A Radiographic Appraisal of the Effects of X-Radiation on the Mandibular Cartilage and Cranio-Facial Growth of the Rat

Jerome John Kozakiewicz
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A RADIOGRAPHIC APPRAISAL OF THE EFFECTS OF X-RADIATION ON THE MANDIBULAR CARTILAGE AND CRANIO-FACIAL GROWTH OF THE RAT

by

Jerome John Kozakiewicz

A Thesis Submitted to the Faculty of the Graduate School of Loyola University in Partial Fulfillment of the Requirements for the Degree of Master of Science

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LIFE

Jerome John Kozakiewicz was born in Chicago, Illinois, December 5, 1931.

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CHAPTER I
INTRODUCTION

The recognition and diagnosis of mandibular prognathism, or overgrowth of the lower jaw, has been greatly simplified with modern radiography. Unfortunately, advances in the treatment of this condition have not kept pace with advances in its diagnosis, and at present, treatment is symptomatic rather than preventive. It is with prevention or early interception of mandibular prognathism in mind that this research was begun.

Mandibular prognathism as a result of systemic pathology, as seen in acromegaly and leontiasis ossea, is not the concern of this study as its treatment lies in the correction of the causative pathology. This investigation deals with mandibular prognathism resulting as a genetically transmitted characteristic. This form of macrognathia exists as a local overgrowth of the mandible. The other portions of the skeleton are unaffected.

Though totally compatible with life in its untreated form, mandibular prognathism and its sequelae of malocclusion of the teeth and unpleasant facial esthetics require early correction
if the condition is to be eliminated in the adult. Since mandibular prognathism is the effect of a disproportionate overgrowth of the mandible locally, it seems logical that treatment of the condition would also be local, that is, restricted to influencing the growth of the mandibular growth center.

At present, for want of better methods, two treatment plans are being used in an effort to correct mandibular prognathism. The first method, supposedly preventative or interceptive, utilizes a "chin-strap" which cups the chin and extends over the occiput and applies pressure to the chin in an effort to "hold-up" or inhibit growth of the mandible in a forward direction. This method is completely ineffectual. The second method is the surgical reduction of the prognathic mandible by osteotomy or ostectomy. Although this method is effective in establishing more pleasant facial esthetics, it also has its disadvantages. Loss of teeth in ostectomy, scarring, paresthesia, and resulting malocclusion of the teeth are but a few of the disadvantages. A major disadvantage is that surgical correction cannot be undertaken until growth of the mandible approaches completion. Earlier surgical inter-
vention is likely to fail because of the unpredictability of the amount of growth which is yet to take place. The psychological trauma resulting from unpleasant facial esthetics cannot be eliminated until mandibular growth approaches completion. Treatment is far from ideal if one must live the first two decades of one's life with the condition before correction can be undertaken.

The orthodontist, in his treatment of mandibular prognathism, is limited to the establishment of a more acceptable occlusion of the teeth and slight modification of the facial profile. His efforts, however valiant, remain unrewarded.

It is possible that prevention or interception of condylar overgrowth could be effected by inhibiting mandibular growth during its active growth period by therapeutic application of x-radiation to the condylar growth centers. By temporarily inhibiting growth of the already oversize mandible in the growing child, the attainment of a normally proportioned adult mandible lies within the realm of clinical possibility. If true, treatment could be undertaken soon after diagnosis, early in the life of the patient, simply and effectively.
STATEMENT OF THE PROBLEM

This study endeavors to investigate the feasibility of utilizing x-radiation for the interception of mandibular prognathism by determining the effects of x-radiation on the condylar growth centers and on cranio-facial growth.
CHAPTER II
REVIEW OF THE LITERATURE

Abnormalities in the growth of the cranium caused by large doses of radiation must be compared with a normal growing cranium if these changes are to be studied and appreciated. It is for this reason that the literature pertaining to the normal growth of the rat cranium will be reviewed first.

Direct measurement of sacrificed specimens of various ages is one method of obtaining information on the growth of the skull. Hatai (1907) used this method to measure the length and width of the cranial vault of the male and female albino rat. He found the male to be larger in all boney dimensions measured and the greatest difference was in the length of the nasal bone. In his study of the growth of the cranial vault of the rat, Massler (1941) substantiated the findings of Hatai. He states that the "female skull grows at a lesser rate than the male at the various suture sites, giving the female skull the appearance of a less mature male skull." Maximal cranial width is attained by the twentieth day and the length of the cranial vault is complete at forty days. The snout of the rat was found to continue in length to three-hundred days and possibly
Masler concludes that growth of the cranial vault occurs primarily by the rapid apposition of bone at the approximating margins of the bones which comprise the various cranial sutures. Weinman and Sicher (1947) agree that cranial growth is accomplished by the appositional growth of bone in the connective tissue of these sutures.

While there is agreement as to the method of growth occurring in the cranium, there remains some disagreement as to when growth of the neurocranium is completed in the albino rat. According to Massler (1941), growth in width of the neurocranium is complete after twenty days, but Jarabak (1941) found that there was a continuous slow linear increase in the width of the neurocranium throughout life. This growth of the cranium was found to continue at a slower rate after one-hundred and fifty days. Jarabak's findings are consistent with those of Donaldson (1924) who observed that the brain of the rat continues to grow in size throughout life, but it grows at a much diminished rate as the rat increases in age. It can be seen that growth changes in the brain can be adequately accommodated by increase in width of the brain case.

The time at which growth in height of the neurocranium is
completed differs greatly as reported by several investigators. Massler (1941) reports that cranial height is complete at about twenty days, Spence (1940) reports completion at seventy days of age, and Jarabak (1941) concludes that growth in height of the anterior portion of the neurocranium is completed by the eightieth day. The disagreement of the investigators as to the exact time of cessation of growth in height of the neurocranium may be due in part to the different methods employed to measure the growth. Although Jarabak found that growth ceased in the vertical plane in the anterior portion of the neurocranium before eighty days, he also found that growth in height of the neurocranium in the region of the occipital bone continued to three-hundred and fifty days. His investigation showed that as cranial length increased, so also did the height in the occipital region. This increase in height in the occipital region of the neurocranium appears to be correlated to the demands placed on the occipital bone by the postcervical musculature and by the growth of the cranium. This continued growth of the occipital bone in a vertical plane is the effect of maturation of the animal--; the change from the greater convexity of the cranium of the young animal to the more angular morphology of the adult.
Rushton (1944) in his study of the growth of the condyle in man stated:

"The condyle is derived from a carrot-shaped wedge of cartilage stemming from the root of the coronoid process. The cartilage wedge is in reality a wedge of bone which has been formed with an intermediate chondroblast stage in contradistinction to the simple fibroblast bone differentiation of the rest of the mandible."

It is proliferation of the cartilage which forms the "main line of growth." According to Rushton, this proliferation causes the mandible to grow downward and forward and its condyles outward. Rushton believes that the growth center is primarily the layer of pre-cartilagenous connective tissue cells beneath the surface fibrous layer. So long as this layer produces new cartilage cells the growth at this center continues. Rushton (1944), Sicher (1945), Weinmann (1944), Brodie (1941), Diamond (1944), Levy (1948), Charles (1925) and Collins, Becks, Simpson and Evans (1946) all agree that it is the formation of cartilage which is the means of growth of the condyle. Its subsequent conversion into bone is merely an incident which effects the mechanical properties and not its size. Brodie (1941) states:

"The condylar growth center is the last center in the head to cease activity, and its growth is not unlike the growth of long bones in potential and mechanism of growth."

That the condylar growth center is the last center to cease activity is in agreement with the findings of the above men-
tioned investigators. They do not agree that the mechanism of growth and the growth potential of the long bones and the condyle are similar.

Collins, Becks, Simpson and Evans (1946) described the growth and transformation of the condylar cartilage in the normal rat and found that the method of growth was identical to that of man. They conclude that since there is persistence of the embryonic cartilage cells in the condyle, there remains the possibility of reactivation of growth and remodeling of the ramus of the mandible throughout the life of the rat.

Levy (1948) investigated the growth of the mandibular condyle of normal mice. His findings, with one exception, are in perfect agreement with those of Collins, Becks, Simpson and Evans (1946). The exception is that Levy could not establish the presence of cartilagenous tissue beneath the fibrous tissue at the cranial (or temporal) portion of the joint. Levy concludes that the only differences that exist in the growth of the condyle and mandibular joint of the rat and mouse are differences in size and chronology of changes due to species.

It is evident from the investigations on the condylar growth center that, as Krogman pointed out in 1930, the growth
process is the same in man and animal. The difference is in degree rather than kind.
Factors Influencing Normal Growth

The factors which influence the growth of tissues and organs has long been the object of investigation. The literature is voluminous with the effects of these factors on the pre and postnatal skeleton. The literature pertaining to factors influencing the growth of the cranio-facial complex will now be reviewed.

The ability of nutritional deficiencies to produce alterations of normal cranio-facial growth has been reported in many investigations. Weinmann (1946) in his study of rachitic white rats found that the cartilage of the condyle showed a characteristic disfiguration. The normal crescent-shaped cartilage had grown to a thick plate, many times its normal thickness. The normal constriction where the head meets the neck was absent and gave the condyle a club-like appearance. Proliferation of cartilage cells continued to increase the mass of the cartilage, but due to lack of ossification, could not be resorbed and replaced by bone. Increase in osteoid tissue adjacent to the uncalcified cartilage was also due to the inability of this tissue to normally calcify. The findings in the cartilage of the mandibular condyle were, in principle,
identical with those of the rachitic epiphyseal or articular cartilage. Warkany and Nelson (1941) report that the offspring of rats that were fed a rachitic diet during pregnancy where born with receding mandibles and shortened extremities of the skeleton.

The effects of pantothenic acid and pyridoxine deficiencies were investigated by Levy (1949). In mice that were fed a pyridoxine deficient diet, growth of the condylar cartilage and formation of bone was inhibited and finally ceased activity after four weeks. Pantothenic acid deficiency in mice inhibited the proliferation of cells in the condylar cartilage and slowed the ossification of all the long bones of the skeleton. The width of the condylar cartilage was reduced, and there was a decrease in the number of cells in the hypertrophic zone of the cartilage. The chondrocytes were abnormally small in all cases of pantothenic acid deficiency. The development of the cartilage was finally suspended and ossification ceased. Levy found that maxillary growth was not retarded as much as was mandibular growth by this deficiency. Malrelation of the jaws was evident.

Nutritional deficiencies have been studied by several
investigators seeking the etiology of cleft palate. Bauer (1949) reported that twenty-two percent of the offspring of rats kept on a riboflavin deficient diet during pregnancy were born with cleft palate and greatly shortened mandibles. Cleft palate, along with harelip and macroglossia, was reported by Warkany, Nelson and Schraffenberger (1943) as the result of Pantothenic acid deficient diet in the pregnant rat. Asling (1961) reports that cleft palate can be the result of pteroylglutamic acid deficiency in the mother. Seven-hundred cleft-palate fetuses were studied and none presented a normal mandible.

The endocrine system has long been known to influence the growth of the skeleton. Lorain-Levi described a hypopituitary infantilism syndrome in 1871. Mortimer (1937) studied the cranial growth of hypophysectomized rats by a roentgenographic method. He found that the greatest disturbance in growth of the cranium was in the anteroposterior direction, while cranial height and width showed little change from the controls. The cranial length was shortened mostly due to diminished size of the nasal and maxillary bones. The mandibles of these hypophysectomized rats were up to forty-three percent smaller than the controls. According to Collins, Becks, Simpson and Evans (1946), the postoperative changes in the mandibular condyles of hy-
pophysectomized rats were similar to those occurring in aging rats. In the young hypophysectomized rat, chondrogenesis is considerably slowed within four days after operation. Conversely, ossification of the cartilage model of the condyle in a twenty-eight day hypophysectomized rat is as advanced as is found in a two hundred and fifty-eight day normal rat. In all cases, they found that some cartilage always remains subjacent to the fibrous covering of the condyle.

By injecting pituitary growth hormone, these investigators found that the above mentioned senile characteristics could be reversed, and chondrogenesis and osteogenesis become active once more. The morphology of a normal appearing condyle can again be achieved after injection of the hormone. The injection of thyroxin did not bring about a reversal of these senile characteristics.

Hellman postulated in 1930 that the formation of the dentition and the eruption of the teeth in humans influences the growth of the cranio-facial complex. He reported that there were transitional changes in the growth of the cranial and facial bones to adjust to the developing dentition. In the development of the dentition, Hellman felt that the upper
and lower portions of the face were wedged apart, bringing additional height to the face. Sicher (1947) reports that though the development of the dentition and the jaws are independent, the development and growth of the alveolar processes are dependent on the development and eruption of the teeth, and conversely, the bone growth in the maxilla and mandible is one of the forces of eruption.

Baker (1941) conducted experiments in rats and pigs to determine the influence of the dental organs on the growth of the bones of the face. He found that the teeth do influence the bones which encompass their formative organs, and that growth of other bones of the cranio-facial complex may be altered when the formative organs are removed. When Baker removed the formative portion of the incisor of the rat, there was a twisting of the facial bones toward the side from which the organ was removed and a facial deformity resulted. Baker concluded that when the formative organ of a tooth is removed, there is a resultant arrest in growth of the facial bones of that side, and the arrest is in the direction in which the tooth normally grows. In the rat the persistently growing incisor grows in the forward direction. The resulting deformity is in the horizontal plane.
The alteration of cranio-facial growth following operative procedures has been investigated and reported by several investigators. Washburn (1947) resected the temporal muscle in the rat and found that the coronoid process absorbs or remains vestigial if its development was advanced when resection of the muscle occurred. Washburn and Detwiler (1943) also describe the effect of section of the splenius capitus on the growth of the cranium. They found that the superstructure to which these muscles attach do not develop after section of the muscle.

Jarabak and Thompson (1949) reported the effect of unilateral resection of the facial nerve at the stylomastoid foramen. There was a nostral deviation toward the side opposite that resected which became more pronounced for four months post-operatively. The bone structure of the face on the resected side appeared smaller than that of the normal side.

Bloom and Bloom (1940) transplanted the mandibles of newborn rats into the leg muscles of mature rats and found that only those portions of the mandible concerned with formation of the dentition where not resorbed. The body of the mandible was not resorbed since it contained the formative organs of the incisor and molar teeth.
In a report of the effects of unilateral condylar resection in the rat, Jarabak, Vehe and Kamins (1949) found that the mandible was deflected toward the resected side and malrelation of the incisor teeth resulted. In five weeks the upper incisor on the side opposite resection formed a complete circle. The molar teeth were shown to tip and elongate in an effort to establish functional occlusion. These sequelae were attributed to the mechanical shortening of the mandible in its most potent growth area. The investigators also found that the measurements affecting the length of the mandible following resection were shortened, whereas measurements associated with the height of the mandibular ramus seemed to increase over the unresected side. The overgrowth of the incisor as reported by Jarabak et al, in this study, has also been mentioned in the literature by Schour (1932) and Berretta (1913).

Jarabak later (1953) studied the effects of bi-lateral resection of the condyles in the rat by serial roentgenograms and direct observation of the sacrificed specimens. The effect on the growth of the cranium, upper face, and lower face was reported. He found that the neurocranium was least affected by condylar resection, while the mandible increased in height below the lower first molar tooth. He also found that there
was an increase in the vertical growth axis of the upper face which was due to the increased curvature of the incisor tooth. This increased curvature was considered the sequela of condylar resection because normal attrition of the incisor teeth was interrupted. The morphological changes observed in the dried specimens were increase in the antegonial notching, increase in size of the coroniod process, and a decrease in the concavity of the posterior border of the ascending ramus. These changes were proportional to the amount of posterior displacement of the mandible following resection.
The Effects of Roentgen-rays on Growth

The ability of roentgen-rays to produce alterations in the growth and development of the body has been known since Perthes (1903) retarded development in the wings of one day old chicks by exposing them to roentgen-rays. Recamier and Tribondeau (1906) also reported that ordinary therapeutic doses of roentgen-rays applied to chicks retarded bone development in both axes. Since these early observations, numerous investigators have endeavored to determine the quality and extent of the effects of roentgen-rays on growth and development. Some of the findings of these investigations will now be reviewed.

Regaud (1922) and Flaskamp (1930) reported that adult bone is highly resistant to radiation. Clark (1936) corroborated their findings and classified the body tissues according to their resistance to radiation. In his report, Clark (1936) disagrees with the premise of Loeb (1922) and that roentgen-rays follow Arndt's Law which holds that minimal doses of roentgen-rays may stimulate growth and cellular metabolism. He concluded that increase in cellular metabolism cannot be induced by roentgen-rays which always produce degenerative changes,
Nageotte (1922) also found that bone is a radio-resistant tissue, but claimed that roentgen-rays alter even adult bone though not distinctively. He reported that bone cells are more radio-sensitive than the interstitial substance of bone lamellae, an observation later corroborated by Ewing (1926) and Heller (1948).

The mode of action of roentgen-rays on bone has been investigated by Regaud (1922), Ewing (1926), Clark (1936), Gates (1943) and Heller (1948). It is generally held that bone is sensitive to radiation due to its high content of calcium and phosphorus that scatters secondary radiation which is more readily absorbed. The actual intensity of a given dose of radiation may be greater in bone than in other tissues because of the secondary radiation from the calcium and phosphorus.

Flaskamp (1930) studied the effects of radiation on bone and states that "retardation or cessation of growth of bone in young animals is a quite constant effect of radiation, provided the dose is above the threshold of tolerance." He estimated the dose of radiation which will cause inhibition of growth of bones of an infant and child at twenty-five and fifty percent, respectively, of the skin erythema dose of the adult.
Brooks and Hillstrom (1933) found the degree of retardation of bone growth to be in direct relation to the dose, up to the point of maximal response. Gall, Lingley and Hilcken (1940) corroborated the findings of Brooks and Hillstrom by finding that in irradiated epiphyseal cartilage, the effect and extent of damage was directly proportional to the dose of x-radiation as measured in roentgens, up to 1800 roentgens, above which point effects were maximal. They also found that 600 to 1200 roentgens applied to the thigh will cause inhibition of growth of the femur. Two findings most frequently observed were swelling of cartilage cells and disorientation of endochondral ossification. One week after exposure to 600 roentgens of x-radiation, cartilage cells show swelling, pyknosis and loss of columnar pattern.

Bisgard and Hunt (1936) localized x-radiation to the epiphyses of long bones of rabbits and measured the growth thereafter by roentgenograms. They found that fractionation of the total dose and protraction of the interval between exposures greatly lessens the inhibition of growth. They learned that the shaft of a long bone could be exposed to 1500 roentgens of x-radiation without causing a disturbance in the growth of the shaft, providing the epiphyseal cartilages are protected from
the rays. They conclude that the only action of x-radiation on cartilage cells is destructive. Extensive changes in the cartilage cells could be observed as early as two days following radiation.

Hinkel (1943) conducted experiments to quantitatively study the radio-sensitivity of the rat femur and to show the influence of age on the effect produced. He wanted to know if a relation could be established between the dose, age, and growth inhibition. Hinkel established that large doses of roentgen radiation caused marked retardation or cessation of growth of the femur, smaller doses had less influence on growth, and still smaller doses failed to cause any change. In this investigation Hinkel established the "minimal stunting dose" as that dose which will cause recognizable retardation of growth at a given or specific age level. This minimal stunting dose was found to rise steadily after the first ten days of life and bears a linear relationship to the age of the animal. The sensitivity of rat bones to roentgen radiation decreases as the age increases. Hinkel also found that roentgen radiation applied to the growing epiphyseal plate caused quantitatively predictable degrees of retardation ranging from temporary
stunting to permanent cessation of growth depending on the dose administered.

Brooks and Hillstrom (1933) could find no essential differences in the reaction of different species to roentgen-rays. Heller (1948) also reported that the only species differences that were observed were due to the difference in rate of bone growth between species.
CHAPTER III
METHODS AND MATERIALS

ANIMALS

Eleven female albino rats of the Wistar stock were used in this investigation. They were divided into three groups according to age. Four animals were in each group, with the exception of group three which had three animals. Group one consisted of animals twenty-one days of age when irradiated; animals in group two were twenty-eight days of age when irradiated; and the animals in the third group were thirty-seven days of age at the time of irradiation. In group one, animals two and three were experimental animals and five and six were the controls. In group two, animals seven and nine were experimental animals and numbers ten and twelve were controls. In group three, number thirteen was the experimental animal and numbers eighteen and nineteen were the control animals. The eleven animals reported on in this investigation are samples of a larger population.

Each group of animals was divided randomly into experimental and control animals. The control animals were maintained and handled in the same manner as the experimental
animals except for initial radiation. All animals were maintained on a diet of Purina rat pellets and water with supplements of soft white bread every two days. Food and water was available to the animals at all times during the experiment.

The animals were housed in small stainless-steel animal cages. The tops of the cages contained the food hopper and a 200 cc rubber-stoppered water bottle and canula. The cages were cleaned every two days.

ANESTHESIA

The anesthesia necessary in this investigation was obtained by injecting Nembutal (Abbott) of 50mg/cc concentration intraperitoneally. Adequate depth of anesthesia was usually obtained in about thirty minutes. It was necessary, in some instances, to supplement the original dose due to the variable reaction of the rats to Nembutal.
RADIOGRAPHIC AND CEPHALOMETRIC PROCEDURE

INSTRUMENT

The cephalometer used in this investigation was constructed by the author and patterned after the instruments used by Spence (1940) and Jarabak (1942). The instrument (Fig. 1) consisted of the two ear-posts (A), two film cassettes (B), the animal cradle (C), the x-ray tube (D), a grooved slide (F), and set screw (G).

The vertical film cassette was attached to the plastic table and was used to hold the film when lateral radiographs were made. The stationary ear-post was attached to the vertical cassette and extended out three-quarters of an inch. The movable ear-post was attached to a precision grooved slide (F) which allowed this ear-post to be moved medially and laterally, in an accurate path. A set screw (G) on the slide locked the mechanism in any given position. The horizontal cassette was attached to the underside of the plastic table and held the film when ventro-dorsal radiographs were made. The position of the horizontal cassette was fixed at 7/8 inch below the ear-posts. A one centimeter long rod was attached to the center of each cassette to aid in enlargement of the
radiographs. Three sixteenth high lead letters were placed on the cassettes at time of exposure to record the date of exposure and number of the animal.

In order that lateral and ventro-dorsal radiographs could be taken without moving the animal, a movable x-ray tube head was used. When taking lateral radiographs the tube head was positioned on two one-inch steel dowel rods which projected up from the wooden base-board. These rods fit into two holes in the base of the tube head and hold the head in a horizontal position and perpendicular to the vertical cassette. When ventro-dorsal radiographs were taken the tube head was placed into a cradle above the cephalometer. Metal lugs in the cradle positioned the tube head in the sagittal plane and perpendicular to horizontal film cassette.

When taking a lateral radiograph the anesthetized animal was placed on its back in the animal cradle (Fig.?). The animal's head was then positioned by placing the fixed ear-post into the animal's right ear hole and moving the movable ear-post into the left ear hole. The slide was then locked by means of the setscrew and the animal's head was suspended between the ear-posts. String was then placed over the upper
incisor teeth and slight tension was exerted in a horizontal plane to parallel the head in the dorso-ventral plane. The central ray from the x-ray tube then passes through the car- 
oposes and to the f

To the head was placed in the hor- 
ray tube- 
ally, in ventro-dor- 
plane and
incisor teeth and slight tension was exerted in a horizontal plane to parallel the head in the dorsal-ventral plane. The central ray from the x-ray tube then passes through the ear-posts and perpendicular to the sagittal plane of the skull and to the film in the vertical cassette.

To take the ventro-dorsal radiograph (Fig.3) the tube head was placed in the overhead cradle and the film was placed in the horizontal film cassette. The central ray from the x-ray tube then passes mid-way between the ear-posts medio-laterally, in the mid-sagittal plane of the animal, and was directed ventro-dorsally in a plane perpendicular to the mid-sagittal plane and to the horizontal film cassette.
ANIMAL POSITIONED FOR LATERAL RADIOGRAPH

- Film in vertical cassette
- Tension string
- Movable ear-post
- X-ray tube

FIGURE 2
Film distance for the lateral radiographs was fixed at 7/8 inch from the tip of the fixed ear-post to the film in the vertical plane. A film holder was used to hold multiple films. The exposed film was developed in the manner advised by the manufacturer.

CHRONOLOGY OF RADIOGRAPHS

Lateral and ventro-dorsal radiographs were taken of all animals. The following figures illustrate the positioning of the animals for the ventro-dorsal radiographs.

**Figure 3**
FILM DISTANCE

Film distance for the lateral radiographs was fixed at 7/8 inch from the tip of the fixed ear-post to the film in the vertical cassette. Film distance for the ventro-dorsal radiographs was fixed at 7/8 inch from the center of the ear-posts to the film in the horizontal film cassette.

The tube head was maintained at a distance of 12 inches from the tip of the fixed ear-post for all lateral and ventro-dorsal exposures.

RADIOGRAPHIC EQUIPMENT

A General Electric portable x-ray machine with a movable tube head was used for all radiographs. The machine was operated at 65 kilovolts and 10 milliamperes. The exposure time for the lateral and ventro-dorsal radiographs was 2 and 1/4 seconds.

Kodak super-speed dental occlusal film was used for all radiographs. Films were developed in the manner advised by the manufacturer.

CHRONOLOGY OF RADIOGRAPHS

Lateral and ventro-dorsal radiographs were taken of all
animals at the start of the investigation. The animals in groups one and two were radiographed every two weeks thereafter up to eight weeks. A power changeover during the tenth week made it impossible to obtain radiographs at the normal two week interval, and a three week interval was substituted. Two week intervals between radiographs were resumed to the end of the experiment at thirteen weeks. The animals in group three were radiographed at one month intervals for a period of three months. The weight of the animals was recorded to the nearest gram each time they were radiographed.

MEASUREMENTS

All measurements were made indirectly from the lateral (Fig.4) and ventro-dorsal (Fig.5) radiographs. The individual radiographs were placed between glass and locked on the stage of a microfilm projector. The 50mm lens used was checked and found to be free of distortion and aberation for the entire field measured. The projector was mounted in place of a dark room enlarger head (Fig.6) and could be moved up and down in a true vertical plane. The radiograph was then projected onto a drafting machine below and the projector raised or lowered until the proper enlargement was obtained. All measurements were made with the image enlarged five times.
Enlargement was aided by the image of the one centimeter long rod which was attached to the cassette during exposure and which appears on the radiograph below the image of the cranium. The measurements made from the enlarged image were recorded to a hundredth of a millimeter.

IRRADIATION

At the start of the investigation all experimental and control animals were weighed and placed under Nembutal anesthesia. While under deep anesthesia, the animals were oriented in the animal cephalometer and each was radiographed from the lateral and ventro-dorsal aspects. (Roentgenographs of the lower extremities were also taken at this time for use by another investigator in an allied investigation.) Immediately after obtaining the cephalometric radiographs, the experimental animals were placed on a rat board to which a head positioning device was attached (Fig.7). The head positioner consisted of two round plastic ear-posts, one attached to the board and fixed and the second post movable in the sagittal plane and in line with the fixed post. The animal was oriented in the positioner in the following manner. Under anesthesia, the animal was tied to the animal board by the front and hind legs
FIGURE 5
with the right side in contact with the board. The head of
the rat was then orientated in the positioner so that the fix-
ed ear-post entered the right ear hole. The second ear-post
was then moved down until it entered the left ear hole and
there


RADIOGRAPH PROJECTOR AND MEASURING
APPARATUS

MICROFILM PROJECTOR

RADIOGRAPH HOLDER
AND STAGE

DRAFTING TABLE

X-radiation in the amount of 1500 roentgens was then de-

livered through a one-quarter inch portal to the left and right
mandibular condyles at a target distance of 25 centimeters

FIGURE 6
with the right side in contact with the board. The head of the rat was then orientated in the positioner so that the fixed ear-post entered the right ear hole. The second ear-post was then moved down until it entered the left ear hole and thereby secured the animal in the sagittal plane. The body and snout of the animal were then secured by looping twine over the snout and abdomen and tying on the underside of the animal board to make movement impossible during irradiation. By this method the right and left mandibular condyles were orientated in the same plane both antero-posteriorly and superio-inferiorly in relation to the board.

The animal was then entirely covered by a one-eighth inch thick lead casket (Fig. 8) through which a one-quarter inch (6.35mm) portal had been drilled. The portal was centered over the left mandibular condyle of the animal, the position of which had been marked with dye, about four millimeters from the skin. The animal and apparatus were then placed in the center of the field under the x-ray tube.

X-radiation in the amount of 1500 roentgens was then delivered through a one-quarter inch portal to the left and right mandibular condyles at a target distance of 25 centimeters
HEAD POSITION DURING RADIATION

RAT BOARD

MOVABLE EAR-ROD
OF HEAD POSITIONER

FIGURE 7
and 220 kilovolts and 15 milliamperes. The radiation was delivered by a General Electric therapy-size x-ray machine equipped with one millimeter of aluminum and one-half millimeter of copper filtration. The animal was removed from the head positioner.

**RADIATION APPARATUS**

- **X-RAY TUBE**
- **LEAD SHIELD**
- **ANIMAL IN HEAD POSITIONER**

**FIGURE 8**
and 220 kilovolts and 15 milliamperes. The radiation was delivered by a General Electric therapy-size x-ray machine equipped with one millimeter of aluminum and one-half millimeter of copper filtration. The animal was removed from the head positioner and reoriented on the board so that a like amount of radiation could be delivered to the distal epiphysis of the femur of the right leg for use in an allied investigation. All parts except the femur were protected by the lead casket during the second irradiation. The animals were placed in their cages upon regaining consciousness.

The condylar growth centers were radiated only at the beginning of the experiment with 1500 r of x-radiation.
ORIENTATION POINT. (O.P.) This point is established by bisecting the superior and inferior cortical plates of the basisphenoid bone and lies midway between the sutures on its anterior and posterior borders.

LINE O.L. or orientation line. This line extends antero-posteriorly through the orientation point and along the inferior border of the palatine process of the maxilla.

LINE IBMP. This line extends along the inferior border of the mandible from the most inferior point below the incisor tooth and along the inferior border of the angle of the mandible.

LINE CL. This is a line drawn from the most posterior point on the mandibular condyle and intersects the plane of the inferior border of the mandible in a right angle. It is used to measure the length of the mandible.

LINE AC. This line is drawn from the tip of the alveolar crest lingual to the lower incisor tooth and intersects the
plane of the inferior border of the mandible in a right angle. It is used in measuring the length of the mandible.

LINE MMP. This line is drawn from the tip of the mesial cusp of the lower first molar and extended to intersect the plane of the inferior border of the mandible in a right angle. Its length represents the height of the mandible anteriorly.

LINE OPMP. This line extends from (and perpendicular to) the plane of the inferior border of the mandible to the orientation point. It is used to measure the height of the mandible posteriorly.

LINE NOL. This is a line erected as a perpendicular to the orientation line (OL) and extends through the most anterior point of the nasal bone.

LINE POL. This is a line drawn perpendicular to the orientation line (OL) and extends through the most posterior point on the occipital bone above the foramen magnum.

LINE CROL. This line is erected perpendicular to the orientation line (OL) and extends from the mesial surface of the
upper first molar at its cervix to the most superior border of the cranium. It is used to measure the upper face height.

LINE CR. This line extends antero-posteriorly parallel to line (OL) and represents the superior border of the cranium.
TOTAL CRANIAL LENGTH. The measurement of total cranial length
is made by measuring the distance between lines POL
and NOL along the orientation line (OL).

LINES AND MEASUREMENTS USED TO STUDY LATERAL RADIOGRAPHS

MANDIBULAR HEIGHT POSTERIORLY. This is measured as the distance
from the orientation point (OP) to the line IMNP and

FIGURE 9
MEASUREMENTS MADE FROM LATERAL ROENTGENOGRAMS

(Fig. 9)

TOTAL CRANIAL LENGTH. The measurement of total cranial length is made by measuring the distance between lines POL and NOL along the orientation line (OL).

CRANIAL HEIGHT. Cranial height is measured as the distance between the lines CR and OL along the line CR-O L. This measurement represents the height of the cranium from the palate to the upper border of the cranial vault.

MANDIBULAR LENGTH. Mandibular length is measured as the distance between the lines CL and AC and is measured along the line IMBP (inferior border of the mandible). This measurement represents the total length of the mandible.

MANDIBULAR HEIGHT ANTERIORLY. This measurement is taken as the distance from the tip of the mesial cusp of the lower first molar to the line IMBP and is measured along the line MMP.

MANDIBULAR HEIGHT POSTERIORLY. This is measured as the distance from the orientation point (OP) to the line IMBP and
is measured along the line OPMP. This measurement represents the height of the mandible in the region of the mandibular angle.

ANTEGONIAL NOTCH HEIGHT. This measurement is taken as the distance from line IMBP (and perpendicular to IMBP) to the highest point in the concavity of the notch.
MEASUREMENTS MADE FROM VENTRO-DORSAL ROENTGENOGRAMS
(Fig.10)

INTERCONDYLAR WIDTH. Intercondylar width is measured as the distance between the most medial points on the medial surfaces of the mandibular condyles.

INTERZYGOMATIC WIDTH. This measurement is taken as the distance between the most lateral points on the right and left zygomatic arches.
MEASUREMENTS MADE FROM VENTRO-DORSAL RADIOGRAPHS

FIGURE 10
CHAPTER IV

GROWTH OF THE MANDIBLE
(CONDYLAR GROWTH CENTER)

Often, as is the case of this study, the reason for scientific investigation is to gain knowledge and experience for clinical application in man. When using lower species of animals as the laboratory media, the data collected and the conclusions drawn from this data, are specific only for the particular species investigated and not always applicable to man. It is, however, the first link in a chain of experiments leading to those upon man.

It is quite evident that the morphology of the craniofacial complex as found in the rat and man differ greatly. But, as there is dissimilarity, there is also great similarity between the rat and man. This similarity is in the composition and physiological mechanisms of the tissues and systems. Though they differ in extent and chronology, the method of growth of tissues in the rat and man are basically the same. This similarity is apparent in the description of the growth of the mandible of the rat.

In the rat and in man growth of the mandible takes place
by both endochondral and intramembranous formation. The condyle of the mandible is formed by the osseous replacement of a pre-existing cartilage model. The endochondral growth of the condyle differs from the growth of long bones in that no secondary center of ossification ever exists. The condyloid process in its early development is narrow and cone-shaped and is composed entirely of hyaline cartilage. This cartilage is separated from the cranial portion of the joint by a layer of loose connective tissue. The loose connective tissue becomes more dense with age and forms the inter-articular disc. The fibrocytes becomes fewer in number and are embedded in dense collagenous fibers. The cartilagenous model is covered by a layer of fibrous connective tissue on its articular surface which constitutes the future perichondrium. The cartilage model grows by both appositional and interstitial growth. Beneath the fibrous covering of the condylar cartilage is a zone of flattened embryonic cells arranged parallel to the articular surface. It is at this site that appositional growth of the cartilage is initiated; the chondrogenic cells of the embryonic layer of the connective tissue differentiate into chondroblasts. These cells then begin production of hyaline intercellular substance and so change into chondrocytes. The condylar cartilage is
surrounded on all surfaces by its perichondrium, except toward the neck with its membrane bone. It is for this reason that the condylar cartilage is able to increase in all dimensions by appositional growth of cartilage.

From this flattened layer or zone of transition the chondrocytes become progressively more mature in nature toward the membrane bone of the mandibular neck. These cells are classified into zones to facilitate description. Immediately beneath the transitional layer, the chondrocytes become rounded and enlarged and are separated by large amounts of intercellular matrix. These cells are usually arranged in groups of two and comprise the intermediate zone. It is in the intermediate zone that interstitial growth of the cartilage takes place, although this does not seem to be the major method of growth in the condylar cartilage.

Below the intermediate zone, the cells become vacuolated and are separated by less intercellular matrix. In this edematous zone the cartilage cells are arranged in a columnar fashion perpendicular to the articular surface. These cells become elongated, the long axes of which establishes the columnar formation. There is almost no matrix separating chondro-
cytes in this zone. Immediately beneath this zone is the zone of osteogenesis. It is here replacement of cartilage by bone is seen; and numerous delicate trabeculae of bone are formed which have remanents of intercellular substance as a core. Abundant blood vessels and clusters of osteoblasts surround the trabeculae. While osteogenesis progresses, the ramus of the mandible increases in width and thickness by both endosteal and periosteal apposition.

In the young animal, proliferation of the cartilage, maturation, and replacement by bone takes place at a very rapid pace. With oncoming maturity of the animal, the process is slowed and changes characteristic of ageing take place in the growth center. Proliferation of cells in the chondrogenic layer of the fibrous perichondrium decreases but osteogenesis at the zone of erosion continues. Slowly, the mainly cartilagenous condyle is transformed into a bony condyle covered by a crescent shaped cartilage. The condyle increases in size but the condylar cartilage itself decreases due to its replacement by bone. The cartilage is never completely replaced.

The character of the cartilage continues to change as maturation progresses; proliferation is diminished and cell
size and intercellular matrix are increased. The bone trabeculae increase in size and become more dense and fused in structure while marrow spaces become constricted. Hemopoiesis begins to take place in the marrow spaces of the trabecular bone and there is an increase in the number of blood forming cells. The decreasing number of osteoblasts on the trabeculae signifies the transition from the phase of rapid growth to one of maturation.

The replacement of cartilage to bone in the condyle is never completed, even in later life. Though bone becomes more dense, the cartilage and its covering of fibrous connective tissue perichondrium remain throughout life. The fibrous covering performs its function in the articulation of the joint, but because of the persistence of the chondrogenic layer in its depths it retains the ability to proliferate and again initiate appositional growth of the condyle. This reawakening of growth in the condyle in later life is apparent in the behavior of the mandible in such cases as acromegaly. This new growth of the condyle is a result of functional disturbance of the ductless gland mechanism.

As was stated in the beginning of this description, the
process of endochondral ossification of the condylar growth center as seen in man and the rat are so similar as to be considered to be identical. For this reason, the facts obtained in these studies on mandibular growth control by radiation may have clinical application in man.

Length of the mandible is also increased by apposition of bone to the alveolar process of incisor tooth, thereby increasing the length of the body of the rat mandible. This does not occur in man.
CHAPTER V
FINDINGS

General Findings

All animals, radiated and controls, appeared to be in good general health for the duration of the experiment. The radiated animals exhibited slight radiation dermatitis and loss of hair in the area of the mandibular condyles four weeks after radiation. Except for the slight burns and loss of hair, general appearance of the radiated animals did not differ from the control animals.

Although no differences in the feeding habits were observed between the radiated and control animals, the radiated animals weighed 12 to 50 grams less than the control animals at the thirteenth week of the experiment (Fig. 11).

Graphical Analysis

These findings are the result of graphical analysis of the growth curves of the radiated and control animals from the beginning of the experiment to the thirteenth week. Measurements were made of cranio-facial growth in three groups of animals, each group having radiated and control animals. The
growth curves of the radiated animals were compared to the
curves of the control animals within each group for each
measurement of cranio-facial growth. In all graphs, the growth
curves of the radiated animals are represented by the bold
black lines, and the curves of the control animals by the light
gray lines. The findings of group I are presented first. The
measurements of cranio-facial for animals 2, 3, 5 and 6 are
presented in figures 12, 13, 14 and 15.

Total Cranial Length

Group I (Fig. 16)

The growth curves of the radiated and control animals as­
cended in close proximity to the fourth week after radiation.
From the fourth week, while the curves of the control animals
(nos. 5 and 6) continued uninterrupted, the curves of the
radiated animals (nos. 2 and 3) assumed a more horizontal path
indicating a reduction of the increment of growth. This
horizontal trajectory of the curves of the radiated animals
continued to the thirteenth week, and indicated a reduction of
the bi-weekly increments of growth contributing to total cra­
nial length between the fourth and thirteenth week. The great­
est reduction of growth is evidenced at the four week level.
Total cranial length continued to increase in both radiated and control animals at the thirteenth week of the experiment.

The growth curves of the animals in group I indicated that the total cranial length of the control animals was .6 to 1 mm greater than the total cranial length of the control animals at the thirteenth week of experiment.

Cranial Height

Group I (Fig. 17)

Analysis of the growth curves of the animals in group I shows that cranial height in one of the radiated animals (no. 3) increased in increments comparable in magnitude with those of the control animals. The curve of this animal did not deviate greatly from the curves of the control animals from the beginning of the experiment to the thirteenth week, and cranial height at the thirteenth week was about the same as found in the control animals.

The growth curve of the other radiated animal in this group (no. 2) deviated greatly from the curves of the control animals after the first two weeks. Increments of growth from the second week to the thirteenth week was greatly reduced,
<table>
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<tr>
<th>WEEKS RECORDED</th>
<th>2</th>
<th>3</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>9</th>
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<td>39</td>
<td>70</td>
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<td>Two weeks</td>
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<td>85</td>
<td>87</td>
<td>129</td>
<td>119</td>
<td>143</td>
<td>123</td>
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<td>Four weeks</td>
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<td>124</td>
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<td>153</td>
<td>158</td>
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<td>Six weeks</td>
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<td>154</td>
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<td>192</td>
<td>189</td>
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<td>208</td>
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<tr>
<td>Eight weeks</td>
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<td>194</td>
<td>211</td>
<td>193</td>
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<td>Ten weeks</td>
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<td>-</td>
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<td>Thirteen weeks</td>
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<td>237</td>
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FIGURE 11
### Animal Number 2

#### Measurements Made from Lateral Radiographs

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<th>Measured</th>
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<th>2 weeks</th>
<th>4 weeks</th>
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<td></td>
<td>4.21</td>
<td>4.56</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Antegonial notch height</td>
<td>0.35</td>
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<td>0.66</td>
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</table>

#### Measurements Made from Ventro-Dorsal Radiographs

<table>
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<tr>
<th>Measured</th>
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<th>2 weeks</th>
<th>4 weeks</th>
<th>6 weeks</th>
<th>8 weeks</th>
<th>10 weeks</th>
<th>13 weeks</th>
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<tr>
<td>Inter-zygomatic width</td>
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<td>11.92</td>
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<td>9.70</td>
<td>10.02</td>
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</table>

**Figure 12**
### ANIMAL NUMBER 3

#### MEASUREMENTS MADE FROM LATERAL RADIOGRAPHS

<table>
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<th>6 Weeks</th>
<th>8 Weeks</th>
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<tr>
<td>Total cranial length</td>
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<td>5.82</td>
<td>5.71</td>
<td>5.80</td>
<td>5.99</td>
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<td>10.56</td>
<td>11.21</td>
<td>11.32</td>
<td>11.89</td>
<td>12.01</td>
</tr>
<tr>
<td>Mandibular height</td>
<td>3.13</td>
<td>3.31</td>
<td>3.58</td>
<td>3.97</td>
<td>4.08</td>
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<td>Antegonial notch height</td>
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#### MEASUREMENTS MADE FROM VENTRO-DORSAL RADIOGRAPHS

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<td>11.78</td>
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**FIGURE 13**
ANIMAL NUMBER 5

MEASUREMENTS MADE FROM LATERAL RADIOGRAPHS

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<th>8 weeks</th>
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<tr>
<td>Total cranial length</td>
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<td>23.58</td>
<td>24.67</td>
<td>25.52</td>
<td>25.81</td>
</tr>
<tr>
<td>Cranial height</td>
<td>5.15</td>
<td>5.40</td>
<td></td>
<td>5.83</td>
<td>5.98</td>
<td>6.10</td>
<td>6.15</td>
</tr>
<tr>
<td>Mandibular length</td>
<td>8.99</td>
<td>10.51</td>
<td></td>
<td>11.90</td>
<td>12.85</td>
<td>13.28</td>
<td>13.58</td>
</tr>
<tr>
<td>Mandibular height anterior</td>
<td>3.08</td>
<td>3.34</td>
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<td>4.30</td>
<td>4.31</td>
<td>4.37</td>
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<td>Mandibular height posterior</td>
<td>2.90</td>
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<td></td>
<td>4.37</td>
<td>4.49</td>
<td>4.72</td>
<td>4.99</td>
</tr>
<tr>
<td>Anteguinal notch height</td>
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<td>0.53</td>
<td>0.70</td>
<td>0.72</td>
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MEASUREMENTS MADE FROM VENTRO-DORSAL RADIOGRAPHS

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<th>8 weeks</th>
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<th>13 weeks</th>
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<tbody>
<tr>
<td>Inter-zygomatic width</td>
<td>9.64</td>
<td>10.51</td>
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<td>12.31</td>
<td>12.40</td>
<td>12.80</td>
<td>13.10</td>
</tr>
<tr>
<td>Inter-condylar width</td>
<td>8.50</td>
<td>9.32</td>
<td></td>
<td>9.54</td>
<td>9.80</td>
<td>9.92</td>
<td>10.32</td>
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</tbody>
</table>

FIGURE 14
### Measurements Made from Lateral Radiographs

<table>
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<th>Measured</th>
<th>Beginning</th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>6 weeks</th>
<th>8 weeks</th>
<th>11 weeks</th>
<th>13 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cranial length</td>
<td>18.38</td>
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<td>22.53</td>
<td>23.91</td>
<td>25.09</td>
<td>25.32</td>
<td>25.89</td>
</tr>
<tr>
<td>Cranial height</td>
<td>5.23</td>
<td>5.25</td>
<td>5.78</td>
<td>5.82</td>
<td>5.97</td>
<td>6.02</td>
<td>6.20</td>
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<tr>
<td>Mandibular length</td>
<td>8.71</td>
<td>9.67</td>
<td>11.42</td>
<td>12.33</td>
<td>12.90</td>
<td>13.49</td>
<td>13.50</td>
</tr>
<tr>
<td>Mandibular height anterior</td>
<td>3.00</td>
<td>3.29</td>
<td>4.02</td>
<td>4.29</td>
<td>4.43</td>
<td>4.65</td>
<td>4.70</td>
</tr>
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<td>Mandibular height posterior</td>
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<td>3.44</td>
<td>3.90</td>
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<td>4.21</td>
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<td>4.66</td>
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<tr>
<td>Antegonial notch height</td>
<td>0.40</td>
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<td>0.62</td>
<td>0.71</td>
<td>0.74</td>
<td>0.80</td>
<td>0.80</td>
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### Measurements Made from Ventro-Dorsal Radiographs

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<th>Measured</th>
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<th>4 weeks</th>
<th>6 weeks</th>
<th>8 weeks</th>
<th>11 weeks</th>
<th>13 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inter-zygomatic width</td>
<td>9.65</td>
<td>10.02</td>
<td>11.32</td>
<td>12.30</td>
<td>12.33</td>
<td>12.90</td>
<td>12.93</td>
</tr>
<tr>
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<td>8.61</td>
<td>9.58</td>
<td>9.79</td>
<td>10.20</td>
<td>10.32</td>
<td>10.43</td>
<td>10.43</td>
</tr>
</tbody>
</table>

**Figure 15**
Figure 16

Total Cranial Length Group 1

Increment of Growth - mm

Weeks 0 2 4 6 7 8 10 11 12 13
FIGURE 17
as is evidenced by the almost horizontal slope of the curve. Cranial height at the thirteenth week was more than .5 mm less than the cranial height of the control animals.

Interzygomatic Width

Group I (Fig. 18)

The growth curves of the radiated and control animals in group I ascended in close proximity to the fourth week. During this period the curves of the radiated animals (nos. 2 and 3) exhibited only slightly reduced growth increments as compared to the control animals. From the fourth to the thirteenth week there appeared to be a reduction on the growth increments of the radiated animals, evidenced by the more horizontal path of their growth curves during this period. At the end of thirteen weeks interzygomatic width of the radiated animals was 1 to 1.5 mm less than the interzygomatic width of the control animals.

Mandibular Length

Group I (Fig. 19)

The growth curves of the radiated animals differed greatly from the curves of the control animals from the time of radiation
INTERZYGOMATIC WIDTH

GROUP 1

INCREMENT OF GROWTH = MM.

TIME - WEEKS

FIGURE 18
Mandibular Length Group 1

Increment of Growth—MM.

Time-Weeks

Figure 19
through the thirteenth week. Whereas mandibular length increased in large increments in the control animals (nos. 5 and 6) in the first few weeks of the experiment, the radiated animals showed evidence of early inhibition of growth in length of the mandible. The growth curves of the radiated animals (nos. 2 and 3) assumed a more horizontal trajectory during the first two weeks of the experiment, indicating a reduced increment of growth for this time. From the second to the thirteenth week the growth increments of the radiated rats appear to be comparable in magnitude to the increments of the controls. This is evidenced by the almost parallel curves of the control and radiated rats from the second to the thirteenth week.

The early reduction of the growth increment during the first two weeks following radiation is evident at the thirteenth week by the shortened mandibular length of the radiated animals. At the thirteenth week, the mandibular length of the radiated rats was from 1.5 to 2.5 mm less in length than the mandibular length of the control animals.

Mandibular Height Anterior

Group I (Fig. 20)

The growth curves of the control animals show a relatively
FIGURE 20
steady ascent from the beginning of the experiment to the thirteenth week, signifying an uninterrupted increase in the height of the mandible below the first molar tooth during this period. The curves of the radiated animals showed less uniformity of the growth curves. The curve of radiated animal (no. 2) ascended in close proximity with the curves of the control animals to the fourth week, then assumed an almost horizontal slope which indicates reduced growth increments from the fourth through the tenth week. Growth increments again increased in magnitude from the tenth through the thirteenth week for this animal, and mandibular height in the anterior region was about the same as found in the controls at the thirteenth week.

The mandibular height (anterior) of radiated animal (no. 3) appeared to increase in reduced but more equal increments from the beginning of the experiment to the thirteenth week. Total mandibular height in the anterior region for this animal was slightly less (.2 mm) than the mandibular height of the control animals at the thirteenth week.

Mandibular Height Posterior

Group I (Fig. 21)
FIGURE 21

MANDIBULAR HEIGHT POSTERIOR GROUP I

INCREMENT OF GROWTH - MILLIMETERS

WEEKS

2  4  6  7  8  10  11  12  13
The growth curves of the animals in group I ascend sharply in the first six weeks of the experiment indicating rapid increase in the height of the mandible in the posterior region. Unlike the control animals, radiated animal (no. 2) exhibited rapid growth for the first two weeks following radiation, and then a diminished growth phase from the second to the fourth week. Growth increments are more consistent with those of the control animals from the fourth to the sixth week, but again become diminished from the sixth to the tenth week. Very slight increase in posterior mandibular height took place during the sixth through the tenth week in this experimental animal. Growth increments again increased after the tenth week but mandibular height in the posterior region was less than was found in the controls at the thirteenth week.

Radiated animal (no. 3) exhibited greatly reduced increments of growth contributing to mandibular height in the posterior region from the beginning of the experiment to the thirteenth week. Almost no increase in height took place for the two weeks following radiation. From the second to the thirteenth week the growth increments are reduced in magnitude, as that mandibular height in the posterior region for this
animal is far less than is found in the control animals at the thirteenth week.

Intercondylar Width

Group I (Fig. 22)

The growth curves of the radiated and control rats in group I exhibited rather erratic paths after the first two weeks of the investigation. All growth curves ascended relatively sharply during the first two weeks indicating large increments of growth for the radiated as well as the control animals. The curve of radiated animal (no. 2) indicated almost no growth in width between the second and sixth week, followed by large increments during the four weeks from the sixth through the tenth week. Growth again diminished to the thirteenth week, so that at the thirteenth week intercondylar width of this animal was about the same as found in the control animals.

The intercondylar width of radiated animal (no. 3) increased in large increments up to the fourth week following radiation. From the fourth week through the thirteenth week the increments were so greatly reduced that the growth curve
FIGURE 23

ANTEGONIAL NOTCH HEIGHT GROUP 1

INCREMENT OF GROWTH - MM.

TIME - WEEKS
assumed an almost horizontal path. Intercondylar width of this animal was much less at the end of the experiment than the width recorded in the control animals.

Antegonial Notch Height

Group I (Fig. 23)

The growth curves of the radiated animals in group I showed no great dissimilarity in the height of the antegonial notch when compared with the growth curves of the control animals. Growth in height appeared to take place at approximately the same rate in the control and radiated animals, except as indicated below.

Although experimental animal (no. 2) appears to exhibit a reduced increment of growth in the height of the antegonial notch during the second to the fourth week, the remainder of the growth increments do not appear to differ in magnitude from those of the control animals. Antergonial notch height in this animal at the thirteenth week is only slightly less than the notch height of the control animals.

The findings of group II will now be presented. The measurements of cranio-facial growth of animals 7, 9, 10 and 12
are recorded in figures 24, 25, 26 and 27.

Total Cranial Length

Group II (Fig. 28)

The growth curves of the control and radiated animals of group II ascended in close proximity until two weeks after radiation. At the two week level in the curve of experimental animal (no. 7) assumed a more horizontal path indicating that growth increments were reduced from the second week to the eight week. After the eight week the curve again paralleled the curves of the control animals. Although the growth curve of this animal deviated from the curves of the controls at the two week level, its total cranial length is only slightly shorter than the cranial lengths of the control animals at the thirteenth week.

The curve of the other radiated animal in this group became more horizontal at the four week level and assumed a plateau between the sixth and eight week, during which time almost no increase in cranial length was evident. After the eight week the growth curve ascended steeply and indicated a larger growth increment during the interval between the eight and tenth week. The curve appeared to parallel the curves of the
control animals from the tenth week to the end of the experiment. Total cranial length of this animal showed no evidence of shortening at the end of thirteen weeks.

Cranial Height

Group II (Fig. 29)

Cranial height in the radiated animals in group II appeared to increase in slightly larger increments than in the control animals during the first six weeks of the experiment. Cranial height of radiated animal (no. 9) was about the same as was found in the control animals at the thirteenth week even though its growth increments from the second to the sixth week were greater than the increments of the control animals. This was possible due to slightly reduced increments of growth in the radiated animal after the sixth week.

The cranial height of radiated animal (no. 7) appeared to increase in greater increments from the time of radiation to the thirteenth week. The slope of the curve was, in general, more vertical in nature than the curves of the control animals. Cranial height at the thirteenth week was greater than was found in the control animals.
ANIMAL NUMBER 7

MEASUREMENTS MADE FROM LATERAL RADIOGRAPHS

<table>
<thead>
<tr>
<th>Measured</th>
<th>Beginning</th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>6 weeks</th>
<th>8 weeks</th>
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<th>13 weeks</th>
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<tbody>
<tr>
<td>Total cranial length</td>
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<td>23.97</td>
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<td>Cranial height</td>
<td>5.28</td>
<td>5.50</td>
<td>5.63</td>
<td>5.70</td>
<td>5.71</td>
<td>5.78</td>
<td>5.82</td>
</tr>
<tr>
<td>Mandibular length</td>
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<td>11.00</td>
<td>11.30</td>
<td>11.51</td>
<td>11.80</td>
<td>12.69</td>
<td>13.01</td>
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<tr>
<td>Mandibular height anterior</td>
<td>3.10</td>
<td>3.55</td>
<td>4.02</td>
<td>4.18</td>
<td>4.23</td>
<td>4.50</td>
<td>4.58</td>
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<td>2.90</td>
<td>3.70</td>
<td>3.85</td>
<td>4.01</td>
<td>4.22</td>
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MEASUREMENTS MADE FROM VENTRO-DORSAL RADIOGRAPHS

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<td>12.58</td>
</tr>
<tr>
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<td>9.61</td>
<td>9.82</td>
<td>9.99</td>
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FIGURE 24
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<th>2 weeks</th>
<th>4 weeks</th>
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<tbody>
<tr>
<td>Total cranial length</td>
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<td>23.83</td>
<td>24.17</td>
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<td>5.10</td>
<td>5.42</td>
<td>5.52</td>
<td>5.80</td>
<td>5.71</td>
<td>5.82</td>
<td>5.91</td>
</tr>
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<td>11.10</td>
<td>11.90</td>
<td>11.42</td>
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<td></td>
</tr>
<tr>
<td>anterior</td>
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<td>3.82</td>
<td>3.91</td>
<td>4.01</td>
<td>4.21</td>
<td>4.34</td>
<td>4.49</td>
</tr>
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<td>posterior</td>
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<td>3.76</td>
<td>3.89</td>
<td>4.01</td>
<td>4.13</td>
<td>4.15</td>
<td>4.16</td>
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<tr>
<td>Antegonial notch height</td>
<td>0.35</td>
<td>0.51</td>
<td>0.80</td>
<td>0.61</td>
<td>0.61</td>
<td>0.65</td>
<td>0.68</td>
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</table>

**MEASUREMENTS MADE FROM VENTRO-DORSAL RADIOGRAPHS**

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<th>4 weeks</th>
<th>6 weeks</th>
<th>8 weeks</th>
<th>10 weeks</th>
<th>13 weeks</th>
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</thead>
<tbody>
<tr>
<td>Inter-zygomatic width</td>
<td>10.19</td>
<td>11.33</td>
<td>11.54</td>
<td>11.90</td>
<td>11.96</td>
<td>12.27</td>
<td>12.52</td>
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**FIGURE 25**
### ANIMAL NUMBER 10

#### MEASUREMENTS MADE FROM LATERAL RADIOGRAPHS

<table>
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<th>4 Weeks</th>
<th>7 Weeks</th>
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<th>13 Weeks</th>
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<tr>
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<td>24.15</td>
<td>24.81</td>
<td>25.19</td>
<td>25.65</td>
</tr>
<tr>
<td>Cranial height</td>
<td>5.91</td>
<td>5.52</td>
<td>5.55</td>
<td>5.80</td>
<td>5.89</td>
<td>5.91</td>
</tr>
<tr>
<td>Mandibular length</td>
<td>10.20</td>
<td>11.29</td>
<td>12.31</td>
<td>12.69</td>
<td>13.23</td>
<td>13.49</td>
</tr>
<tr>
<td>Mandibular height anterior</td>
<td>3.22</td>
<td>3.32</td>
<td>4.21</td>
<td>4.34</td>
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<td>Mandibular height posterior</td>
<td>2.96</td>
<td>3.70</td>
<td>4.26</td>
<td>4.35</td>
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<td>4.71</td>
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<td>Antegonial notch height</td>
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<td>0.63</td>
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#### MEASUREMENTS MADE FROM VENTRO-DORSAL RADIOGRAPHS

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<td>Inter-condyalar width</td>
<td>9.10</td>
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<td>9.82</td>
<td>10.10</td>
<td>10.10</td>
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</table>

**FIGURE 26**
### ANIMAL NUMBER 12

#### MEASUREMENTS MADE FROM LATERAL RADIOGRAPHS

<table>
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<th>Measured</th>
<th>Beginning</th>
<th>2 Weeks</th>
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<th>8 Weeks</th>
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<td>24.32</td>
<td>25.00</td>
</tr>
<tr>
<td>Cranial height</td>
<td>5.22</td>
<td>5.32</td>
<td>5.38</td>
<td>5.60</td>
<td>5.61</td>
<td>5.69</td>
<td>5.70</td>
</tr>
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<td>Mandibular length</td>
<td>9.89</td>
<td>11.08</td>
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<td>Mandibular height anterior</td>
<td>3.07</td>
<td>3.72</td>
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<td>4.18</td>
<td>4.18</td>
<td>4.38</td>
<td>4.39</td>
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<tr>
<td>Mandibular height posterior</td>
<td>2.71</td>
<td>3.88</td>
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<td>4.31</td>
<td>4.35</td>
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#### MEASUREMENTS MADE FROM VENTRO-DORSAL RADIOGRAPHS

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<th>4 Weeks</th>
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<th>8 Weeks</th>
<th>11 Weeks</th>
<th>13 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inter-zygomatic width</td>
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<td>11.79</td>
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<td>Inter-condylar width</td>
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<td>9.82</td>
<td>10.09</td>
<td>10.10</td>
<td>10.25</td>
<td>10.25</td>
</tr>
</tbody>
</table>

**FIGURE 27**
FIGURE 28

TOTAL CRANIAL LENGTH GROUP II
Interzygomatic Width

Group II (Fig. 30)

The growth curves of the control animals and radiated animal (no. 7) indicated that a rather large increase in interzygomatic width took place in these animals during the first two weeks of the experiment. While the curve of radiated animal (no. 7) ascended to close proximity with the curves of the control animals, the growth curve of radiated animal (no. 9) showed that interzygomatic width in this animal increased considerably less in the first two weeks following radiation. From the second through the thirteenth week of the experiment the slope of the curves of both radiated animals appeared to be more horizontal in character as compared to the control animals. This indicates that the growth increments of the radiated animals were less in magnitude, as compared to the controls, from the second through the thirteenth week. Interzygomatic width at the end of the thirteenth week is less in the radiated animals than the width recorded in the control animals.

Mandibular Length

Group II (Fig. 31)
The growth curves of the control and radiated animals were quite closely grouped to the second week of the experiment. From the second week, the curves of the radiated animals (nos. 7 and 9) become strongly horizontal in nature and indicated that the increments of growth were reduced from the second to the eighth week. Growth also took place at a reduced rate in the control animals from about the third week to the end of the experiment.

The period between the eighth and tenth week shows considerable deviation between the curves of the radiated and control animals. While the curves of the control animals indicate that growth continues in almost equal increments, the curves of the radiated animals exhibit that the increment of growth from the eighth to the tenth week is considerably larger than in the controls. Due to this rapid growth, the curves of the radiated animals almost approximate the curves of the controls at the tenth week level. Growth increments of the radiated animals from the tenth week to the end of the experiment are slightly reduced as compared to the increments of the control animals.

The radiated animals in group II exhibited only slightly shortened mandibles at the end of the thirteenth week of the
FIGURE 31

MANDIBULAR HEIGHT ANTERIOR GROUP II

FIGURE 32
investigation. This shortening ranged from .2 to .5 mm shorter than the mandibular length of the control animals.

Mandibular Height Anterior

Group II (Fig. 32)

The growth curves of the control and radiated animals ascended quite uniformly to the second week of the experiment, indicating uninterrupted growth during this period. Mandibular height in the anterior region increased at a reduced rate in radiated animal (no. 7) from the second to the sixth week, as evidenced by the horizontal trajectory of the growth curve during this period.

Growth increments increased again in magnitude from the sixth through thirteenth week for this animal, and mandibular height in the anterior region at the thirteenth week was only slightly below the level of the control animals.

The growth curve of experimental animal (no. 9) showed little deviation from the curves of the control animals to the eight week following radiation. From the eight week to the tenth week the increment of growth is larger than is experienced by the control animals. This period of rapid growth in height
of the mandible is followed by increments which are consistent with growth taking place in the control animals. Mandibular height of this animal at the thirteenth week is very slightly greater than the mandibular height of the control animals.

Mandibular Height Posterior

Group II (Fig. 33)

Both radiated rats in group II showed evidence of reduced mandibular height in the posterior region. This reduction of the growth increments was indicated graphically from the second through the thirteenth week of the experiment.

The growth curve of radiated animal (no. 9) ascended continuously with the curves of the control animals to the second week after radiation. From the second week, while the curves of the controls continued upwards, the curve of this animal became more horizontal, indicating a reduction of the growth increments after the second week. The curve continued in this path to the thirteenth week, thus terminating at a lower graphical level than the curves of the control animals and indicating less growth of the mandible in the posterior region in the radiated animal than was found in the controls.
FIGURE 33

MANDIBULAR HEIGHT POSTERIOR GROUP II

AGGREGATE OF GROWTH = MM

WEEKS
The growth curve of radiated animal (no. 7) indicated that slightly less growth in height took place in the two weeks following radiation in the radiated animal as compared to the controls. The curve of this animal also became more horizontal at the second week after radiation and continued in an almost horizontal path to the thirteenth week. This animal (no. 7) showed greatly reduced growth increments of mandibular height from the second to the thirteenth week, with only .35 mm of growth in height taking place during the eleven weeks following radiation. Mandibular height in the posterior region for this animal was far less than the mandibular height of the control animals in group II.

Intercondylar Width

Group II (Fig. 34)

The growth curves of the radiated animals in group II showed considerable deviation when compared to the curves of the control animals. The curves of the control animals show great variability in the magnitude of consecutive increments of growth throughout the experiment.

The growth curves of the radiated animals assumed a more
INTERCONDYLAR WIDTH GROUP II

FIGURE 34
horizontal path immediately following radiation, indicating considerably less growth in intercondylar width in the two weeks following radiation. Intercondylar width increased at about the same rate in the control and radiated animals from the second to the eight week. From the eight week in the case of radiated animal (no. 7), and the tenth week in radiated animal (no. 9), the curves become almost horizontal and indicated almost no increase in intercondylar width to the end of the experiment. The lack of growth experienced by the radiated animals during the first two weeks and the last five weeks of the experiment is seen in the graphical difference in the curves of the control and radiated animals at the end of the experiment. The radiated animals showed reduced increments of growth over sustained periods resulting in intercondylar widths which are less than the intercondylar widths of the control animals.

Antegonial Notch Height

Group II (Fig. 35)

Unlike group I, the growth curves of the radiated animals in group II exhibit a marked dissimilarity from the curves of the control animals. The more horizontal growth curves of the radiated animals during the two weeks following radiation in-
dicates a reduced increment of growth in height of the antegonial notch during this period. The slope of the curves during the next two weeks, that is the second through the fourth week, parallels the curves of the control animals signifying approximately equal growth increments taking place in control and radiated animals during this time.

The radiated animals appeared to experience a six week period of reduced growth from the fourth through the tenth week. Although this period of reduced growth increments is followed by a very mild increase in the increments from the tenth to the thirteenth week, the antegonial notch height shows an increased contouring in the radiated animals than is seen in the control group at the end of the thirteenth week.

The findings of the animals in group III will now be presented. The measurements of cranio-facial growth of animals number 13, 18 and 19 are recorded in figures 36, 37 and 38.

Total Cranial Length

Group III (Fig. 39)

Increase in total cranial length of the radiated animal (no. 13) in group III took place at a reduced rate during the
ANTEGONIAL NOTCH HEIGHT GROUP II

FIGURE 35
first month after radiation. The growth curve of the radiated animal during the first month assumed a more horizontal path than the curves of the control animals indicating that the control animals experienced larger increments of growth during this period. The increments of growth of the control animals for the first month were almost twice the magnitude of the increment of the radiated animals.

Cranial length in the radiated animal continued to increase at a reduced rate as compared with the control animals during the second and third months. Total cranial length of the radiated animal was approximately 2 mm shorter than in the control animals at the end of the second month, and 2 1/2 mm shorter at the end of the third month.

Cranial Height

Group III (Fig. 40)

Cranial height of the radiated animal (no. 13) appeared to increase at a reduced rate from the time of radiation to the end of the thirteenth week. The growth increments for the animal were less in magnitude than the increments of the control animals during the first, second and third months. This is evidenced by the lower graphical level and more horizontal slope of
### MEASUREMENTS MADE FROM LATERAL RADIOGRAPHS

<table>
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<tr>
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<th>1 month</th>
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<td>0.42</td>
<td>0.70</td>
<td>0.70</td>
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### MEASUREMENTS MADE FROM VENTRO-DORSAL RADIOGRAPHS

| Inter-zygomatic width        | 10.21     | 12.12   | 12.04    | 13.03    |
| Inter-condylar width        | 8.98      | 10.02   | 10.06    | 10.17    |

**FIGURE 36**
ANIMAL NUMBER 18

MEASUREMENTS MADE FROM LATERAL RADIOGRAPHS

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<th>3 months</th>
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<td>5.98</td>
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<td>13.72</td>
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<td>Antegonial notch height</td>
<td>0.32</td>
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<td>0.72</td>
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MEASUREMENTS MADE FROM VENTRO-DORSAL RADIOGRAPHS

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<td>8.91</td>
<td>9.36</td>
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FIGURE 37
### ANIMAL NUMBER 19

#### MEASUREMENTS MADE FROM LATERAL RADIOGRAPHS

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<td>22.61</td>
<td>23.92</td>
<td>24.70</td>
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<td>Cranial height</td>
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<td>5.30</td>
<td>5.48</td>
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<td>3.70</td>
<td>3.81</td>
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<tr>
<td>Antegonial notch height</td>
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#### MEASUREMENTS MADE FROM VENTRO-DORSAL RADIOGRAPHS

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<td>Inter-condylar width</td>
<td>8.89</td>
<td>9.51</td>
<td>9.28</td>
<td>10.20</td>
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</tbody>
</table>

**FIGURE 38**
CRANIAL HEIGHT GROUP III

FIGURE 40
the growth curve of the radiated animal during these periods. Cranial height at the end of the third month was less than the cranial height of the control animals.

Interzygomatic Width

Group III (Fig. 41)

Interzygomatic width of the radiated animal in this group (no. 13) appeared to increase at about the same rate as the control animals during the first month following radiation. During the second and third month, interzygomatic width appears to increase in slightly greater increments in the radiated animal. The slope of the curve of the radiated animal is only slightly more vertical than the curves of the control animals during the second and third month, indicating only slightly greater increments of growth during this time. Interzygomatic width of the radiated animal is slightly greater than in the controls at the end of three months.

Mandibular Length

Group III (Fig. 42)

The growth curve of the radiated animal (no. 13) ascended contiguously with the curves of the control animals to the end
INTERZYGOMATIC WIDTH - GROUP III

FIGURE 41
of the first month. During this period, the increments of growth were large for both radiated and control animals. During the second month of the experiment the slope of the curve of the radiated animal was only slightly more horizontal than the controls, and indicates only slight reduction of the growth increment for the second month. The increase of mandibular length of the control animals during the third month is slightly more than is found in the radiated animal. At the end of the third month, mandibular length of the radiated animal is less than the mandibular length of the control animals. The shorter mandibular length of the radiated animal is the result of retarded growth increments during the second and third month following radiation.

Mandibular Height Anterior

Group III (Fig. 43)

Growth curves of the radiated and control animals ascended in close relation during the first month of the experiment. All animals experienced large increments of growth in height of the mandible in the anterior region during this time, the increment of the radiated animal being only slightly larger than the increments of the control animals. The growth curves of the radiated and control animals during the second and third month showed no
MANDIBULAR LENGTH GROUP III

FIGURE 42
appreciable differences in the rate of increase of mandibular height in the anterior region. At the end of the third month, there was no evidence of difference between the height of the mandible in the anterior region of the control and radiated animals.

Mandibular Height Posterior

Group III (Fig. 44)

Mandibular height in the posterior region increased at a slightly greater rate in the radiated animal (no. 13) during the first month of the experiment. After the first month, the growth curve of the radiated animal assumed an almost horizontal path, indicating greatly reduced growth increments during the second and third month of the investigation. Although very little increase of mandibular height in the posterior region was seen in the radiated animal during the second and third month, mandibular height at the end of the third month did not differ greatly from the mandibular height of the control animals.

Intercondylar Width

Group III (Fig. 45)

The growth curves of the control animals in group III indi-
MANDIBULAR HEIGHT ANTERIOR GROUP III

FIGURE 43
cated that intercondylar width increased in width in almost equal increments during the first, second and third month. The curve of the radiated animal (no. 13) show a great difference in the magnitude of the increments for the first, second and third months. Intercondylar width increased rapidly during the first month in this animal, achieving a growth increment almost twice the magnitude of the control animals. This large increment was followed by an almost horizontal path of the growth curve, indicating reduced increments during the second and third month. Intercondylar width of the radiated animal at the end of the third month did not appear to be less or greater than the intercondylar width of the control animals.

Antegonial Notch Height

Group III (Fig. 46)

The growth curves of the radiated animal in group III indicated that antegonial notch height increased in about the same increments as the control animals to the end of the first month. Both control and radiated animals showed large increments of growth of the antegonial notch in height during the first two months and smaller increments during the third month. The growth increment from the second to the end of the third
month is reduced in magnitude as indicated by the almost horizontal slope of the curve of the radiated animal during this period. The curves of the control animals also show smaller increments of growth during the third month, but the reduction is not as pronounced as is found in the radiated animal. The height of the antegonial notch at the end of the third month is only slightly less in the radiated animal as compared with the control animals.
MANDIBULAR HEIGHT POSTERIOR GROUP III

FIGURE 44
INTERCONDYLAR WIDTH - GROUP III

FIGURE 45
ANTEGONIAL NOTCH HEIGHT - GROUP III

FIGURE 46
CHAPTER VI
DISCUSSION

The significance of mandibular condylar growth in the development of the mandible is a well established fact. Although the diagnosis of mandibular prognathism is relatively simple, its treatment frequently remains a surgical problem which is dependent upon the achievement of almost adult proportions of the mandible before correction can be effectively undertaken. It is with prevention or early interception of mandibular prognathism in mind that this research was begun.

This investigation was undertaken as a preliminary study to investigate the feasibility of utilizing x-radiation for the interception of mandibular prognathism by determining the effects of x-radiation on the condylar growth centers and craniofacial growth, and to determine the radiation effects on cartilage derived from connective tissue origin.

An effort was made to control the variables of roentgenographic procedures, the radiation of animals, and the measurement of the radiographs. The use of the animal cephalometer allowed a serial study to be made of the changes in the cranio-
facial complex following radiation of the condylar growth centers. By its use, the increments contributing to the total growth of a part could be measured, and the specific effects of x-radiation applied to the mandibular condyles determined. The effects on the configuration of the cranio-facial complex will now be discussed.

EFFECTS ON THE NEUROCRANIUM

Total Cranial Length

Graphical analysis of the growth curves of the animals subjected to condylar radiation (Figs. 16, 28, 39) indicated that, in most cases, there is some interference with growth in length of the cranium following radiation. This interference becomes evident at about four weeks after radiation of the condylar growth centers. The amount of shortening of cranial length varied between the three age groups of animals, from .6 to 1 mm shorter in the youngest animals to about 2.5 mm in the oldest age group.

The interference with growth contributing to total cranial length of the radiated animals is best explained as a result of the method of radiation rather than an effect of the radiated
condylar growth centers. As was described in the chapter on methods, x-radiation was applied from the lateral aspect of the cranium to the left condylar growth center. The x-rays continued on through the basal structures of the cranium and passed through the right condylar growth center. With the portal of the lead casket centered over the condyle, it is evident that a considerable amount of radiation was delivered to the body of the basisphenoid bone before reaching the opposite condyle. It is almost possible that the basispheno-occipital synchondrosis received a portion of the delivered dose.

Growth in length of the cranium is accomplished to a major extent by the growth in length of the basisphenoid bone and endochondral growth at the basispheno-occipital synchondrosis. It is then evident that if the amount of radiation delivered to the basisphenoid bone and associated structures was inhibitory to the growth of the basisphenoid bone, total cranial length may be reduced.

An explanation remains necessary for the lack of cranial length reduction found in the radiated animals of the second age group. In these animals there appeared to be no reduction
of cranial length, and as will be discussed later, no reduction in cranial height. It is possible that the portal of the lead casket was placed in a more superior position over the mandibular condyle during radiation of the animals, allowing radiation to be delivered to the condyles by restricting the radiation from the basisphenoid bone and synchondrosis. This accounts for the uniform growth of the cranial base and lack of reduction of the cranial length as was found in these animals.

Cranial Height

Analysis of the growth curves revealed that although two of the radiated animals (no. 2, fig. 17 and no. 13, fig. 40) showed evidence of reduced cranial height, reduction of the height of the cranium was not a general finding of this investigation. There appeared to be no observable differences in the morphology of the cranial outline of the radiated and control animals in each group. The morphologic changes of the superior border of the cranium as seen on the lateral radiographs were those changes associated with maturation of the animals.

In this investigation, cranial height was measured from the orientation line to the highest point on the superior border of the cranium as seen on the lateral radiograph. The orientation
line OL. (fig. 9) was down thru the center of the basisphenoid bone and inferior border of the palate. When measuring cranial height, the morphological changes associated with maturation of the animal become evident in the changing position of the highest point on the superior border of the cranium. In the young animal, the superior cranial border outline is strongly convex, placing the highest point near the middle of the cranium. As age increases, the cranial outline becomes more flattened antero-posteriorly, placing the highest point on the outline more posterior.

Washburn (1943) investigated the growth of the superstructures of the cranium to which the post-cervical musculature attaches. He found that the superstructure failed to develop following the resection of muscles.

Jarabak (1953) found that as cranial length increased, so did cranial height in the occipital region. Height of the cranium in the occipital region continued to increase after neurocranial length has ceased. This was attributed to the continued growth of the superstructures associated with the attachment of the post-cervical musculature.

Both Washburn and Jarabak report that there appears to be
a correlation between growth in height of the cranium in the occipital region, and the demands placed on the occipital bone by the post-cervical musculature.

Since it is highly doubtful that the x-radiation applied to the mandibular condyles in this experiment had any effect on the post-cervical musculature, it is not probably that any difference should be evident between the cranial height of the radiated and control animals. No differences were seen in this investigation.

Interzygomatic Width

Growth in width of the zygomatic arches appeared to be reduced in the radiated animals of the first and second age groups (groups I and II). This reduction in the increments of growth became apparent on the lateral radiographs two and four weeks following radiation (fig. 18 and 30) and was still evidenced at the end of the experiment by the lesser interzygomatic width of the radiated animals.

Two possible explanations can be offered for the reduction in interzygomatic width following radiation. The first explanation is that x-radiation delivered to the condylar growth centers effected the growth in width of the zygomatic arches. Jarabak (1953) in a study of the cranio-facial changes following complete removal of the mandibular condyles, found no evidence of
reduction of interzygomatic width in the operated animals.

The second explanation is that interzygomatic width was reduced in the radiated animals due to concurrent radiation of the posterior root of the temporal part of the zygomatic arch during radiation of the mandibular condyles. The molar teeth were in occlusion during radiation of the condylar growth centers, placing the condyles in the posterior portion of the articular fossae at this time. Since the articular fossae are located on the underside of the posterior roots of the temporal part of the zygomatic arches, it is seen that the path of x-rays must necessarily pass through the roots of the zygomatic arches in order to be directed through the mandibular condyles. It is possible that the reduced interzygomatic width seen in the radiated animals of the two younger groups, is the effect of radiation of the roots of the zygomatic arches. Appositional growth of the temporal bone, along with concurrent growth of the other cranial bones, directly contributes to the increase in interzygomatic width (and zygomatic length). Interference with appositional growth of the temporal bone as an effect of x-radiation may be manifested in a decrease in the measurements to which its growth contributes, explaining the reduction in interzygomatic width of the radiated animals.
The reduced interzygomatic width as found in the irradiated animals is probably the result of x-radiation of the mandibular condyles.

Review of the findings of previous investigations concerning the effects of radiation on bone growth are necessary to propose an explanation of the apparent lack of reduction of interzygomatic width exhibited by the radiated animal in the oldest age group (group III).

The mode of action of roentgen-rays on bone has been investigated by numerous investigators, including Ewing (1926), Clark (1936), Gates (1943), and Heller (1948), Flashamp (1930). Flashamp (1930) studied the effects of radiation on bone and states that "retardation or cessation of growth of bone in young animals is a quite constant effect of radiation, provided the dose is above the threshold of tolerance." Hinkel (1943) conducted experiments to quantitatively study the sensitivity of the rat femur and to show the influence of age on the effect produced. Besides confirming the findings of others, that retardation of growth was in direct proportion to the dose, Hinkel clearly established that age of the animal at time of radiation did indeed influence the effect of radiation on bone growth.
The radiated animal in group III was 37 days of age at the time of radiation. Interzygomatic width in this animal showed no decrease from the width of the control animals. This animal received the same dose (1500 r) as the radiated animals in the first two groups. It is possible, that due to the older age of this animal, the dose of radiation which was effective in the younger animals was below the threshold of tolerance of this animal and did not effectively interfere with growth contributing to interzygomatic width.

Mandibular Length

The importance of the mandibular condyles has been discussed in a previous chapter. The ability of x-radiation to retard growth of the mandible by inhibiting proliferation in the condylar centers has been studied by Burstone (1950) from a histological aspect. Burstone's conclusions, based on these histological findings, were that inhibition of the growth process in the condylar growth centers was the prime effect of x-radiation applied to the growth centers and that the amount of inhibition was determined by the dose of radiation. In view of Burstone's findings, this investigation endeavored to utilize a radiographic technique to appraise and measure the gross changes in mandibular dimensions following radiation of the
condylar growth centers.

It was found in this investigation that the application of 1500 r of x-radiation to the mandibular condylar growth centers caused a measurable reduction in the growth increments contributing to mandibular length. This reduction, or inhibition of growth, was apparent in all cases within two weeks following radiation. The duration for which the increments were reduced, that is, the length of time in which inhibition of growth in length was evident, varied in the three age groups of animals. While all irradiated animals showed shortened mandibular length at the thirteenth week of the experiment, the amount of shortening varied between the irradiated animals of the three groups. As illustrated in (fig. 19), the growth curves of the radiated animals indicate that the increments of growth during the first two weeks after radiation exhibits far greater reduction than any of the growth increments which follow. Although mandibular length in these animals was shortened at the end of thirteen weeks, all growth increments were not equally inhibited.

The duration for which the increments of growth were inhibited appeared to vary more between the animals of the three age groups than between animals of the same group. Several important findings are evident concerning the effect of x-
radiation on the condylar growth centers. First, it is possible to inhibit the growth contributing to total mandibular length by applying x-radiation directly to the condylar growth centers, and the effect can be demonstrated in linear measurements. This finding may provide the stimulus for further investigation regarding the use of x-radiation for the interception of developing prognathic mandible.

The second finding concerns the dose of x-radiation used in this experiment. Since no previous studies had been reported concerning the effects of x-radiation on mandibular growth in the rat, the dose of radiation which would be effective in inhibiting mandibular growth was unestablished. The dose of 1500 roentgens used in this experiment has proved to be an effective dose in inhibiting growth of the rat mandible in length. While it has proved to be an effective dose for the age of animals utilized in this experiment, one can only speculate if the optimal dose lies above or below the dose utilized in this experiment.

The third finding concerns the effect of x-radiation on cartilage derived from connective tissue origin and cartilage derived from interstitial growth of cartilage cells. It is
generally agreed that growth of the mandibular condyle is the result of appositional growth from the connective tissue overlying it. This investigation found that growth of the mandible and condylar cartilages is inhibited by x-radiation applied to the condylar growth centers.

An allied investigation (part II) carried on in conjunction with this investigation, investigated the effects of the same dose of x-radiation (1500 r) applied to the distal epiphysis of the femur. The findings of Part II were not unlike the findings reported previously by Gall, Lingley and Hilcken (1940), and Hinkel (1943), and demonstrated the ability of x-radiation to inhibit the growth of long bones following radiation of the epiphyseal cartilages. The findings of this investigation, when compared with the findings of Part II and previous studies concerning the effects of x-radiation on epiphyseal cartilages, indicates that the effects on cartilage derived from connective tissue origin by apposition do not differ from the effects on cartilage whose origin is the interstitial growth of cartilage cells.

Mandibular Height

There appeared to be no appreciable difference in the height
of the mandible below the first molar tooth of the radiated animals as compared to the control animals. Although the growth curves of the radiated animals (fig. 20), in some instances, indicated that the increments of growth were not as uniform in magnitude as the increments of the controls, the mandibular height of the radiated animals at the end of the experiment did not significantly differ from the controls.

In a previous investigation, Jarabak (1953) found that mandibular height below the first molar tooth increased following the removal of the mandibular condyles. In his investigation, the increase in height in this area was attributed to the lack of function and attrition of the lower incisor tooth with its antagonist due to posterior displacement of the mandible following operation. The incisor was found to continue to grow in the arch of a perfect circle, and the increased dimension of the mandible below the molar tooth was considered the sequela of its continuous eruption without attrition, rather than actual increase in alveolar process height.

Radiation of the mandibular condyles did not cause an observable change in the antero-posterior relation of the mandible, and function and attrition of the incisor teeth did not
appear to be interfered with in the radiated animals. Although these findings are not sufficient to corroborate or deny the findings of Jarabak's (1953) investigation they add credence to the theory that the increase of mandibular height below the first molar tooth was the sequela of continual eruption of the unopposed lower incisor, rather than growth in the body and alveolar process.

While height of the mandible in the anterior region did not appear to differ between radiated and control animals, mandibular height in the posterior region, that is, in the region of the angle, did appear to be reduced in the radiated animals. This finding is not considered unusual in light of the findings concerning mandibular length. Growth in the condylar growth centers is expressed in a downward and forward migration of the mandible. Inhibition of condylar growth as an effect of x-radiation delivered to these growth centers is then expressed in a reduction of the measurements associated with growth in length and height of the mandible. Reduction of the height of the mandible below the condylar centers is considered to be the direct result of reduction in growth of the condylar growth centers as an effect of x-radiation.
Intercondylar Width

The erratic nature of the growth curves associated with intercondylar width of both radiated and control animals leads this author to believe that the method employed in this investigation was not suitable to record accurately the changes in intercondylar width. The increments of growth contributing to intercondylar width varied so greatly between consecutive measurements as to cast doubt on the reliability of these measurements.

When placing the animals in the animal cephalometer (fig. 3) to take the ventro-dorsal radiograph, it was found that the ear-rods, which hold the cranium in the proper position during radiography, exerted varying amounts of pressure to the soft tissues behind the mandibular condyles. It was found that the pressure exerted in this area was of sufficient magnitude to cause varying amounts of constriction of the intercondylar width. This was possible due to the fact that the union of the mandible in the symphysis is a fibrous one, allowing compression of the inter-condylar width when the ear-rods were firmly placed. Therefore, although the findings concerning growth in intercondylar width are recorded in this investigation, the veracity of these measurements remains doubtful.
Antegonial Notch Height

Measurement was made of the height of the antegonial notch on the inferior border of the mandible because a previous investigation (Jarabak 1953) had demonstrated that its height increased following surgical removal of the condyles. Jarabak in explanation of this finding stated, "lack of growth of the condyle brought about by resection."

This investigation did not find the antegonial notch height to be increased in the radiated animals. On the contrary, some of the radiated animals experienced a slight decrease in the height of the notch. In general, no difference could be established between the antegonial notch height in the radiated animals as compared to the control animals. These findings tend to indicate that the increase in height of the notch as found in Jarabak's (1953) study were probably morphological changes more closely associated with change in muscle relation and altered function due to posterior displacement of the mandible following resection of the condyles, rather than a direct result of arrested growth in the condyles.

The results of this study, represent some of the craniofacial changes which take place following x-radiation of the mandibular condyles.
CHAPTER VII
SUMMARY AND CONCLUSIONS

Summary

The effects of x-radiation on the mandibular cartilage and cranio-facial growth were appraised radiographically.

Eleven female albino rats of the Wistar stock served as the subjects of the investigation. A single dose of 1500 r of x-radiation was delivered to the mandibular cartilages of the experimental animals. Using a small animal cephalometer, lateral and ventro-dorsal radiographs were taken of the skull at two week intervals for a period of approximately three months. Measurements of cranio-facial growth were made indirectly from the enlarged images of the projected radiographs. The measurements were analyzed graphically.

Observations made from the findings are:

1. Total cranial length was shortened in the animals subjected to condylar radiation. This effect is believed to result from extraneous radiation during condylar radiation.
2. Cranial height did not appear to be affected by condylar radiation.

3. Interzygomatic width is reduced following x-radiation of the mandibular condyles, providing the dose of radiation is above the threshold of tolerance of the animal.

4. Mandibular length was measurably shortened following x-radiation of the condylar growth centers.

5. 1500 roentgens of x-radiation was found to be an effective dose when applied to the condylar growth centers of the rat.

6. Mandibular height in the region of the first molar tooth, was not affected by x-radiation of the mandibular condyles.

7. Mandibular height in the region of the angle of the mandible, was shortened following x-radiation of the condylar growth centers.

8. Height of the antegonial notch was not effected by condylar radiation.

The conclusions drawn from these findings are:

1. Growth of the mandible is effected by x-radiation
applied to the condylar growth centers. The effects of x-radiation on cartilage of connective tissue origin are the same as on cartilage which grows by interstitial growth.

2. From the findings of this investigation, on rats, it does not appear feasible to utilize x-radiation for the interception or prevention of mandibular prognathism, due to the unfavorable concomitant effects of radiation on adjacent parts of the cranio-facial complex.
CHAPTER VIII

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APPROVAL SHEET

The thesis submitted by Dr. Jerome John Kozakiewicz has been read and approved by members of the Departments of Anatomy and Oral Biology.

The final copies have been examined by the director of the thesis and the signature which appears below verifies the fact that any necessary changes have been incorporated, and that the thesis is now given final approval with reference to content, form, and mechanical accuracy.

The thesis is therefore accepted in partial fulfillment of the requirements for the Degree of Master of Science.

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Date

Signature of Adviser