range	Sex	Right Mean	Left Mean	SE	Right Mean	Left Mean	SE
3-5	Male	32.18	39.17	1.83	37.36	41.09	1.30
	Female	32.96	40.22	2.12	38.99	39.90	1.39
6-8	Male	40.19	39.17	2.12	41.06	45.05	1.30
	Female	40.21	38.50	1.83	41.71	43.54	1.11
9-11	Male	40.66	42.09	1.30	45.89	45.93	1.66
	Female	40.75	41.82	1.50	44.04	46.29	1.11
12-15	Male	46.23	45.69	0.82	49.98	49.34	0.92
	Female	43.59	43.94	1.06	46.74	47.71	0.98
16-19	Male	46.92	48.06	0.89	52.99	45.28	1.11
	Female	43.76	43.65	1.06	52.12	48.21	1.16
Adult	Male	47.55	47.71	0.84	52.94	54.39	0.98
	Female	43.20	46.21	0.84	49.71	50.35	0.92

GLOSSARY

I. LANDMARKS ON POSTERO-ANTERIOR CEPHALOGRAM

The cephalometric landmarks used in this study are alphabetically listed and defined below. The numbers following the abbreviation of a landmark denotes the order in which the landmark was digitized. In the text the letters "R" and "L" following the abbreviation signify "right" and "left" respectively, whenever bilateral structures were used.

Anterior Nasal Spine (ANS) (12)

The most inferior and central point of the nasal septum on the palatal shelf.

Condylion (Cd) (3 and 25)

The most lateral point on the head of the mandibular condyle.

Fronto-Zygomatic Suture (Fz) (17 and 22)

The most medial point of the fronto-zygomatic suture as seen on the orbital margin.

Gonion (Go) (8 and 27)

The lowest, posterior and most outward point of the angle of the mandible (Salzman).

Inferior Orbital Margin (Io) (45 and 37)

The most inferior point on the bony outline of the orbit.

Lateral Orbital Margin (Lo) (46 and 36)

The outermost point on the concavity of the bony lateral outline of the orbit.

Latero-Nasale (Nl) (14 and 32)

The most lateral point on the contour of the lateral nasal wall.

Mandibular Alveolar Crest (La) (10)

The most superior midpoint on the alveolar crest between the mandibular right and left central incisors.

Mandibular First Permanent Molar (Lm) (7 and 28)

The most lateral point on the buccal contour of the crown of the mandibular first permanent molar.

Mastoidale (Ms) (4 and 26)

Lowest point on the contour of the mastoid process (Sassouni).

Maxillare (Mx) (5 and 30)

Uppermost point on the maximum concavity of the lateral contour of the maxilla. Corresponds closely to the key ridge (Sassouni).

Maxillary Alveolar Crest (Ua) (11)

The most inferior midpoint on the alveolar crest between the maxillary right and left central incisors.

Maxillary First Permanent Molar (Um) (6 and 29)

The most lateral point on the buccal contour of the crown of the maxillary first permanent molar.

Medial Orbital Margin (Mo) (47 and 39)

The most medial point on the bony outline of the orbit.

Menton (Me) (9)

The lowermost point of the contour of the chin (Sassouni).

Nasal Base (Nb) (13 and 31)

The most inferior and lateral point on the floor of the nasal cavity.

Nasal Concha (Nc) (40 and 43)

Most medial point on the contour of the inferior nasal concha.

Root of Crista galli (Cg) (20)

The midpoint of the root of crista galli where it joins the cribriform plate of the ethmoid bone.

Superior Cranial Vault (Cv) (35)

The most superior point on the outline of the cranial vault.

Superior Orbital Margin (Ro) (18 and 21)

The most superior point on the bony outline of the orbital roof (Sassouni).

Temporal Bone (Te) (1 and 23)

The most lateral point on the outline of the cranial vault usually located on the temporal bone.

X Point (X) (19)

A geometrically constructed point located at the intersection of the supraorbital plane and a perpendicular line erected to this plane and passing through the midpoint of the root of Crista galli (Colby).

Zygomatic Process (Zy) (2 and 24)

The most lateral point on the bony outline of the zygomatic arch (Sassouni).

II. LINE AND PLANE CONSTRUCTED ON POSTERO-ANTERIOR RADIOGRAPH

Midline (X-Cg) (19 and 20)

A line constructed by erecting a perpendicular to the supraorbital plane which passes through the center of the base of Crista galli (Colby).

Supraorbital Plane (RoR-RoL) (18-21)

A line passing through the most superior points on the orbital outlines as viewed on a postero-anterior radiograph.

III. SOFT TISSUE LANDMARKS

Pupil (P)

The center of the pupil as seen in the position of distant vision.

Ectocanthion (OE)

The most lateral point on the palpebral fissures where the upper and lower eyelids meet when the eyes are open (Kisling).

Endocanthion (IE)

The most medial points on the palpebral fissure taken when the eyes open (Kisling).