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The Application of Differential Diagnosis to the Paleopathology of Acromegaly and Giantism

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ABSTRACT

The Application of Differential Diagnosis to the Paleopathology of Acromegaly and Giantism

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The diagnosis of giantism and acromegaly were examined in case studies from paleopathology literature. Major diagnostic characteristics were noted as used by the authors and analyzed to examine how the diagnoses of giantism and acromegaly were actually being applied to skeletal material. Autopsied soft tissue case studies were also used. The results of this study showed that diagnoses of giantism and acromegaly have been inconsistently applied, and that a clear understanding of the disease process in the living is necessary to understand the skeletal changes that can occur. Also, researchers did not offer enough information to allow for independent assessment of diagnosis by others. Statistical analysis showed that a majority or researchers made the diagnosis of giantism based upon "greater than average height" and the diagnosis of acromegaly based upon the "elongation of the mandible". Finally, an overall system of differential diagnosis for giantism and acromegally was generated.

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INTRODUCTION

The accurate assessment of disease processes in human skeletal materials is important in the generation of a biological profile. This in turn is essential to the study of other areas, such as paleodemography, prehistoric community health, and forensic anthropology. This study will systematically examine the disease processes of giantism and acromegaly, both of which have been identified in a number of historic and prehistoric case studies. Giantism and acromegaly, the juvenile and adult forms of the same disease process, are associated with the overproduction of growth hormone (GH), which is often associated with a pituitary adenoma.

Both acromegaly and giantism have been identified in human skeletal remains. Giantism and acromegaly result from an imbalance in the endocrine system, which is specifically linked to the presence of a specific pituitary tumor, an acidophilic adenoma. What separates the hyperpituitary giant from the acromegalic is the age of onset of the disease process. Children or those individuals who have not reached puberty could show the clinical signs and symptoms of giantism. Adults or those individuals who have gone through puberty could be considered acromegalic (Aegerter and Kirkpatrick 1975:379).

Overproduction of growth hormone, usually associated with these pituitary adenomas or tumors, often leads to many of the characteristic clinical features of acromegaly and giantism. Giantism is characterized by excessive height with normal body proportions, whereas acromegaly is characterized by excessive growth of the extremities and the skull (particularly in the mandibular condyle). Uncomplicated

giantism is characterized by bones that are long but are not massive. Many clinical symptoms such as cardiac disease, depression and diabetes are also associated with pituitary adenomas (Robbins and Cotran 1979:1338-1339, Jaffe 1972, and Hayles 1980).

"In acromegaly, bone deposition occurs and leads to... extreme height" (Roberts and Manchester 1997:181). While the most commonly cited feature is excessive height, Aufderheide and Rodriguez-Martin (1998: 327) point out that acromegaly occurs in "normal adults whose tumors develop after growth has ceased." These authors also note that those suffering from giantism can become acromegalic in adulthood if their pituitary tumors remain active. Since other diseases produce skeletal characteristics that overlap with acromegaly and giantism, it is necessary to distinguish among these similarly appearing conditions. In order to address this issue, differential diagnosis can be used. Differential diagnosis, usually used to assess the disease state in a living individual, is implemented in skeletal biology and paleopathology to distinguish among disease processes with similar lesions (Buikstra 1976).

This thesis will examine the diagnosis of acromegaly and giantism in human skeletal remains through a systematic review of the literature. Using present medical knowledge of the clinical presentations of these diseases, as well as information from paleopathology, a systematic method of differential diagnosis will be generated. Within this framework, variations of the presentation and distribution of skeletal pathologies of giantism and acromegaly will be discussed using a number of case studies. Cultural concepts will also be addressed as they relate to the observer's ability to accurately identify giantism and acromegaly in the human skeleton.

CHAPTER 1

DISCUSSION OF GIANTISM AND ACROMEGALY

Anatomy of the Pituitary

Tumors of the pituitary can affect the individual in two ways. First: the physical presence of the tumor as it affects adjacent structures. Second: changes can result in the production and secretion of pituitary hormones or "hypothalamic principles" (Anderson and Kissane 1977:1616). Knowledge of the anatomic relationships of the pituitary to its environs, therefore, is essential in understanding the symptoms caused by pituitary tumors (Anderson and Kissane1977:1603, Robbins and Cotran 1979:1338). Growth of this tumor can cause erosion and remodeling of the sella turcica as well as surrounding bony structures (Aufderheide and Rodriguez-Martin 1998: 327-328, Ortner and Putshcar 1999:298).

In the adult, the pituitary gland is situated in the hypophyseal fossa of the sella turcica in the sphenoid bone of the skull. The optic chiasm, hypothalamus, and the third ventricle lie directly above the gland. Lateral to the pituitary on each side are the cavernous sinuses, each containing the internal carotid artery and cranial nerves III, IV, IV, and VI. If the tumor expands, these structures can be impacted (Weinreb 1984:277-283, Moore 1992:637-782).

As the pituitary tumor expands, its physical presence can exert pressure on the sella turcica and its surrounding tissues. Space-occupying lesions in general cause nausea, vomiting, headaches and increased intercranial pressure (Robbins and Cotran

1979, Jaffe 1972:333, and Cushing and Davidoff 1927). Headaches are one of the first signs that press people to seek medical help (Cushing and Davidoff 1927). As the optic chiasm and nearby nerves are compressed by the expanding tumor, visual disturbances can result. If the pituitary tumor expands such that the blood flow is cut off to the tumor, this disease can burn itself out (Jaffe 1972:333, and Robbins and Cotran 1979:1340).

If the tumor continues to grow and expand, the posterior lobe of the pituitary and the hypothalamus can be affected (Weinreb 1984:277-283). The pituitary gland itself can be compromised, which can lead to an insufficiency of pituitary hormones or diabetes. Production and transport of releasing substance and inhibitory factors can be affected when a pituitary tumor physically crowds the hypothalamus. The hormones secreted by the pituitary and their actions are listed in Table 1 (modeled after Weinreb 1984:282-283).

Table 1: Hormones Secreted by the Pituitary and Their Actions

- Growth hormone: promotes bone growth
- Thyrotropin: involved in metabolism regulation
- Adrenocorticotropin: stimulates secretion of glucocorticoids

Gonadotropins
- Follicle-stimulating hormone: involved in functioning of ovary and testis
- Luteinizing hormone: ovary function: secretion of estrogen and progesterone
- Interstitial cell-stimulating hormone: testis function, secretion of testosterone
- Prolactin: lactation and mammary glands
- Melanocyte-stimulating hormone: Stimulates melanin/pigment production on skin

Hypothalmus
- Oxytocin: affects mammary glands and uterus
- Vasopressin/antidiuretic hormone: affects kidneys water reabsorption, vasoconstriction, too little causes diabetes

As functions of the pituitary and hypothalamus are affected, imbalance of the endocrine system can occur (Robbins and Cotran 1979:1338). The pituitary gland, along with many other glands found throughout the body, is part of the endocrine system. These glands secrete specific hormones that are involved in the regulation of body activities. The endocrine system's operations involve all tissues in the body, which is why its influence "is widespread, of longer duration, and results in more diversified, slower effects suitable to responses that require time, such as metabolism, growth and reproduction"(Weinreb 1984:272) With this information, it is easy to see why involvement of the pituitary would lead to a slow progression of the disease with whole body involvement.

Tumors in the anterior pituitary are responsible for two distinctive, but interrelated, syndromes. Giantism or acromegaly occur with the overproduction of growth hormone. Amenorrhea-galacctorrhea results from the overproduction of prolactin. "Structurally GH is similar to prolactin and many patients with acromegaly have hyperprolactinaemia" (Bouchier and Morris 1982:577). Cessation of menstruation and infertility can result (Robbins and Cotran 1979:1339).

In order to understand the distribution of lesions in a systematic manner, acromegaly and giantism will be examined as one disease-state that is differentiated by developmental age of onset. Hyperpituitarism is the general term used to designate increased levels of growth hormone regardless of age at disease onset (Robbins and Cotran 1979:1339). "The term hyperpituitarism should, in reality, apply to any syndrome resulting from hypersecretion of any one of the trophic hormones. Clinically, this usually refers to acromegaly and giantism" (Robbins and Cotran 1979:1339).

Description of Giantism and Acromegaly

Giantism and acromegaly occur in approximately three people out of one million (Robbins and Cotran 1979). In contrast, Bouchier and Morris (1982:575) suggest one in 10,000 for acromegaly. At autopsy, pituitary tumors were evident in 25% of the population examined (Harrison 1981:1899). Males and females show an equal rate of occurrence. Diagnosis is usually not made until the disease has progressed for 10-15 years. The average age at diagnosis is in the early 40's. Researchers suggest that acromegaly might have a genetic component in some cases. Inheritance is thought to be autosomal dominant (McKusick (c) 1986, Nabarro 1987 and "National Institutes of Health" 1995).

A pituitary adenoma is a cause of giantism and acromegaly. Overproduction of growth hormone before puberty can lead to excessive height due to the unrestricted growth at the epiphyseal plates. Because hypogonadism commonly accompanies giantism, the lack of sufficient gonadal hormones delays puberty and epiphyseal closure. Connective tissue of the skin and other subcutaneous tissues, such as ligaments and synovial membranes are also affected by the overgrowth (Jaffe 1972, and Robbins and Cotran 1979).

When height is increased, growth is increased proportionality through out the entire skeletal system. If height is extreme, other lesions often result from the increased weight of the individual, such as spinal curvature, vertebral arthritis, and general arthritis. Fractures of weight-bearing bones can occur due to simple mechanical stress from the increased weight load. This is complicated by the osteoporosis that can occur with acromegaly and giantism (Anderson and Kissane 1977:1928, Aufderheide and

Rodriguez-Martin 1997:327). The sella turcica can be enlarged due to the pituitary tumor (Ortner and Putschar 1981).

Acromegaly, characterized by continued overgrowth of soft tissues and connective tissue, develops in adulthood after epiphyseal closure takes place. This overgrowth results in many of the identifying facial and skeletal characteristics of acromegaly. "Acral" refers to the hands and feet. "Mega" refers to large. Together, these two concepts refer to the large hands and feet found in advanced acromegaly (Robbins and Cotran 1979:1340). Because of the characteristic growth in the bone and soft tissue of the face and skull, acromegalics are often said to look more like each other than like members of their own family (Harrison 1981:1899).

Initially, there are few observable physical signs of acromegaly. Often the first indication of the process is frequent, debilitating headaches often accompanied by nausea and vomiting. Hat, shoe, and glove sizes increase, but often the people do not take much notice until commented upon by others. Gradually, changes in skin coloration and texture occur. The skin becomes thickened and darkened with an increased production of sebaceous substances (Cushing and Davidoff 1927).

Women experience ammenorrhea, the cessation of menstruation without pregnancy or menopause (Jaffe 1972:334). Men often experience decreased libido and degeneration of the testicular tissue (Hamwi 1960:695). Increasing duration of the disease tends to increase the reproductive system changes (Nabarro 1987).

In general, the facial features of an individual with acromegaly become broader and coarser. Supraorbital ridges, or brow ridges, and the malar prominences, or cheeks, become more pronounced, and the exterior occipital protuberance becomes exaggerated

(Ortner and Putschar 1981). The jaw lengthens due to the increased growth at the mandibular cartilage. Mandibular deformation occurs with increasing severity as judged by increasing length of the lower jaw in relation to the maxilla. The chin juts forward due to bone growth at the mental eminence. As this disease progresses, an increasing prognathism can occur due to the bone growth expanding the maxillary and mandibular radii. Teeth become widely spaced. Radiographs often reveal huge frontal sinuses and a noticeably thickened skull (Ortner and Putschar 1981, and Jaffe 1972).

The appendicular skeleton also exhibits distinctive changes as result of the bone and connective overgrowth. Fractures can occur due to simple mechanical stress, which is complicated by osteoporosis (Robbins and Cotran 1979:131339). Tufting of the distal phalanges may occur, giving the fingers a clubbed appearance upon physical examination. Increased growth at the costo-chondral junction results in elongation of the ribs, which leads to an increased diameter of the thorax (Bouchier and Morris 1982:575, and Ortner and Putschar 1981). Overall, all prominent points of the skeleton demonstrate increased rugosity (Ortner and Putschar 1981).

Clinically, the individual presents with a series of symptoms that can be life threatening. Cardiovascular disease including hypertension is common, due to the overgrowth of connective tissue. Upper airway obstruction occurs due to soft and hard tissue overgrowth. Endocrine system imbalances such as hyperprolactinemia, diabetes, hypogonadism, hypothyroidism, hypoadrenalism and decreased reproductive and sexual functions can occur due to the physical presence of the tumor or the abnormal production of secretions (Weinreb 1984, and Nabarro 1987).

The skin becomes coarse and leathery. Skin coloration can become either very pale or dusky. Pores are apparent and sebaceous gland activity produces oily skin with increased sweating. Acne is a common complaint. There is thickening of heel pads and other soft tissue particularly in the hands, face, and feet. The tongue and lips become thicker and larger, interfering with speech and eating. Enlargement of the internal organs such as the heart, liver, spleen, stomach etc. can cause other serious health problems such as cardiovascular disease and strokes (Cushing and Davidoff 1927).

Most often noted are the neurological changes that alter the person's intellect and consciousness. As the disease progresses, lethargy and exhaustion increase. It is difficult for the person to orient and focus to tasks, and visual fields become limited. Metabolic disturbances often add to the clinical symptoms. Diabetes, the inability to adequately metabolize sugars such that physical wasting occurs, is common (Robbins and Cotran 1979:1339). Frequent urination, thirst, and incessant hunger are other developments. Scoliosis occurs in a way characteristic to acromegaly (Cushing and Davidoff 1927) Thoracic kyphosis is often present (Aegerter and Kirkpatrick 1975:380).

Constipation is a common complaint of those affected by acromegaly/giantism. Appetites are often curtailed by the physical changes in the teeth, tongue and jaws. Chewing, swallowing and talking are also compromised. A grossly enlarged tongue is very common in acromegaly. Often, the tongue is so large it does not fit in the mouth. Drooling results from the lack of space and in the inability to swallow. As the jaw grows, malocclusion of the teeth occurs. Since the teeth do not fit together well, chewing can be difficult. This growth in the jaw also causes the teeth to become spaced

farther and farther apart, which also can create difficulties in speech and eating (Cushing and Davidoff 1927, and Ortner and Putschar 1981).

As the person's weight increases, their lower extremities are stressed by the increased weight bearing demands (Aufderheide and Rodriguez-Martin 1998, and Aegerter and Kirkpatrick 1975:377). Muscles weaken, which can cause kyphosis and gracile lower extremities (Ortner and Putschar 1981). Not only do the feet grow in width and length due to an increase in bone dimensions, but extreme soft tissue overgrowth occurs as well (Aufderheide and Rodriguez-Martin 1998:327, and Ortner and Putschar 1981).

Giantism and Acromegaly Literature Researched

Giantism and acromegaly have been discussed in the literature for over a hundred years. In order to collect as large a sample as possible of reported acromegaly and giantism in skeletal populations, the first stage of this research is a thorough review of the literature. A literature search was conducted first using the Magic system at Michigan State University. Acromegaly, giantism, giants, giant skeletons etc., were used to search this database. The MSU system has an agreement with other collections at Midwestern university libraries, which were also searched. ERL Databases were searched from the MSU library system. Other potential references were identified from articles and books.

The internet search system was also used to find references to skeletal remains designated as acromegalics and giants. A request for information was circulated on a biological anthropology list serve. Contacts were made through referrals from people

with information of private collections or other sources such as museums and private libraries. Smithsonian records and materials were made available, as were materials housed in the Mutter Museum and Library, located in Philadelphia. In addition, one private collection of documents, photographs, and medical records dealing with nationally and internationally recognized giants was examined. Skeletal case studies were included only if no medical treatment was involved, and they were used as examples of acromegaly or giantism in the medical and archaeological literature.

After reviewing the available literature regarding acromegaly and giantism, it was apparent that a fundamental problem existed. Overall, it was difficult to determine from the literature on giantism/acromegaly a generally accepted definition of individuals with "giantism" or "acromegaly." This paper, therefore, will attempt to take information from archaeology, medical literature and physical anthropology and synthesize a single view of acromegaly and giantism from the varying literature. In this way, a single concept of diagnosis will be achieved out of the very different views and definitions of what it means to be a "hyperpituitary giant" or an "acromegalic".

Because modern medical interventions will add more variables than can be addressed within the scope of this research, modern cases will be included in the study only as long the individual was not treated. The cited examples of acromegaly and giantism used in this project will be re-examined, types of pathologies and locations will be noted, and differential diagnoses will be carried out.

In her research on tuberculosis, Jane Buikstra incorporated modern examples of pathology resulting from similar disease states. These examples were then used as the pool for comparison with her data. She emphasizes " ... that an attempt was made to

use sources that described pathology in the absence of modern chemotherapy and surgical treatment. Although other texts were surveyed, greatest weight was given to earlier sources, provided that accurate diagnosis had been made." (Buikstra 1976:325) She then uses a process of elimination or differential diagnosis, to remove from the list, disease forms which were least likely to be associated with the characteristic pathologies. This thesis will follow a similar methodology.

CHAPTER 2

METHODS

Differential diagnosis, the second stage of this research, examines the pattern of distribution of lesions throughout the entire skeletal system. This assessed pattern is then compared to the distribution of lesions of known diseases with similar presentation. If there is a good fit between the observed and expected pathology distribution, a diagnosis is made. If not, the process begins again with a new set of parameters/possible diseases being chosen. If the individual was diagnosed with giantism or acromegaly by other sources, it remained in the study although the documented diagnosis would be evaluated.

Differential diagnosis is a tool used by medical practitioners to identify disease states of patients so that treatment can be initiated. Physical anthropologists have modified this tool for work with skeletal material. Diagnosis becomes differential diagnosis when two or more diseases could be the causative agents for the clinical presentation (Bouchier and Morris 1982:29). Bouchier and Morris (1982:29) represent the diagnostic process through a number of steps: (#1) Acquisition of data, (#2) Therapeutic decisions OR (#1) Acquisition of data, (#2) Analysis of Data, (#3) Are the Data Accurate?, (#4) What is the Problem?, (#5) What is the Cause?, (#6) Therapeutic Decisions. This diagnostic system will be modified for use in this project since therapeutic decisions are not relevant with skeletal material.

To examine the diagnosis of the cases presented, phrases that were used to describe the skeletal characteristics of acromegaly will be noted for each case. These

phrases will be condensed into a comprehensive list of all the characteristics mentioned in all the cases in an attempt to judge the accuracy of diagnosis overall (see Appendix 2). Buikstra (1976) states that accurate diagnosis is essential to generate an accurate profile of a population.

Diagnosis of each case will be given as described in the literature. The diagnoses used are giantism, acromegaly with giantism and acromegaly. Heights are stated in centimeters for ease in analysis. The characteristics are ranked according to the frequency in which they were used amongst all the cases, all the acromegalic cases, all the hyperpituitary giant-acromegalic cases and all the hyperpituitary giant cases. In this manner, it will be possible to assess what characteristics were actually being provided as evidence for each diagnosis. A list of the characteristics used in the literature is presented in Appendix 1.

Individual diagnosis is examined in differential diagnosis. A t-test will then be used to examine these diagnoses as a distinct population to better understand differential diagnosis of acromegaly and giantism as used in the literature. This statistical testing will be presented in the Analysis and Discussion chapter.

An examination of what is not present will also be conducted for each individual case study. For example, the absence of characteristics in the presence of an eroded sella turcica should be noted as well, thereby allowing comparison between expected characteristics and those actually observed. In addition, this will define what was noted as not present as opposed to what characteristics were not used. Hamwi *et al* (1960:698) stated that, "A review of 30 clinical cases of acromegaly showed

radiological evidence of sella abnormalities in only 25". Therefore, acromegalics do not necessarily present an enlarged sella turcica.

Conversely, since destruction of the sella turcica can occur as a result of tumors that do not affect hormone secretions (Aufderheide and Rodriguez-Martin 1998:326), it is possible to have an eroded sella turcica without having giantism or acromegaly. It is interesting to note that Aufderheide and Rodriguez-Martin (1998:328) do not equate an eroded sella turcica with giantism, but Ortner and Putschar (1981:298) do. These examples underscore the need for a thorough and systematic definition of giantism and acromegaly in skeletal remains. Understanding the disease process is key to diagnosis.

Differential Diagnosis

As has been mentioned, differential diagnosis is a tool commonly used in the medical field to treat patients. Cummins and Eisenberg (1986:xvii) describe the process as follows:

> "*Step One:* Clinical information is gathered....
> "*Step Two:* Possible diagnoses come to mind....
> "*Step Three*: Possible diagnoses are evaluated and refined....
> "*Step Four*: A tentative diagnosis is selected....
>
> "Clinicians evaluate the possible diagnoses primarily by asking further questions. There is an enduring clinical axiom that most diagnoses are made during the history-taking... Research into clinical problem – solving suggests that the central strategy clinicians use is "feature-matching" or family resemblance. Clinicians possess knowledge about various diagnoses. They attempt to match the features of the patient's problems with their prior knowledge of the diagnoses they consider possible. They catalog features from the patient's history, physical examination, or laboratory tests that might match a mental picture of various diagnoses" (Cummins and Eisenberg 1986:xv).

It is important to note that Bouchier and Morris (1982:31) state that the diagnostician affects the success of the diagnosis by the fullness of his or her knowledge base. The more possible disease states that the clinician is familiar with, the greater potential for successful diagnosis.

Medical diagnosis is an art and not a science. This is true for physical anthropologists also. Diagnosis is based upon the experience of the observer. Medical diagnosis is not like a test for syphilis, where a sample is tested in a lab with the results either being "yes/present" or "no/not present". It is not that simple. A test gives data, a diagnosis gives results after data is analyzed. For example, there is no height divider when dealing with giantism and acromegaly. A long, prominent chin is not conclusive evidence of acromegaly. It is a constellation of symptoms that indicates "giantism" and "acromegaly" in modern medical diagnosis. Modern diagnosis is based on the observation of the whole and on the presence or absence of certain characteristics. Within the diagnostician's mind, when doing a diagnosis, it is a process of matching observed characteristics as the best fit to a specific disease (Cummins and Eisenberg 1986:xv).

Differential diagnosis in paleopathology begins with understanding/noting the provenience of the individual in regard to time and space, which helps to place the individual in context of a population. A biological profile of the individual is preformed and recorded; a biological profile includes sex, age, ethnicity, height and describes lesions and other markers present (intentional modifications, taphonomic changes, etc.). A list of the general condition of the skeleton and the bones present is therefore generated.

Age and sex might be determined before any pathological processes can be explored. Aging of those with hyperpituitarism is unfortunately suspect, as will be discussed later. Sexing acromegalics might prove difficult as well as acromegalics can exhibit severely coarsened facial features and overgrowth in the area of the pubic symphysis. This implies that sex, age and ethnicity should be re-examined after differential diagnosis is initially performed to discern how the diagnosed disease-state could affect conclusions in these three areas.

As has been stated, lesions present are noted. These lesions are referenced with other diseases that have concordant lesions to find a best fit. The constellation of lesions are compared to the constellation of lesions of similar disease states. The lesion pattern of the skeletal material is found to have a convincing match or not to an array of lesions that are commonly associated with a given disease. The more characteristics that are in common between the known array with the sample, the more convincing the diagnosis. The compiled list of lesions noted in the literature for acromegaly is found in Table 2 and for giantism in Table 3[1]. Some characteristics are more strongly associated with a specific disease than other characteristics. For example, a remodeled or enlarged sella turcica with other lesions strongly suggests hyperpituitarism. However, lack of an enlarged or remodeled sella turcica if there are other acromegalic lesions, does not mean than acromegaly is not a possible diagnosis.

[1] In some cases, different descriptions were used in the literature to potentially refer to the same condition. For this project, ALL descriptions used in the literature are presented without interpretation.

Table 2: Compiled List of Lesions Associated with Acromegaly.

Malocclusion
Periosteal Reaction
Cranial Vault Thickened
Enlarged Frontal Sinuses
Prognathism
Kyphoscoliosis
Vertebral Arthritis
Scalloping of Vertebral Bodies
Robust Skeleton
Cystic Bone Lesions
Rugged Face
Bony Obliteration of Skull Structures
Spondylosis
Robust Skull
High Temporalis Origin Markings
Robust Zygoma
Hypertrophied Nasal Bones
Osteoporosis in Skull
Blunt Mandible Angle
Fusion of Vertebrae
Degenerative Changes in Epiphyses
Fan-Shaped Position of Anterior Teeth
Enlarged Sella Turcica
Elongation of Ribs
Fractures
Enlarged Supraorbital Ridges
Tufting of Terminal Phalanges
Elongation of Mandible
Enlarged Mandible
Enlarged Occipital Protuberance
Osteoporosis
Arthritis-Not Vertebral
Prominent Chin
Increased Bone Deposition at Insertions.
Large Face
Pigeon Breast
Postcranial Exostoses
Enlarged Maxillary Sinuses
Increased Pneumatization of Mastoid Cells
Narrowing of Phalangeal Shafts, Broad Bases and Heads
Thickening and Squaring of Shafts of Metatarsals
Hyperlordosis of Lumbar Vertebrae
Enlarged Sinuses
Evidence of Weight Loading in Vertebrae

Table 3: Compiled List of Lesions Associated with Giantism.

Kyphoscoliosis
Vertebral Arthritis
Excessive Height
Degenerative Changes in Epiphyses
Proportional Growth
Enlarged Sella Turcica
Fractures
Osteoporosis
Arthritis-Not Vertebral
Epiphyses Not Closed
Hyperlordosis of Lumbar Vertebrae
Evidence of Weight Loading in Vertebrae

A difficulty encountered in the diagnosis of giantism and acromegaly are the concepts of "greater than average height" and "extremely or unusually tall". These terms can add to the confusion of the diagnoses of these diseases. Many authors and sources (Roberts and Manchester 1983, Brothwell 1981:162, and Egypt Government Document 1907, Wells 1964 and Brothwell 1970) emphasize height in the diagnosis of acromegaly and giantism. It is the purpose of this work to describe acromegaly and giantism in such a way that other characteristics will also be considered during diagnosis.

The cultural context of the observer is also important in medical diagnoses. When many of the physicians involved in the skeletal case studies presented in this thesis observed their patients, the diseases "acromegaly" and "giantism" had not been labeled as a disease. They had no idea that the symptoms were indeed related to a pituitary tumor, or what caused the physical changes. However, they did recognize that these patients were unique. By conducting autopsies and assessing characteristics, such

as pituitary tumors, skeletal changes, and soft tissue changes, etc., they were able relate the observed changes to a single, common condition (Cushing 1927:1-5)

Often, their first impression of something being "abnormal" with individuals expressing gigantism or acromegaly was that the individuals were "tall" within the physician's own cultural context. The individual was also evaluated based on his/her family history and population characteristics. Moreover, since "physician" was a Western concept, the Western cultural concept was used to identify those individuals who were "abnormally" tall. Because physicians, and archaeologists, were historically interested in the extremes of the populations they were observing, only those individuals (either alive or skeletal) who were labeled as "abnormally tall" by the observer were considered for further study. The entire process of differential diagnosis is linked to the experience, culture, and affiliation of the individual doing the diagnosis. The existence of "abnormal height" is therefore in the eye of the beholder

Modern archaeological samples can be designated "giant" because individuals fall within the upper third of the height distribution of a population (Wells 1964:107, Aufderheide and Rodriquez-Martin 1998:327). These individuals studied may or may not have characteristics of giantism or acromegaly by the modern medical definition. They are just studied because they are the biggest bones in the sample. This study will produce a list of observed characteristics for giantism and acromegaly that have been used in the literature. Hopefully, this list will be used by people working with skeletal material to recognize the many variations in skeletal lesions found in acromegaly and giantism.

Differential Diagnosis in Physical Anthropology and Archaeology

Differential diagnosis has been borrowed by physical anthropologists as an aid in identifying and describing pathologies present in skeletal material. Unlike those in the medical field, anthropologists are not able to get a history from the patient nor are we/they able to do diagnostic tests on soft tissues or body fluids/secretions. This limits the ability of the physical anthropologist to definitively diagnosis a disease from skeletal materials. This difficulty is increased with some diseases such as giantism since the presentation of lesions is variable (Aegerter and Kirkpatrick 1975:377).

Although not common, both giantism and acromegaly have been noted in the archaeological record (Ortner and Putschar 1981, and Gladykowska-Rzeczycka 1998), in museum collections (Ortner and Putschar 1981), and in a modern forensic case (Sauer and Marushia 1997). The small sample size from archaeological material could be due to several representative factors. Since life span in general was shorter, the diseases may not have reached the advanced stages more recognizable in more modern populations. Also, examples of the disease would be decreased due to earlier death from the disease. Lastly, women who were acromegalic or hyperputitary giants could be "lost" as males as these diseases are often associated with enlarged bone diameter, increased bone rugosity, larger chins, enlarged supraorbital ridges, and prominent muscle attachments. Renewed growth also occurs in the pubic symphysis, which remodels areas used in sexing individuals.

As stated previously, other conditions might potentially be confused with giantism and acromegaly. In the past, the diagnosis of acromegaly and giantism in skeletal material has not been systematic. Such conditions as Marfan Syndrome,

adrenal tumors and genetic predisposition to extreme height could be confused with acromegaly (Wells 1960:107 and Gladykowska-Rzeczycka 1998). It has been suggested that hypertrophic osteoarthropathy (HOA) and Paget Disease of Bone have also been confused with acromegaly (Carcassi 1992).

Because of the confusion that can occur in distinguishing acromegaly and giantism from other diseases, it is important that a person have experience with many other disease states. Since differential diagnosis is based upon the experiences of the observer, it is necessary to keep abreast of new information and re-examine previous cases to minimize error.

CHAPTER 3

DISEASES COMMONLY CONFUSED WITH ACROMEGALY AND GIANTISM

A number of disease states and conditions have been mistaken with acromegaly and giantism. In addition to the five disease states Marfan Syndrome, HOA, Secondary HOA, Paget Disease of Bone and Adreno-Genital Syndrome, two other classifications, "genetic predisposition for greater than average height" and "Neandertal" will be discussed (see Appendix 1).

Marfan Syndrome

Marfan Syndrome appears to be due to a mutation in the fibrillin-1 gene located on chromosome 15 (McKusick (a) 1986). One quarter of all affected individual's disease results from new mutations. Paternal age is thought to be a factor in some new mutations. Expression of Marfan is variable. Homozygous and heterozygous forms have been reported although this is still under discussion (Fairbank 1976:152-155). Researchers agree that Marfan is autosomal dominant, but there is conflicting evidence regarding a recessive form of the disease (Fairbank 1976:152-155, McKusick (a) 1986, and Aegerter and Kirkpatrick 1975:187-190).

It is estimated that the frequency of incidence in the human population is 1.46 people per million (Fairbank 1976:152-155). Diagnosis usually becomes apparent in the first few years following birth, however mild cases can exist that are not diagnosed even into adulthood. Life expectancy of people with Marfan is thought to be shorter

than average, however, Silverman et al (1995) reported an increase in life expectancy for Marfan patients of over 25% from 1972-1995. They attributed this increase to advancements in medical care and an increase in the life expectancy of the population in general (McKusick (a) 1986). Although males and females are equally affected in numbers, life expectancy of men is much less than that of women. Severity of the disease was seen as the best independent indicator of life expectancy. The average age at death is 30 to 40 years of age. Cardiovascular involvement is common and often life-threatening (Robbins and Cortan 1979: 236). A primary cause of death is rupture of aneurysms, followed by cardiac failure (McKusick (a) 1986).

Primarily three systems manifest characteristic changes in fibrous connective tissue —the ocular, the cardiovascular and the skeletal. Myopia, cataracts, increased axial globe length, corneal flatness, retinal detachment and secondary glaucoma and subluxation of the lenses are common clinical findings (McKusick (a) 1986, and Fairbank 1976:152-155).

Cardiovascular findings include valve prolapse and aortic involvement including aortic aneurysm and aortic dissection. Skeletal features include maxillary overbite, crowded teeth and a highly arched palate. Increased height, disproportionately long limbs, abnormal vertebral curvature, pectus excavatum or anterior chest deformity, and narrow shoulder girdle are common appendicular and axial characteristics. This syndrome has also been referred to as arachnodactyly (spider fingers) due to the increased length of the extremities especially the fingers. Spider fingers and general joint laxity are characteristic of this syndrome (McKusick (a) 1986, and Robbins and Cortan 1979: 236).

Marfan Syndrome differs from giantism in that the increased height of Marfan is disproportionate in the extremities. While many characteristics of Marfan can be found in giantism, there are two characteristics, which are not associated with giantism: spider fingers and maxillary overbite (McKusick (a) 1986, and Fairbank 1976:152-155).

Marfan Syndrome has been described in a skeleton housed in the Museum of Pathological Anatomy, Vienna, Austria. This skeleton was initially diagnosed as "physiologically tall stature". It was later re-diagnosed as Marfan Syndrome. The skeleton is 191cm (6 feet 3 inches) in height with limb length disproportionately long compared to the trunk. Arachnodactyly or "spider fingers" is evident, but there is no noted tufting of the terminal phalanges. The skeleton does not exhibit any acromegalic characteristics other than increased height. A photograph of the skeleton confirms this observation. The mandible shows neither prognathism nor overgrowth. Supercilliary ridges and points of muscle attachment are not prominent; there is no visual evidence of overgrowth. The skull looks small in comparison with the remainder of the skeleton (Beighton, P. et al 1993).

Primary Hypertrophic Osteoarthropothy (HOA) or Pachydermoperiostosis Idiopathic

This is primarily an autosomal dominant disease. Recessive forms of the disease seem to exist but with less frequency. HOA has been recognized in people of all geographic areas and nationalities. Males are affected more frequently and with more severity than females (Fairbank 1976:118-119), and the disease is not indigenous to any one country (Jaffe 1972:292).

There are none of the causative factors in Primary HOA, such as the pulmonary, cardiac, gastrointestinal or hepatic disorders that are associated with Secondary HOA (Singh and Menon 1995). Secondary HOA will be discussed more fully later. According to Ortner and Putchar (1981:294-297), the disease begins in puberty and progresses throughout life. Because the disease is self-limiting, a normal lifespan is usual. The physical characteristics and symptoms of HOA have similarities to those described in acromegaly. Hyperhidrosis (sweating) is the major symptom, but if there is joint involvement, there can be diffuse joint pain. Skin becomes thickened. Facial features become coarser with a concurrent increase in oiliness of the skin. The ends of the fingers can exhibit clubbing, usually due to the soft tissue changes. The extremities can appear disproportionately large, although height is not affected (Jaffe 1972:291-300, and Ortner and Putchar 1981:294-297).

Thickening of the calvarium and base of the skull occur with the disease and the "frontal and paranasal sinuses are enlarged" (Fairbank 1976:118-119). The vertebral bodies are affected and the vertebral foramina often become narrowed. The extremities can be disproportionate to body height, but height is usually within normal limits. Subperiosteal reaction usually occurs in the distal ends of radius, ulna, tibia and fibula (Ortner and Putschar 1981:297, and Jaffe 1972:291-3). This reaction produces periosteal bone which and is deposited on the original cortex, that is consistently thick, rough and irregular (Carcassi 1992:4, and Jaffe 1972:296). In advanced cases of the disease, the diameter of the long bones show a marked increase and spinal ligaments and interosseous membranes may be ossified (Ortner and Putschar 1981:297, and Jaffe 1972:291-3).

In the past, HOA has been confused with acromegaly. It is distinguishable from acromegaly as all the bones show periosteal build up or hyperostosis, not just areas of cartilage as in acromegaly. Tufting of the terminal phalanges is not characteristic of HOA (Fairbank 1976:118-119, Singh and Menon, 1995, and Carcassi, 1992).

Secondary HOA

Secondary HOA is primarily associated with pulmonary diseases, however, it is defined by the same characteristics as HOA in all other respects. Metastatic or primary cancer of the lung, breast cancer, tuberculosis or other pulmonary lesions can initiate a lymphocytic infiltration of the periosteum[2]. Diffuse periosteal hyperostosis, found at the ends of long bones or at mid-diaphyses, and cortical bone resorption with pronounced vascular grooving often occurs. The bones of the trunk are rarely affected (Jaffe 1972:286-300). Metacarpals and metatarsals are affected more than the phalanges; the terminal phalanges usually remain unaffected. The skull is usually unchanged, except for infrequent occurrences of bone deposition on the inner table (Jaffe 1972:286-300).

Secondary HOA, just like HOA has been confused with acromegaly. It is distinguishable from acromegaly because all the bones show periosteal build up or hyperostosis. Tufting of the terminal phalanges is not characteristic of Secondary HOA (Fairbank 1976:118-119, Singh and Menon, 1995, and Carcassi, 1992).

[2] This is the only difference between the two diseases, though authors make distinctions based on specific case studies they have experienced. Since Secondary HOA is assoicated with such diseases as cancer and tuberculosis, Secondary HOA rarely reaches advanced stages.

Paget Disease of Bone (PDB)

There seems to be evidence linking the occurrence of Paget Disease of Bone (PDB) to several factors. Because of the identification of virus-like inclusions in Pagetic bone, many researchers are exploring the hypothesis that PDB is linked to viral infection. Autosomal dominant inheritance with a high penetrance by the age of 65 has been presented as a possible route of inheritance (Van Hul et al. 1997, McKusick (b). 1986). A locus on chromosome 6 has also been tentatively linked to PDB and is referred to as PDB1. Another locus on chromosome 18 has been potentially linked with PDB and is referred to as PDB2 (McKusick (b). 1986).

Since the disease is very rare before the age of forty, a population incidence of 3% has been estimated from several populations above the age of forty. Incidence seems to increase with age. Men apparently are more often affected than women are, by a proportion of four to three (Fairbank 1976:120). Populations with low incidence of the disease are those of China and Africa. European, North American and Australian populations have a higher incidence, as the disease is relatively common. Interestingly, Jamaicans of European or African ancestry have a similar incidence of the condition (McKusick (b). 1986, Hamdy 1981:4, Barry 1969:17).

As previously mentioned, Paget disease often goes unnoticed until the fifth decade of life (Barry 1969:17). Pain in the affected bone is often the first symptom. Enlargement, deformity or pathological fractures of the bone can also be presenting features of this disease. Any bone may be involved, but some bones are more commonly involved than others are. The vertebral column is most often involved. In descending order of frequency, other commonly affected bones are-- the right femur,

the skull, the pelvic bones, the left femur, the tibia and fibula and the arm bones. The mandible and teeth can also be affected. The hands and feet are rarely affected and it is uncommon for the whole skeleton to be involved. One or more bones can be involved, but the presentation is usually asymmetrical (Hamdy, 1981:12).

The affected bones go through phases of destruction and sclerosis. During the lytic or destructive, phase there is increased vascularization in the resulting spaces. Vascularization decreases during the sclerotic phase, as areas of increased bone density become apparent. Both phases can exist concurrently. Life expectancy is normal and for the most part the people with this condition are surprisingly fit (Fairbank 1976:120).

The only confusion of Paget Disease of Bone and acromegaly and giantism is that increased bone density of the skull can occur in both conditions. Although skull thickness can be increased in PDB, the bone would be porous. The diploe or the space between the inner and outer tables of the cranial vault contains nodular bony masses, which give the appearance of pumice. However, radiographs show patchy areas of sclerosis and increased thickness. Giantism and acromegaly show involvement of the facial bones, while PDB usually does not involve the facial bones even if the skull is involved. Bony overgrowth similar to that found in acromegaly also occurs in Paget's disease. Unlike acromegaly, the distribution is not confined to areas of cartilage and remodeling of the jaw, as is found in acromegaly, is not characteristic for Paget Disease of Bone

Adrenal-Genital Syndromes

Adrenal (suprarenal) tumors can affect the production of hormones necessary for normal growth and development. Over or under-production of certain hormones such as testosterone and estrogen can delay or inhibit puberty and physical development. Puberty is associated with the closure of epiphyses that coincide with the cessation of growth. If puberty is delayed, growth can continue. However, although growth occurs faster than usual, height is not usually dramatically increased in adulthood (Weinreb 1984:288-294, Hayles 1980:164, and Aegeter and Kirkpatrick 1975:378).

Eunichoidal giantism is characterized by periosteal bone growth is inhibited in hypogonadism, which results in a gracile skeleton. Since endochondral growth is increased, the upper and lower limbs can be of greater than usual length compared to the rest of the body. Elongation of the mandible and proganthism can result as well. Castration in boys would result in a tall, long-legged, gracile skeleton. This would also be true of any tumors that would severely limit or stop testosterone production. Growth and development would also be affected for girls with hypogonadism. Skeletal manifestations of these processes would not necessarily include modifications in the sella turcica unless a pituitary tumor was involved in creating the hormonal imbalance (Hayles 1980:164, and Aufderheide and Rodriguez-Martin 1998).

Anderson and Kissane (1977:378) describe eunichoidal giantism as a condition of males where descent and maturation of the testes are halted or where castration occurred before puberty. Delayed epiphyseal closure would allow for a longer period of

growth, which would account for the greater height. Height would be found disproportionately in the lower extremities

Genetic Predisposition for Greater Than Average Height

Height can be influenced by many factors. Genetic limits on an individual's height are determined by the genes provided by the parents. Nutrition has also been shown to be an important factor in stature. An individual with a genetic propensity for increased height who has nutritious food available in plentiful amounts may reach their maximum height (Wells 1969:454). Psycho-social events may also limit height. In other words, stress can also affect height[3] (Weinreb 1984:299, and Wells 1969).

It is important to remember that an individual is part of a population. A person who is taller than average in one population may not be taller than average in another. Known population heights are important to determine where an individual falls within the population distribution of heights.

The Neandertal Question

Keith (1931) discussed the similarity in characteristics of acromegalics and Neandertals. This brings up two very important points to remember in the assessment of a disease. It is necessary if possible to study the skeletal material as both an individual and as a member of a population. Keith's discussion of the Gardar skull clearly illustrates the potential difficulty in diagnosing "lesions" that are in fact the normal variation within the population in question.

[3] Height for all individuals is potentially affected by the same factors such as nutrition and genetics.

Archaeologically, provenience of skeletal material is essential to provide a firm foundation on which to base further study/analysis. The skull found at Gardar, southern Greenland, was said to have been found in a 12th century Norse graveyard. However, the features resembled those designated as "Neandertal" according to Hansen. Since the base of the skull was missing, this diagnosis has been questioned by many including Keith. The discussion engendered by the analysis of the Gardar skull highlights the concept that ancestral, ethnic, and geographical variation can occur which may mimic pathology. In short, ancestral features must be considered when performing a differential diagnosis when generating a biological profile.

Similar characteristics assigned to the Neandertal and the Gardarene Skull include: robust features, thickened skull table, prominent supraorbital ridges, and an enlarged occipital bun. Another distinguishing feature of the Neandertal is a "football" shaped vault. The Gardarene Skull also had this characteristic (Keith 1931). Keith (1931) determined that Neandertal and acromegalic characteristics were similar, though differences could be discerned. The Gardarene Skull had a longer face, large mastoid processes, and an especially narrow skull.

Trinkaus (1985:528) examined the following characteristics in Neanderthals and acromegalics: malocclusion, excessive development of chin, expansion of the paranasal sinuses, large supraorbital tori, projecting external occipital protuberance, enlargement of the sella turcica, increased cranial vault thickness, excessive apposition of bone on vertebral bodies, kyphosis, marked rib elongation and curvature, thick cortices of diaphyseal bone, increased rugosity of musculoligamentous insertions, degeneration of articular cartilage, and apposition of bone on the pubic symphysis. Trinkaus concluded

that only two characteristics were remotely similar for Neanderthals and acromegalics; large distal phalangeal tuberosities and slightly-thickened cranial vault bones, both of which could be confused with acromegalics.

Neandertal morphology is discussed in this paper as it relates to the differential diagnosis of acromegaly. Some features ascribed to the Neandertal population have been thought by some to also be characteristic of acromegaly. Keith's (1931) discussion of the Gardar skull illuminates the difficulty in assessing pathology of incomplete materials and the need to place "pathology" in context of normal physical variation within a population and the provenience of the skeletal remains. Keith concluded that the Gardar skull was acromegalic, based on his comparisons with other acromegalic and Neandertal skulls.

CHAPTER 4

ACROMEGALY AND GIANTISM: SKELETAL AND SOFT TISSUE CASE STUDIES

Presented in this chapter are the reported skeletal case studies of 17 individuals that make up the primary data for this project. These case studies are presented as information/data to understand and define the diagnosis of giantism and acromegaly. Embedded within this presentation of data is an analysis of each case study. Found in the appendices is data regarding the individuals as a group. In addition, the original diagnosis of each individual will be re-examined (using the flow charts presented in Appendix 2).

1. The Polish Giant (Gladykowska-Rzeczycka 1998)

This individual was found in the area of Lenogora, Poland and was dated to between the end of the 11th Century to the beginning of the 14th Century. The skeleton's height was estimated by the authors at 215.5 cm (7 feet 1 inch) using the Trotter and Glesser stature method (Gladykowska-Rzeczycka 1998: 147, 153). Analysis of the skeleton suggested a female of 25-30 years of age. She was diagnosed as having giantism. The authors of this article gave a thorough presentation of the material. Photographs were plentiful and detailed descriptions of all lesions present were related. The criteria mentioned for the diagnosis were enlarged dimensions of all

bones[4] and a disproportionately large mandible with "a fan-shaped" configuration of the anterior teeth. The skull was thickened especially in the anterior region. The jugular foramen and fossa were almost obliterated, and the sella turcica was enlarged and flattened (Gladykowska-Rzeczycka 1998: 169).

Postcranial lesions were present as well, with the vertebral column being particularly affected. Diffuse degenerative changes were noted in the entire vertebral column and the epiphyses of all bones. Fusion and partial fusion of thoracic and lumbar vertebrae was noted. Ossification of the right anterior longitudinal ligament was apparent, and exostoses were present on the vertebrae. Evidence of extensive loading on the vertebral column included such lesions as scoliosis, Schmorl's nodes and flattened vertebral bodies. Fractures in the right humerus and left tibia were also noted (Gladykowska-Rzeczycka 1998: 169).

Harris lines were visible on the radiographs. This is an interesting fact if there is any validity to the correlation between nutritional stress and the generation of Harris lines. In cases of extreme growth, often the body systems are stressed by extreme size (weight stress fractures, as an example). Ironically, inadequate nutrition could have decreased this woman's size so that she was less afflicted by acromegaly that she might have been. Adequate nutrition might have caused even more weight bearing lesions!

I would concur with the authors that this individual probably suffered from a pituitary tumor that caused giantism and acromegaly. For a thorough review of characteristics, see Table 2. Compared to her contemporaries she was at the extreme end of the distribution of height for both men and women.

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[4] Gladykowska-Rzeczycka also states that there is excessive body height (1998:169) and enlarged dimensions of all bones (1998:153), which suggests proportional body build or growth.

The diagnosis of "acromegalic giant" is imbedded in the text, although the article's title suggests a diagnosis of "hyperpituitary giant." A clear example of this is found in the Gladykowska-Rzeczycka et al.'s *Summary of Conclusions* (1998:169-170), which states "...the female from Ostrow Lednicki suffered from serious disturbances of the pituitary gland which caused gigantism at a young age and acromegaly after epiphyseal closure." Many characteristics are used to assess the health state of the individual. Differential diagnosis is used by the authors to define the cluster of traits. The diagnosis appears to be accurate, based upon the information presented by the authors. The age and the sex are not consistent with a diagnosis of PDB. As this individual was described as having all bones enlarged, Marfan and Adreno-Genital Syndromes can also be eliminated. HOA and secondary HOA are not likely because height is not affected and the bone was not described as being thick, rough, and irregular.

Table 4. The Polish Giant Authors' Described Characteristics

Male/Female	Female
Age	25 to 30
Height	215.5 cm (7 feet 2 inches)
Documented Diagnosis	Both Acromegaly and Giantism
Cranial Vault Thickened	
Enlarged Frontal Sinuses	
Prognathism	
Kyphoscoliosis	
Vertebral Arthritis	
Bony Obliteration of Skull Structures	
Tall (Excessive) Height	
Osteoma	
Fusion of Vertebrae	
Degenerative Changes in Epiphyses	
Fan-Shaped Position of Anterior Teeth	
Proportional Growth	

Enlarged Sella Turcica
Length and Diameter of All Bones Enlarged
Fractures
Enlarged Mandible
Enlarged Maxillary Sinuses
Increased Pneumatization of Mastoid Cells
Evidence of Weight Loading in Vertebrae

2. The Tergenesse Giant (Nerhlich et al. 1991 and 1994, and Pirsig et al. 1994)

Nerlich et al. (1994) presented a poster on Thomas Hasler, the Tergenesee Giant. His skeleton is maintained at the Institute of Pathology at Munich University. During life, he was reported to have attained a height of 235 cm (7 feet 8.5 inches). His skeleton as measured by Nerlich et al. was 210 cm (6 feet 10.6 inches) in length. Hasler died suddenly in 1876 at the age of 25. He showed symptoms of acute cerebral distress (cerebral hemorrhage) as a cause of death.

Analysis of his skeletal remains revealed an "extensively" enlarged and thickened skull. The frontal bones measured up to 7 cm (2.75 inches) in thickness. This cranial bone overgrowth noticeably decreased the cranial capacity. The mandible was described as very prominent. The sella turcica was significantly enlarged with indications of a cystic defect at the posterior border. A microcystic bone pattern was reported upon cross section of cranial bone.

Bones were elongated but proportional throughout the entire skeleton. All epiphyseal plates were open. The lower extremities showed several lesions. The left fibula was widened irregularly throughout its length with no compact bone involvement. Pathological fractures were present. The left femoral head showed a

change in position that was attributed to a healed fracture. The femoral shaft adjacent to the healed fracture seemed to be widened and enlarged. Lastly, the skeleton showed signs of "spondylosis with focal osteophytic bone formation" (Nerhlich et al. 1991:S90). Spondylosis is the term used when a major portion of the neural arch separates from one or more vertebrae (Ortner and Putschar 1981:357).

Pirsig et al. (1994) used radiology and endoscopy to examine Thomas Hasler's skeleton. They found obliteration of the left optic canal and left nasal lacrimal duct, a compressed left internal acoustic canal, the left nasal canal filled with bone, both cribiform plates thickened and lacking foramina, an atretic left ear and reduced volumes in the oral cavity and pharynx.[5] Cystic bone replaced normal bone structure in the skull, especially the mandible. Cystic lesions of the long bones of the left upper and lower extremities and the left os illium and left clavicle also showed a small rim of sclerotic bone. Histological examination of the skull disclosed trabecular bone that was made up of immature woven bone which is typical of fibrous dysplasia[6].

Nerhlich et al. (1991 and 1994) and Pirsig et al. (1994) concluded that Hasler was affected with giantism and with a form of fibrous dysplasia. I would argue that since his skull enlarged enormously with advancing age, his mandible was very prominent and cranial thickness of up to 7 cm (2.75 inches) was noted, that acromegalic characteristics were present as well as those of giantism. Fibrous dysplasia can cause thickening of the cranial vault, but has not been found to affect either the length of the

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[5] *Nasal canal* is the author's term. It is unclear what the author is specifically referring to, however it is important in that nasal structures were compromised by abnormal bone growth.

[6] Fibrous dysplaia is a condition of the bone in which the normal structure is replaced by lesions of fibrous tissue and poorly-formed, woven bone trabeculae (Robbins and Cottran 1979:1496). These lesions may appear in one of three distributions: monostotic, polyostotic (rarely in the spine), and Albright's syndrome characterized by polyostotic fibrous dysplaia, café au lait spots and associated

mandible nor the size of the skull. (Ortner and Putschar:315-322). Fibrous dysplasia is more frequently found in females than males, and often begins in childhood, but ceases upon epiphyseal closure or end of the growth period (Uehlinger 1960:283).

Table 5. The Tergensee Giant Authors' Described Characteristics

Male/Female	Male
Age	25
Height	210.0 cm (6 feet 10.6 inches)
Documented Diagnosis	Hyperpituitary Giant
Cranial Vault Thickened	
Cystic Bone Lesions	
Bony Obliteration of Skull Structures	
Spondylosis	
Tall Height	
Robust Skull	
Enlarged Sella Turcica	
Length and Diameter of All Bones Enlarged	
Fractures	
Elongation of Mandible	
Epiphyses Not Closed	

3. *The Mutter Giant (Hinsdale 1898, Humberd 1939, McFarland 1938)*

Housed at the Mutter Museum in Philadelphia, Pennsylvania, this individual's origins are shrouded in mystery. The "American Giant," as he was called, arrived during the hey-day of interest in giants and other human "freaks." During the 1700's through early 1900's, there was a society interest in viewing "giants"—alive and dead. "Giants" such as Charles O'Brien were pursued by individuals interested in possessing the "giant's" skeleton after death. (It might be interesting to psychoanalyze the pursuers

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endocrine dysfunctions such as precocious puberty in females, hyperparathyroidism, hyperthyroidism, acromegaly or Cushing's syndrome.

and their need to possess the biggest human body but it is beyond the scope of this work.)

The Mutter Giant was brought to the museum in 1877 at which time it was prepared for display. The skeleton was described as that of a twenty-three year old male. Dr. Hinsdale (1898) estimated that the Giant was 22 to 24 years old. Humberd gave an age of 17 years old (Mutter Museum Archives). His height was 235.6 cm, or 7 feet 8.75 inches. Estimating age has been an admitted problem in this instance due to the reliance upon methods that involve areas of cartilaginous growth. Epiphyseal closure was not complete, according to Humberd (Mutter Museum Archives). The delay in epiphyseal closure leads to the difficulty in aging this individual. Epiphyseal closure delay is a characteristic of giantism (Aufderheide and Rodriguez-Martin 1998).

Hinsdale (1898) in his essay "Acromegaly" described the lesions present in the remains. The skull was described as being proportionate to the size and height of the axial skeleton, but dolicocephalic. The frontal sinuses were enlarged. An enlarged pituitary fossa was recorded by Hinsdale (1898). The mandible, which was slightly prognathous, was also massive. The sacrum consists of four vertebrae, and the coccyx consists of three vertebrae.

The ribs were long and narrow. The thorax was large but narrow. Periosteal inflammation was apparent on the borders of the pelvis. Arthritis was evident in the iliac crests and above the acetabulum. Thin bone was noted in the acetabula and the iliac bones. Hinsdale (1898) notes that the femora were slender, but proportionate to

the rest of the bone.[7] The shafts were well formed and not "unduly curved." The femoral heads were misshapen, and the necks were semi-lunar in cross-section. Compact bone was very thin at the extremities of the femur, barely covering the cancellous bone. The fibulae were curved and lie posterior to the tibiae. McFarland (1938) added to this account that the individual had a pigeon breast and ununited epiphyses.

The array of features presented strongly supports the literature's consensus of giantism with acromegalic features. However, unlike other individuals in the case studies presented, this individual's bones were not disproportionately enlarged (which is one of the identifying characteristics for acromegaly and giantism). Bone diameter could have been decreased by two factors. One is muscle wasting which would decrease the forces placed upon the bone thereby affecting modeling. The second is that eunichoidal giantism with the pituitary tumor has characteristics of slender bones and longer extremities with increased height. However, the height was stated to be proportional. Eunichoidal giants and individuals with Marfan tend to have disproportionately longer legs. Remodeling of the jaw is unusual in PDB. HOA and secondary HOA are associated with hyperostosis of all bones of a skeleton.

[7] This observation seems contradictory. Hinsdale could be noting that the femoral length is proportional to the other bones or that the femora were slender but not so slender as to be extreme. Both can be

Table 6. The Mutter Giant Authors' Described Characteristics.

Male/Female	Male
Age	17 to 24
Height	235.6 cm (7 feet 8.75 inches)
Documented Diagnosis	Both Acromegaly and Giantism
Enlarged Frontal Sinuses	
Prognathism	
Kyphoscoliosis	
Tall Height	
Blunt Mandible Angle	
Proportional Growth	
Length and Diameter of All Bones Enlarged	
Elongation of Ribs	
Elongation of Mandible	
Enlarged Mandible	
Arthritis-Not Vertebral	
Large Face	
Epiphyses Not Closed	
Pigeon Breast	
Enlarged Maxillary Sinuses	
Dolichocephalic	
Evidence of Weight Loading in Vertebrae	

4. The Persian Giant (Ortner and Putschar 1981, Fuchs 1935, and Material from the Collection of Warren Raymond).

Ortner and Putschar (1981:298) present a skeleton housed in the Pahlavi University Medical School as an example of giantism. The features presented include "giant" stature, massive bone apposition and acromegalic features. However, the overgrowth present throughout the whole skeleton and the irregularity of the surfaces of the bones as visualized in the photograph suggest an additional diagnosis, perhaps HOA or neurofibromytosis.

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characteristic of giantism.

Accounts are given of a "giant" in Persia in the 1930s (See Fuchs, 1935). Fuch's gave a presentation regarding this person to the Society of Physicians in 1935. His presentation, which included photographs, was noted in the *1935 Journal of the American Medical Association.* Unfortunately, the photographs were not reproduced in the notice. Associated with this "giant" individual are clinical accounts and a diagnosis (Fuchs 1935, Hayles 1980, and the Collection of Warren Raymond). The individual was said to be 19 years old and 220 cm, or 7 feet 2.6 inches, tall (Hayles 1980:164).

Fuchs (1935:490) described the individual as being from Persia, and was:

> "... 10 feet 6 inches (3.2 meters) tall and was 19 years old. He had developed normally up to his tenth year, when he began to grow enormously. Mighty humps developed on his forhead, chin and behind the ears. The head became so heavy that the man could not hold it up. The humps on the forehead caused a great forward curvature. They have the appearance of tumors. There are many other lighter, loose nodules in the wrinkled skin. In the enormous head the eyes appear, in spite of their normal size, extremely small; the vision is good and the teeth are normal. The extremities are of an enormous length, the proximal phalanx being as long as the index finger of a normal man. The legs are too weak to enable him to walk, so he is generally lying down; but he is able to stand up when supported by a cane. His intelligence is almost normal; he complains frequently of vague pains. Recklinghausen's disease has been considered as the etiologic factor and it is assumed that an early localization of the process in the hypophysis or in the growth center is responsible for the giant growth. The patient was unable to ride in an ordinary carriage and he had to be placed on a boat by means of a crane. His weight exceeded 200 Kg. (450 pounds)"

It is possible that the giants described by Fuchs and Ortner and Putshcar are not the same individual. However, I am confident that the skeleton found in the Museum is the same person represented in photographs from a private collection (Collection of

Warren Raymond)[8]. The clinical information, albeit from secondary sources, seems to fit both the photographs of the living man and the skeletal photograph. The individual's skeleton seems to have a depression of at least one rib to the left of the sternum as is described in the clinical accounts. The side view of the person's face as compared to the photograph of the skeleton is quite compelling. The supraorbital torus is unique, as is the projection of the mandible. It would be amazing to think that two individuals from Persia (present day Iran) would both manifest with such distinctive skeletal changes.

The museum specimen is diagnosed by Ortner and Putschar (1981:298) with giantism and acromegaly. They do not mention sella turcica enlargement or height. A measurement of height was given to Charles C. Hart as being 220 cm (7 feet, 2.6 inches) (Letter from the Honorable Charles C. Hart to person unknown, date unknown, from the private collection of Warren Raymond)[9], which is the same height given by Hayles 1980:164). Increased diameter of bones was visible, and bone apposition on his face and skull was readily apparent. Upon physical examination, his tongue was found to be of normal size. Acromegaly often causes a great increase in the size of the tongue. Scoliosis was described as curving to the right. Fingers and toes began enlarging at ten years of age. Exostoses were found upon examination *(ibid*, Collection of Warren Raymond).

Given the clinical information of the living individual, a diagnosis of giantism, with some other major contributing disease process, is likely. PDB is eliminated as the

[8] Warren Raymond has a collection of documentation on unusual human variation both soft tissue and skeletal. Mr. Raymond has been consulted for numerous television programs and museum exhibits.
[9] Based on evidence found within the Fuchs (1935) and Hayles (1980) articles, the date of this letter is probably between 1934 and 1935.

skeleton showed widespread periosteal overgrowth involving the facial bones. Marfan and Eunichoidal giantism are less likely as the skeleton was described as massive. HOA and secondary HOA are possible, as both are associated with widespread skeletal hyperostosis. Fuch's giant had a family history of tuberculosis, which has been associated with secondary HOA (*ibid*, Collection of Warren Raymond). With the information from the document research (which was probably not available to Ortner and Putschar), other diagnoses present themselves. Potentially Von Recklinghausen's Disease, as suggested by Fuchs) is likely as well.

Von Recklinghausen's Disease (neurofibromatosis), caused by an autosomal dominant allele, presents an extremely varied array of lesions. It has tumors throughout the body that arise from nerve sheets. Fairbank (1976:148-149) describes the disease as follows; "Fibromatous skin tumours and multiple tumours of nerve trunks are typical features, varying in size from a few millimetres to several centimetres, together with hypertrophy of one limb, or part of it, or of other areas, such as the skull. This local gigantism may affect the underlying bone as well as the soft tissues." Hayles (1980:164 goes on to say, "An occasional patient with neurofibromatosis has been quite tall, often with asymmetric growth, but none has been of exceptional height."

Ortner and Putschar (1981:325) also describe the disease as having a characteristic type of kyphosis. They state that:

> "A special type of kyphoscoliosis can occur in neurofibromatosis, a condition characterized by formation of multiple nerve sheath tumors on spinal and peripheral nerves. In this disease, the maximal scoliotic deformity more frequently involves the cervical spine. The tumors of spinal nerves in this condition lead to smooth widening of interspinal foramina in the affected area. This feature would permit recognition of

such a scoliosis as due to neurofibromatosis even on the dry skeleton" (Ortner and Putschar 1981:325).

Re-examination of the skeleton of the "Persian Giant" could therefore provide more information for a more definitive diagnosis of this individual.

Clinical information is rarely if ever available to test the accuracy of paleopathological diagnosis. This case afforded me the opportunity to assess the diagnosis with the added clinical information. It would of course be necessary to examine the skeleton housed at the Pahlavi University Medical School to support my assumptions of identity. It is brought up here to show that literature research can give potentially electric information about the lives of individual people through historic skeletal remains.

Table 7. The Persian Giant Authors' Described Characteristics

Male/Female	Male
Age	Either 19 or 42
Height	220.00 cm (7 feet 2.6 inches)
Documented Diagnosis	Both Acromegaly and Giantism
Cranial Vault Thickened	
Tall Height	
Length and Diameter of All Bones Enlarged	
Enlarged Supraorbital Ridges	

5. Smithsonian Individual #2 (Ortner and Putschar 1981:301-302)

Documentary evidence suggests that this individual was a Native American male from Tennessee. Age was estimated to be 35-45 years at death. The individual lived in the historic period before the 1900's. In general, the skeleton was massive and

the skull was rugged. The temporalis muscle origins were found close to the saggital suture. The mandible showed overgrowth past that of the maxilla. The chin was prominent and had bony projections on the anterior inferior border. New growth on the mandibular condyles and an increased angle between the ramus and the mandibular body were evident on the roentgen film. The pituitary fossa was large, but according to the authors, not unusually so, and there was secondary growth on the rib ends[10].

The long bones were elongated and heavy. Stature was estimated for this individual as being 189.75 cm (6 feet 3 inches). Hands were large but proportionate to the rest of the skeleton. "This suggests greater pituitary function during growth, but with major morphological changes occurring after the normal growth period had ended" (Ortner and Putschar 1981:302). Diagnosis in this account was "possible acromegalic."

Given the above information, my diagnosis would be giantism with acromegaly. Epiphyseal closure occurs later in those whose secretion of GH is increased before puberty. Therefore, manifestation of acromegalic symptoms would be delayed, though present, as growth would not yet be restricted to only areas of cartilage. This might account for the decreased severity of the acromegalic skeletal lesions. Remodeling of the jaw suggests that PDB is not a probable diagnosis. As the long bones were elongated and heavy, Marfan and Adreno-Genital Syndrome are unlikely. HOA and secondary HOA are unlikely as the skeleton does not exhibit widespread periosteal overgrowth of all bones.

[10]This case presents an excellent example that an enlarged sella trucica alone is not indicative of giantism or acromegaly. Conversely, a sella turcica that is of normal size does not rule out giantism and

Table 8. Smithsonian Individual #2 Authors' Described Characteristics.

Male/Female	Male
Age	35 to 45
Height	189.75 cm (6 feet 3 inches)
Documented Diagnosis	Acromegaly
Prognathism	
Robust Skeleton	
Tall Height	
Robust Skull	
High Temporalis Origin Markings	
Blunt Mandible Angle	
Proportional Growth	
Length and Diameter of All Bones Enlarged	
Elongation of Ribs	
Tufting of Terminal Phalanges	
Elongation of Mandible	
Prominent Chin	

6. Smithsonian Individual #3 (Ortner and Putschar 1981:298-300)

Vienna was home to another skeleton of an individual used as an example of acromegaly by Ortner and Putchar. Described and pictured were the skeletal remains of a reported 39 year old male of undocumented ancestry (Ortner and Putschar 1981:298). Enlargement of the sella turcica was visible due to the pressure erosion of a tumor. Marked elongation of the mandible was apparent; especially the ramus, which produced a pronounced prognathism and malocclusion. A prominent chin, malocclusion of teeth and prominence of the inferior and superior nasal spines were also present. A photographic view of the cranial interior (skull cap removed) showed enlarged frontal sinuses and the previously noted enlarged sella turcica accompanied by resorption of the anterior and posterior clinoid processes. Tufting of the terminal

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acromegaly. See Harrison 1991:1899.

phalanges and periosteal hyperostosis was evident in the hands. Vertebral involvement included subperiosteal apposition.

Height was not mentioned for this individual. Since, the authors suggested that there was no gigantism, only acromegaly exhibited in this individual, it is assumed that height was not increased. Marfan, PDB, HOA, Secondary HOA, and Adrenal-Genital Syndromes were excluded as tufting was observed in the distal phalanges. The information provided in the above paragraphs supports a diagnosis of "acromegaly" for this individual. It would be interesting to have this individual's height measurement, to examine the heights of acromegalics used as examples of acromegaly in the literature as a population.[11]

Table 9. Smithsonian Individual #3 Authors' Described Characteristis.

Male/Female	Male
Age	39
Height	Unknown
Documented Diagnosis	Acromegaly
Malocclusion	
Enlarged Frontal Sinuses	
Prognathism	
Vertebral Arthritis	
Hypertrophied Nose Bones	
Enlarged Sella Turcica	
Tufting of Terminal Phalanges	
Elongation of Mandible	
Prominent Chin	
Increased Bone Deposition at Insertions	

[11] A list of other lesions characteristic of acromegaly were also given by Ortner and Putschar, although they are not specifically attributed to this individual (Ortner and Putchar1981:298-299). These included exaggeration of the supraorbital ridges and of the posterior occipital protuberance. Paranasal sinuses and facial bones were enlarged and the cranial vault was thickened. Marginal build up of bone on the alveolar process caused separation of the teeth. Increased diameter of the thorax was caused by elongation of the ribs. All prominent points on the bones demonstrated increased rugosity. Kyphosis is common due to muscle weakness in acromegalic individuals.

7. Gardarene Skull (Keith 1931)

Keith (1931) describes a fragmentary skull from Gardar, Greenland dated to the twelfth century. The individual had been determined to be a male of 40-50 years of age by Professor Hansen in the late 1920's. The skull was not completely preserved: only the skullcap and a major portion of the posterior part of the mandible survived. Unfortunately, the chin portion was missing. The angle of the Gardarene mandible and the width of the ascending ramus were greater than those of O'Brien (see next case study). The torus occipitalis was "enormous"[12]. The skull was "extraordinarily" narrow. Keith suggested that the skull was distorted due to taphonomic forces.

Although some of the other males buried in the graveyard were strongly built, the Gardar skull was massive in comparison. The skull shape was long and low, similar to Neandertal. The bony attachment for the neck was enormous. The temporal lines that mark the attachment of the upper boundary of the temporal muscles, almost met along the saggital suture. Professor Hansen, in communication with Keith (1931:488-489), suggested that these traits were not acromegalic but a genetic throw–back to "early man" because he had noted similar traits, though of lesser degree, in other members of the Norse cemetery population. Knowing what these similar traits for the Gardar individual's population were would also be helpful in re-assessing Keith's diagnosis.

Dr. Barnard Davis, a craniologist from the mid-Victorian era, compared the Neandertal skull presented by Huxley (1863) to an example of an acromegalic skull (with an enlarged sella turcica) in his possession. Keith (1931) compared the same

[12] Actual terms that were used by the authors were used whenever possible to decrease error of translation.

materials as did Davis and came to the same conclusion that Neandertal and acromegalics share similar characteristics. However, he noted that acromegalic features were indicative of an endocrine disorder, whereas Neandertal characteristics were not pathologic for that population.

Keith judged the skull to be that of an acromegalic not a throw back to "early man". With the information available, I would not be comfortable making a diagnosis of acromegaly or any other disease.

Table 10. Gardarene Skull Author's Described Characteristics.

Male/Female	Male
Age	40 to 50
Height	Unknown
Documented Diagnosis	Both Acromegaly and Giantism
Robust Skull	
High Temporalis Origin Markings	
Enlarged Supraorbital Ridges	
Elongation of Mandible	
Enlarged Mandible	
Enlarged Occipital Protuberance	
Increased Bone Deposition at Insertions	

8. Charles Byrne or O'Brien (Bergland 1965, Landolt and Zachmann 1980, and McAlister 1974)

Although there was documentary evidence of O'Brien's life, he was included in this work because his skeleton is viewed as one of the primary examples of a giantism. During his lifetime and up until 1912, the involvement of a pituitary adenoma in the disease process was unknown. Many years after his death, O'Brien's skull was opened to reveal an expanded sella turcica (Hayles 1980:166). O'Brien died in 1783 at the age of 22 years. He had reached a documented living height of 8 feet 2 inches (250 cm)

(Bergland 1965:265-269). Two hundred thirty-one centimeters was the recorded measurement of standing height by Landolt and Zachman (1980:1311).

O'Brien's skeletal maturation was retarded. He had the skeletal development of 17 years as estimated by epiphyseal closure, though he was 22 years old at death. O'Brien's height was proportional; suggesting that gonadotrophin production was not affected. In other words, he did not have eunuchoidal giantism (Landolt and Zachmann 1980:1311-1312). Acromegaly was suggested by the thick skull, large sinuses, and wide protuberant mandible (Keith 1931). PDB is not probable as he was much younger than 40 years of age. Marfan would be excluded as his height was proportional and an enlarged sella turcica was present. HOA and secondary HOA would be unlikely as there is no suggestion of widespread hyperostosis and height was above average. Given the above information, I believe Charles O'Brien had acromegaly and giantism. The decreased severity of his acromegalic features was due to delay in the process of epiphyseal closure.

Table 11. Charles O'Brien Authors' Described Characteristics.

Male/Female	Male
Age	22
Height	231.00 cm (7 feet 8.4 inches)
Documented Diagnosis	Both Acromegaly and Giantism
Cranial Vault Thickened	
Tall Height	
Robust Skull	
Enlarged Sella Turcica	
Elongation of Mandible	
Enlarged Mandible	
Prominent Chin	
Epiphyses Not Closed	
Enlarged Sinuses	

9. Rhine's New Mexico Acromegalic (Rhine 1985:210-219)

Stanley Rhine presented an acromegalic individual in his paper, "A Possible Case of Acromegaly from New Mexico." Differential diagnosis suggested that acromegaly was present in an individual from the pre-Columbian New Mexico pueblo of Pottery Mound. This individual was estimated to be a 30-40 year old male from "just immediately pre-contact" (Rhine 1985:212). His stature was calculated to be 165 cm (5 foot 5 inches), which is only 2 cm above the Pottery Mound male population mean of 163 cm (5 foot 4 inches). Examination of the sella turcica was problematic as the condition of preservation of this area was poor. However, radiologists found the sella to be within normal limits upon radiograph. Mastoid, frontal and maxillary sinuses were deemed large, and the "ungunal tufts" were enlarged[13].

Diagnosis was made both with individual and population characteristics kept in mind. In comparison to the individual's counterparts, this individual was quite robust. His cranial vault was thickened with enlarged supra orbital ridges and a "deep" mandible.

Rhine (1985) used Lang and Bessler's (1961) report on the radiographic features of acromegaly as diagnostic criteria. These criteria include:

- Enlargement of the sella turcica
- Enlargement of the maxillary sinuses
- Prominence and enlargement of frontal sinuses
- Prominence of brow ridges and zygomatic arches
- Greater pneumatization of the mastoids
- Prominence of the occipital torus
- Localized thickening of the skull

[13] Ungunal tufts are equivalent to distal phalanges.

- Coarsening of trabecular patterns
- Enlargement and elongation of the mandible
- Abnormally large joint spaces
- Degenerative osteoarthritis, with exostoses at origins and insertions of muscles
- Enlargement of ungual tufts of terminal phalanges
- Narrowing of phalangeal shafts, broad bases and heads
- Thickening and squaring of shafts of metatarsals
- Kyphosis of upper dorsal spine, hyperlordosis of lumbar
- Scalloping of vertebral bodies (formation of bone collar on centrum) from Stuber and Palacios (1971)

Rhine used a systematic method with detailed and clear criteria to diagnose the individual from New Mexico. Unfortunately, they were intended for diagnosis of a living person, so a few of the characteristics were not applicable to skeletal material. Characteristics were noted as being either present or absent. A diagnosis was made upon the majority of criteria being present. Enlargement of the sella turcica is not characteristic of all cases of acromegaly[14]. Acromegaly is not defined exclusively by increased height in any way shape or means. PDB is eliminated because of the wide distribution of skeleton involvement, as are Marfan and Adreno-Genital Syndromes because the person is of average height. HOA and Secondary HOA are possible as the pattern of bony overgrowth was not discussed. His argument was convincing that the individual had acromegaly. No photograph was available, so it is difficult to assess what other, if any indicators of disease were present.

[14] See Case I of the soft tissue case studies. The individual was diagnosed with acromegaly during life but showed no appreciable enlargement of the sella turcica.

Table 12. Rhine's New Mexico Acromegalic Author's Described Characteristics.

Male/Female	Male
Age	30 to 40
Height	165 cm (5 feet 5 inches)
Population Mean	163 cm (5 feet 4 inches)
Documented Diagnosis	Acromegaly
Cranial Vault Thickened	
Enlarged Frontal Sinuses	
Kyphoscoliosis	
Vertebral Arthritis	
Scalloping of Vertebral Bodies	
Robust Skeleton	
Rugged Face	
Enlarged Supraorbital Ridges	
Tufting of Terminal Phalanges	
Elongation of Mandible	
Prominent Chin	
Increased Bone Deposition at Insertions.	
Postcranial Exostoses	
Enlarged Maxillary Sinuses	
Increased Pneumatization of Mastoid Cells	
Narrowing of Phalangeal Shafts, Broad Bases and Heads	

10. Egyptian Skull (Brothwell 1981)

Brothwell (1981) refers to an example of acromegaly in an Egyptian, probably early dynastic, skull retained in the British Museum (Natural History). Sex is ascribed as female. Brothwell (1981) notes the extreme length of the face as the diagnostic feature of this individual. He notes that the supra orbital ridges were not abnormally large which he suggests was a due to the fact that the individual was female.

Differential diagnosis of acromegaly as outlined by Brothwell (1981) included

- Disease of adults
- Tumor of pituitary
- Growth reinitiated especially in hands, feet, and skull
- Enlarged vertebral bodies
- Enlarged ribs
- Considerable thickening of long-bones
- Enormous development of supraorbital ridges
- Thickening of occipital bone in region of nuchal crests
- Enormous development of frontal sinuses
- Lengthening of face due to reinitiation of growth in the mandibular and palatial regions

The diagnosis of acromegaly was based upon the appearance of the mandible alone. No other information was given regarding the condition of the post-cranial skeleton, if it existed at all. While acromegaly is not incompatible with the evidence presented, the evidence presented is wanting. Mandibular growth is one of, if not the, most conspicuous characteristics of acromegaly but it is not the only one. Sellar turcica condition was not discussed as present or absent. Sinuses were not discussed, nor were a number of other characteristics. Overall, Brothwell's description of this individual was incomplete. A more detailed description of the skeletal material would be necessary to allow for an independent assessment of diagnosis. The variation of features of the population would also be helpful to determine the diagnosis.

Examination of the photograph of the front of the skull shows indeed that the person's face was quite long. In addition, it appears that the lower jaw has an underbite. Given the list of markers that Brothwell used in diagnosis, it is not convincing that the individual is acromegalic. A radiograph would give more information regarding the

internal structure of the skull, revealing the size and configuration of the sinuses, the shape and dimensions of the sella turcica, and the thickness of the cranial vault.

Table 13. Egyptian Skull Author's Described Characteristics.

Male/Female	Female
Age	Unknown
Height	N/A
Documented Diagnosis	Acromegaly
Elongation of Mandible	

11. Marushia/ Sauer Individual (Sauer and Marushia 1997)

An individual identified in a forensic case was diagnosed with acromegaly and giantism by Sauer and Marushia in 1995. A biological profile was generated from the almost complete skeleton: male, 35 to 50 years in age, race/ethnicity was Caucasian, and height was estimated to be between 6 foot 2 inches and 6 foot 6 inches (193.04 cm by femur length). The individual was later identified by dental records, and was determined to be a 35 year old male, 6 foot 6 inches (198.12 cm) in height . This individual presented an unusual opportunity to compare a skeletal diagnosis with some life history information.

The individual was not diagnosed during life with a pituitary tumor or acromegaly/ giantism. However, skeletal characteristics were noted, which suggested a possible diagnosis of acromegaly. The individual was of great height and robustness. Growth appeared proportional, although no measurements were performed. The skull was robust, with prominent supraorbital ridges, and occipital and zygomatic

protuberance. The skull was also long and narrow in shape, with a noticeable sagittal keel.

The mandible was elongated and enlarged. Upon radiographic and visual examination, increased vault thickness, enlarged paranasal sinuses, and an enlarged and remodeled sella turcica were noted. Arthritis and osteophytic lipping were noted in the vertebral elements. PDB is excluded as the skeleton shows evidence of extensive skeletal involvement. As the bones were not slender and an enlarged sella turcica was present, Marfan and Adreno-Genital Syndromes are discarded as possible diagnoses. HOA is disregarded as hyperostosis was not noted in all bones. Upon re-examination of the evidence, the conclusion of "acromegaly with possible giantism" is correct.

Table 14. Marushia/Sauer Individual Authors' Described Characteristics.

Male/Female	Male
Age	30 to 50
Height	193.04 cm (6 feet 5 inches)
Documented Diagnosis	Both Acromegaly and Giantism
Cranial Vault Thickened	
Enlarged Frontal Sinuses	
Vertebral Arthritis	
Robust Skeleton	
Tall Height	
Robust Skull	
Robust Zygoma	
Proportional Growth	
Enlarged Sella Turcica	
Length and Diameter of All Bones Enlarged	
Enlarged Supraorbital Ridges	
Elongation of Mandible	
Enlarged Mandible	
Enlarged Occipital Protuberance	
Arthritis-Not Vertebral	
Enlarged Maxillary Sinuses	
Dolichocephalic	

12. San Cristobal Individual (Brauer 1991:2)

Bauer (1991:2) described a late prehistoric female from the San Cristobal Ruins, New Mexico; an adult of no specified height. An enlarged and elongated mandible, with a massive chin growth, was noted. The frontal sinuses were enlarged, as was her remodeled sella turcica. Areas of bone and muscle insertion showed increased bone deposition. Severe arthritis and osteoporosis were present throughout the entire skeleton. Recovered thoracic vertebral bodies showed bony build-up on the anterior body. The condition was described as severe.

Acromegaly, as diagnosed by Bauer is a convincing conclusion. PDB was unlikely as the lesions were widely distributed throughout the skeleton. Marfan was ruled out because of rugosity of insertion points. Adreno-Genital Syndrome was not likely because the individual is female. HOA and Secondary HOA present with periosteal build-up evenly over all the bone, not just areas of muscle insertion. The list of characteristics fits the characteristic profile of acromegaly. The severity of the disease suggests that the process was adult onset, as pre-puberty onset delays the epiphyseal closure, thereby decreasing the severity of the lesions. "Severe" arthritis and osteoporosis was an indicator of severity, as was massive chin growth. These observations suggest that the disease has been occurring for a longer time or with greater severity than the Marushia/Sauer individual (see Skeletal Case 12).

Table 15. San Cristobal Individual Authors' Described Characteristics.

Male/Female	Female
Age	"Adult"
Height	Unknown
Documented Diagnosis	Acromegaly
Enlarged Frontal Sinuses	
Vertebral Arthritis	
Enlarged Sella Turcica	
Elongation of Mandible	
Enlarged Mandible	
Osteoporosis	
Arthritis-Not Vertebral	
Prominent Chin	
Increased Bone Deposition at Insertions	

13. Dick's Mound Skull (Morse 1969:124)

Morse (1969:124) describes the skull of a Native American male from Dick's mound, Adams County, Illinois dating to ca. AD900 (Late Woodland). He stated that the individual "probably suffered from acromegaly." Characteristics noted were elongation and thickening of the long bones and elongation of the mandible. The teeth were not separated by large spaces and the frontal sinuses were not enlarged. There was no mention of the size or shape of the sella turcica though a radiograph was presented in the account.

Several characteristics are mentioned as indicative of acromegaly in this skeleton. A radiograph is even included. Due to the lack of clarity of the reproduction or my ability to read radiographs, it is difficult to determine the configuration of the sella turcica. There is no mention of the condition of the sella turcica. Again, as in several other of the skeletal case studies it would be more convincing if more information was presented regarding the absence of characteristic lesions. For example,

phalangeal tufting was not mentioned as being present or absent nor were prominent insertion sites. The variation of features of the population would also be helpful to assess the diagnosis.

With the paucity of information it is almost impossible to do an independent diagnosis for this individual. PDB cannot be ruled out. Marfan and Adreno-Genital Syndromes are unlikely since the bones were described as thickened. HOA and Secondary HOA are a possibility since the long bones were described as thickened. While it is possible and probably likely that Brothwell's diagnosis of acromegaly is correct, a more detailed and complete description of the lesions present and absent would make a stronger presentation for this diagnosis.

Table 16. Dick's Mound Skull Author's Described Characteristics.

Male/Female	Male
Age	Unknown
Height	Unknown
Documented Diagnosis	Acromegaly
Length and Diameter of All Bones Enlarged	
Elongation of Mandible	

14. Hosovski Individual (Hosovski 1991:273-279)

Hosovski describes an individual with acromegaly who lived in the Central Balkans in the 14Th or 15Th century. The skeletal remains of a male estimated to be about 30 years of age are described. Much of this individual was missing, with the following bones available for analysis: the skull with lower jaw (but no teeth), the right

clavicle, two right ribs, thoracic vertebrae #12, lumbar vertebrae #1, the right "iliac" bone, both femurs, and the right fibula.

The skull was described as being "characteristic in appearance" (Hosovski 1991:275). Hosovski (1991:275) refined this description by stating that all bones of the skull were changed by a "hyperplastic process." Growth was described as uneven with the glabella and supra orbital arches, zygomatic bones and arches showing the most growth. Thickness and mass in skull bones was increased, although there were holes present, which the author attributes to osteoporosis.

The lower jaw was elongated. The bite was modified with a progenia mandible (prominent chin) present. The paranasal sinuses were enlarged while the sella turcica showed normal dimensions (Hosovski 1991:276). Examination of the post-cranial skeleton revealed robust bones with exostoses present; the exostoses were found in greater frequency on the femurs and vertebrae. Osteal-sternal dysostosis with the signs of osteoporosis of newly-formed bone, osteoarthrosis, bilateral coxarthrosis (a condition of bone overgrowth in the joint of the femur head and acetabulum) and gonarthrosis (a condition of bone overgrowth in the area of the knee or femoral condyles), and proliferous periosteal reaction (fibulae especially) were evident. Height was calculated by Hosovski to be about 173 cm or 5 feet 8 inches tall. The right femur was significantly larger than the left (Hosovski 1991:277).

Hosovski generated his diagnosis from a list of skeletal features attributed to Matovinovic and Kicic (Hosovski 1991:274). This list of characteristics is reproduced here:

- The increase of the skull, with all the bones of face and skull being thicker, and due to disproportional growth of jaws, orbital arches and nose, the patient has an unusual
  appearance. There is an increase in all the paranasal cavities, especially of a front sinus, the mastoid cells, and cavities of temporal and zygomatic bone.
- Sella turcica is often broadened (over 20mm).
- Due to longitudinal growth, the lower jaw is prolonged and separate from the upper one, so that prognathism appears, and because of the complex remodeling of a bite, a
  blunt angulus mandibullae is formed ("a jaw in the form of a lamp")
- On all the bones, and especially on finger phalanges, there is periosteal thickening of bones ("a hand in the form of a shovel").
- Periosteal thickenings are located especially on muscle joints, which are manifested in the form of a (sic) exostoses.
- In rare cases osteoporosis is found
- As terminal cartilage plates of spine vertebrae can create a bone permanently, their growth begin in ante-posterior direction, and due to static changes, kyphosis appears with reduced capability of spine flexibility.
- After proliferation of joint cartilage in many joints there is osteoarthrosis(sometimes with deformations), etc. (Hosovski 1991:274)

Hosovski systematically examines this individual using a list of specific criteria for acromegaly as described above. Giantism was ruled out due to the relatively "normal" height of the individual, although a population mean was not given. However, the author implied that the case appeared mild even, though the estimated age at death was 30 years of age. This estimated age might be older than the chronological age of the individual. Aging was estimated using the condition of the saggital suture and the heads of the femurs attributed to Ferembach et al. (Hosovski 1991:274). Estimating age in individuals with acromegaly by standard aging methods is suspect (this concept will be explored more fully in the Discussions Chapter). The state of epiphyseal closure throughout the skeleton was not mentioned. As previously mentioned, epiphyseal closure is often delayed in those with a pre- and peri-puberty onset of the condition. As in the case of O'Brien, the decreased severity of the

Hosovski individual's acromegalic features could be due to a delay in the process of epiphyseal closure and the fact that he died young (thereby decreasing the length of time the disease would affect him).

PDB is possible, but unlikely, as the asymmetrical growth is associated with discrete areas of periosteal exostoses, not an overall reaction of the right femur. The fibula also shows involvement, which would be unusual in PDB (Ortner and Putschar 1981: 314). Marfan is unlikely as height was described as "normal" and the skeleton, "robust". Adreno-genital syndromes exhibit greater than average height and disproportionately longer legs. HOA would produce a periosteal overgrowth that would be evident in all bones of the individual. Hosovoski's diagnosis of acromegaly is credible, however giantism should be considered.

Table 17. Hosovski Individual Author's Described Characteristics.

Male/Female	Male
Age	30
Height	173 cm (5 feet 8in)
Population Mean	171.3 cm (5 feet 7 inches)
Documented Diagnosis	Acromegaly
Periosteal Reaction	
Cranial Vault Thickened	
All Sinuses Enlarged	
Prognathism	
Vertebral Arthritis	
Robust Skeleton	
Rugged Face	
Robust Skull	
Robust Zygoma	
Hypertrophied Nose Bones	
Osteoporosis	
Blunt Mandible Angle	
Length and Diameter of All Bones Enlarged	
Enlarged Supraorbital Ridges	

Elongation of Mandible
Enlarged Occipital Protuberance
Increased Bone Deposition at Insertions.
Postcranial Exostoses

15. The Norfolk Giant (also called the Suffolk Giant) (Wells 1964 and Brothwell 1967)

Wells (1964) described a skeleton, determined to be male, from an Anglo-Saxon cemetery at Burgh Castle, Norfolk. This skeleton dated from the Middle Saxon period c. AD 650. The height of the individual is estimated to be 232.52 cm (7 feet 7.5 inches). Severe, well-healed fractures were apparent on the right humerus, both ulnae, the right talus and calcaneus. Brothwell (1967:523) suggested that, though this individual might represent an individual whose height is at the upper limit of the normal curve of stature variation, the fractures may actually be indicative of giantism. No other information was given. It is apparent that a more thorough analysis of this individual's skeleton would be needed to determine a diagnosis. The variation of features of the population would also be helpful to assess the diagnosis.

The list of what was not mentioned, potentially not even considered, include the condition of the sella turcica, scoliosis, muscle and tendon insertion points, state of epiphyseal closure, cranial thickness, arachnadactyly etc. Age estimation of the individual including assessment of epiphyseal closure would also help in diagnosis. Since the diameter of the bones in relation to bone length for the Norfolk Giant was not indicated, Marfan syndrome should also be considered as a possible diagnosis. With the available information, a diagnosis of giantism is unconvincing.

Table 18. The Norfolk Giant Authors' Described Characteristics.

Male/Female	Male
Age	Unknown
Height	232.52 cm (7 feet 7.5 inches)
Documented Diagnosis	Hyperpituitary Giant
Rugged Face	
Tall Height	
Fractures	

16. The Archaeology of Nubia #1 (Egyptian Government Document 1907:47)

A massive skeleton of a phenomenally big man was found in a Nubian cemetery dated to the12th –20th Egyptian dynasty. Height must have exceeded 189 cm (6 feet 2.5 inches (see subsequent case). The researchers stated that there was no evidence of a pathological cause of his giantism. The average height of men in the cemetery population was 164.8 cm (5 feet 5 inches).

This individual was designated "giant" on the basis of height alone as he showed no pathologies according to the 1907 Egyptian government document. This individual fits the diagnosis of "giant" based upon the criteria set forth by Wells (1969) that a "giant" is defined as an individual above three standard deviations above the mean height of their population, but this individual does not necessarily fit the medical definition of the term "giant."

An examination of the skeletal material would need to be conducted to better define this individual's disease status. It was not mentioned whether the sella turcica or any other hyperpituitary giant and acromegalic characteristic was examined or not. Only the conclusion that no pathologies were present was recorded. Epiphyseal closure could also give more information regarding the cause of this individual's greater than

normal height, especially as it relates to estimated age at death. No photographs were available for viewing this individual. Analysis of the skeleton, if done, was not available. The variation of features of the population would also be helpful to assess the diagnosis. For these reasons, the appellation "giant" is not consistent with the diagnosis of giantism as outlined in this thesis.

Table 19. The Archaeology of Nubia #1 Authors' Described Characteristics.

Male/Female	Male
Age	Unknown
Height	189.0 cm (6 feet 2.5 inches)
Documented Diagnosis	"Giant"
Rugged Face	
Tall Height	

17. The Archaeology of Nubia #2 (Egyptian Government Document 1907:47)

Another male skeleton was discussed in the same book because of his extreme height and massive size. This individual dated to between the first and the twelfth dynasty, Nubian Egyptian. Height was measured as 189.0 cm (6 feet 2.5 inches). Again, it was stated that there was no evidence of a pathological cause for his giantism. The average height of males in the cemetery population was 166.1cm (5 feet 5.4 inches) in height.

This individuals was designated "giant" only on the basis of height as he showed no pathologies according to the 1907 Egyptian Government Document. The height of the individual was at the extreme upper limit of the normal curve of stature for his

population. This individual fits the diagnosis of "giant" based upon the criteria set forth by Wells (1969) that a "giant" is defined as an individual above three standard deviations above the mean height of their population, but this individual does not necessarily fit the medical definition of the term "hyperpituitary giant."

An examination of the skeletal material would need to be conducted to better define this individual's disease status. It was not mentioned whether the sella turcica or any other hyperpituitary giant and acromegalic characteristic was examined or not. Only the conclusion that no pathologies were present was recorded. Epiphyseal closure could also give more information regarding the cause of this individual's greater than normal height, especially as it relates to estimated age at death. No photographs were available for viewing this individual. Analysis of the skeleton, if done, was not available. The variation of features of the population would also be helpful to assess the diagnosis. For these reasons, the appellation "giant" is not consistent with the diagnosis of giantism as outlined in this thesis.

Table 20. The Archaeology of Nubia #2 Authors' Described Characteristics.

Male/Female	Male
Age	Unknown
Height	189.00 cm (6 feet 2.5 inches)
Documented Diagnosis	"Giant"
Tall Height	

Soft-Tissue Case Studies

The following soft-tissue case studies fulfill a third purpose for this project, which is to integrate soft-tissue case study information into a better understanding of the skeletal analysis of an individual with acromegaly and giantism. These case studies will allow the comparison of clinical life histories that can be associated with skeletal changes. The soft-tissue case studies also lead to a fourth purpose for this project, which is to present a better understanding of the lives and experience of those individuals with acromegaly and giantism as it impacted them personally, as opposed to life experiences based on postmortem conjecture (see Appendix 4).

The purpose of this section is to examine the soft-tissue and skeletal manifestations of acromegalics/giants who had detailed clinical histories and post-mortems. The first four case studies were gathered by Cushing and Davidoff as an aid in "diagnosis and mild examples of the disease" (Cushing and Davidoff 1927:81). The four case studies described by Cushing and Davidoff (1927) demonstrate the variability in the physical presentation of acromegaly and giantism.

Cushing and Davidoff's (1927) work followed a number of individuals' clinical courses. Two of the individuals donated their bodies to allow the examination of their skeletal system as well. These people's gifts allowed the association of skeletal changes to the documented progress of their disease. (It is to these people that this work is dedicated.) Reconstruction of the life of an individual is often based on conjecture with little documentary evidence. The association of a life history with skeletal pathologies will allow the bio-archaeologist/forensic anthropologist to infer possible skeletal

changes to the individual's lifestyle. How the person was affected physically can be explored with a concept of the individual's perception of the disease.

Case Histories of Individuals with Acromegaly

Case I

Individual number one (Cushing and Davidoff 1927) was a 42 year old man, a teacher, who first sought medical treatment for "incapacitating headaches associated with obvious acromegaly". As a young man at the age of 23, the individual was described as delicate-featured and light complexioned. He graduated that year as valedictorian of his college class. A photograph indeed represents a well-groomed and dressed young man of delicate feature and light complexion. He was 23 years old, 6 feet tall (182.88 cm) and weighed 140 pounds.

> "The first of these reports concerns a man who had faced his disfiguring and painful affliction with extraordinary fortitude. He had become greatly interested in the disease to which he was a victim, had written an autobiographical account of his individual case, and had left instructions for an autopsy. He had submitted frequent reports to the senior author regarding the progress of his malady up to the time of his death which occurred in his home in 1921, 10 years after he first came under observation at the John Hopkins Hospital." (Cushing and Davidoff 1927:6)

The acromegaly began sometime after his graduation; the exact time of onset was impossible to define due to its insidious presentation. However, the year of presentation is given as 1892, the year he graduated from college. At 27 years of age, surgery was performed for "enlarged cervical glands". The author suggests that

overgrowth was sufficiently obvious to be noticeable to the surgeon. He married at 30 years of age, 1898, but there were no children born to the couple.

In 1900 at 32 years of age, he sought medical advice for "increasing" headaches. These headaches were to plague him the rest of his life. Measurements were taken at this time. Height had increased to 6 feet 2 inches (187.96 cm), weight had increased to 202 pounds, and his collar, shoe and hat sizes had also increased.

The headaches were suboccipital but became more generalized over time. Any muscular effort increased the accompanying "bursting" feeling. Erect posture also increased his cephalgia or headache. Horizontal positions provided some relief. There was no nausea or vomiting. Mental and physical inertia became more difficult to live with as the duration of the affliction increased. Numbness in the extremities was constant. He often experienced shortness of breath, which was linked to an occasion of "pseudo-angina" or false cardiac pain. He felt that he was very susceptible to infections. His hypertrophied nasal bones caused increasing obstruction to his breathing, as did his enlarged tongue especially during sleep. He sweated copiously night and day. Sexual libido and testes' size decreased progressively over time. Diabetes was not diagnosed.

A photograph records this man's appearance at 42 years old, about 15 years after the disease became apparent[15]. Comparison of this photograph to his college graduation photograph showed increased facial length and larger features. In the later photo, a huge skeletal frame with noticeable signs of acromegalic growth was apparent. Rounding of the shoulders was not visible upon external examination. X-rays showed

[15] This time span is important for understanding the development of the disease and will be discussed later in this chapter.

closed epiphyses in the hand with characteristic tufting of the terminal phalanges. Rontgenography of the sella was not a highly developed procedure at the time, but the sella was not increased in size. The clinoid processes were heavy with tips that appeared to be fused or overlapped.

His head was large (length of 27 cm), with enlarged supraorbital ridges. The alveolar arch of the jaw was heavy with no apparent prognathism nor increased spacing between teeth (prognathism appeared later). There was enlargement of his thyroid gland.

A right subtemporal decompression was performed in July 1, 1910, but the headaches resumed. Glandular extracts were prescribed in large amounts. Certainly, on the basis of an active hyperpituitarism, this was distinctly contraindicated. Whether it had anything to do with the continued accession of skeletal growth is unknown. At this time, it was also noticed that the individual had a decreased temperature.

During the 10 years that followed the failed operation, his headaches increased. He became tired easily, yet he continued to teach. Skeletal overgrowth was continuing. His lower jaw finally became so large that it was almost impossible for him to chew. He had a stroke, which produced transient right-sided hemiplegia (paralysis) with some residual weakness. He retired from teaching in 1918, as he could no longer concentrate. In the time that followed until his death, he experienced increasing weakness and drowsiness along with the previously described headaches. He was alert and optimistic until his death on April 16, 1921.

A post-mortem examination was conducted per the gentleman's wishes. He died of broncopneumonia at the age of 52. Tufting of the terminal phalanges had

increased, with the greatest size change in the great toes. The sella turcica had not increased in size since it was visualized on a x-ray in 1910. However, the floor was found to be partially absorbed. The outline of the gland was distinct and appeared to be of normal or even sub-normal size. A histological examination described a pituitary adenoma.

All body measurements had increased slightly in his last ten years of life. The bones were markedly hypertrophic or enlarged, but they were said to show no histopathological alterations. Cortex was thin with a large medullary cavity, and there were hyperostotic changes in the vertebral centrums. Ribs were broad and heavy configured with an abnormally large anteroposterior diameter. The skull was greatly thickened, especially the frontal (2 cm). The increase in the thickness was observed to occur in the inner table, which showed rough hyperostoses over much of the frontal bones. The occipital bone was thinner (1 cm), and the longitudinal sinus was noticeable as it was broad and deep. This case is important because no enlargement of the pituitary was visible.

Case II

Case number two (Cushing and Davidoff 1927) was of a 35 year old man, a farmer, who had a childhood onset of acromegaly[16]. A family history was given by the individual. His father was six feet (182.88 cm) tall and weighed over 190 pounds, while his mother was described as having massive features. He was the oldest of six children,

[16] Acromegaly, in Cushing and Davidoff 1927, is used to describe acromegaly specifically, and giantism and acromegaly generally, much like hyperpituitarism is currently used.

and weighed 10-12 pounds at birth. No physical abnormality was noted until he reached 13 at which time he began to grow rapidly.

By 19 years of age, he was 6 feet 4 inches (198.12 cm) tall and weighed 200 pounds. He was alert, powerful and intelligent, with what was described as "an uncontrolled libido". A severe undefined illness was noted in his 23rd year; the major symptoms were polyuria or frequent urination and persistent furunculosis.

The author states that a photograph taken at 25 shows no signs of acromegaly. Growth resumed for this man at 27 years of age, when a diagnosis of acromegaly was made. During this period, he experienced intense frontal headaches and pain in the arms and legs. Blood and muco-haemorrhagic discharge from the nose gave respite from these headaches. His vision was impacted at this time with diplopia, or double vision, and bitemporal blindness. He later became crippled by his excessive overgrowth. He experienced a loss of vigor, weakness, drowsiness, and became easily fatigued and impotent. Although his height increased two inches from 1904-1910, his spine exhibited a progressive bowing.

In 1910, his height was 6 feet 6 inches (198.12 cm) and his weight was 269 pounds. His frontal sinuses were greatly enlarged. The mandible was protruded and tilted, and the diameter of the thorax was increased. A lateral x-ray of the cranium showed a sella turcica that had been greatly expanded. It was described as being heavy and hypertrophied, with a posteriorly tilted dorsum sellae. Increasing blindness and a divergent squint was attributed to pressure against the optic chiasm. An attempt was made to relieve the inter-cranial pressure affecting the eyesight with a transphenoidal operation.

Hospitalization was necessary in 1914 due to the level of severity of the symptoms; he could no longer stand erect. A photograph of the naked man *standing* next to a fully clothed, average man was included to show the patient's stature, acral enlargements, and crippled posture. Spinal changes occurred that resulted in the bowing and rigidity of the spine. His facial features had enlarged even more since the last documented observations. His skin and underlying structures had become loose and fluid-filled. Fibromata mollusca (skin tags) were apparent over his back and chest, and his scalp had become very thick with deep corrugations. He vomited occasionally and his temperature was subnormal. Reclining offered relief from the intolerable headaches that were at times accompanied by vomiting. The individual was often drowsy. Another surgery was preformed as an attempt to offer some relief from the excruciating headaches.

Five months of hospitalization ensued. Headaches and projectile vomiting continued. At the behest of his family, a final surgery was preformed in an effort to provide some comfort to this man. "He gained his release by death the following day" on February 15, 1915. He was forty years old and had lived with acromegaly for approximately 27 years. Permission was granted for an unrestricted autopsy with removal of the skeleton. All that was noted of the skeletal changes was "(a)cromegaly with typical skeletal changes" (Cushing and Davidoff 1927:42).

Case III

Individual number three (Cushing and Davidoff 1927) was a male, married, who was referred to hospital admission in 1913 at 34 years of age, with a diagnosis of acromegaly and complicating diabetes. He had not sought medical help before this

time, although symptoms of acromegaly could be traced back to his twentieth year. It is recorded that he worked as a Canadian fisherman up until just a matter of weeks before this admission.

Family history revealed no family members of outstanding stature, and he had the usual childhood diseases. He had pronounced prognathism but was unaware of the progression of this feature. He did not recognize that he had this prominent feature according to the authors. They suggested that this reflected his generally unobservant nature.

When he was twenty years of age (1899), he began to increase in size. His hands and feet became so large that he had a difficult time finding shoes and gloves to fit them.

During this period, he found that his appetite increased notably, although he had always had a good appetite. He did not keep track of his weight, but he did state that he had gained 50 pounds in 2 years. In 1908, he weighed 220 pounds according to his recollection. He married at 29 years of age (1908), soon after which, he became impotent. He and his wife had no children.

Throughout the following years, he suffered from night sweats and profuse sweating during the day and his hands and feet were often numb. Even with these physical problems, he did not change his daily activities. His life was impacted in 1910 at the age of 31 when he noticed that he was increasingly drowsy and that his output of urine increased. Dispositional changes were noted by family and friends from 1910 up until his hospital admission. He was irritable and more forgetful. He had noted headaches occasionally in previous years, but now they were occurring every few

weeks. Vomiting often relieved the pain. Seizures and nocturnal attacks, which left him unconscious, had started about one year before he sought out this only episode of medical help.

Physical examination at the age of 34 described a man who was a "distractable (sic), drowsy and irritable acromegalic of 5 foot eight inches in height, weighing 178 lbs. Vision was normal" (Cushing and Davidoff 1927:45). He was diagnosed with diabetes as well as acromegaly.

On April 29, 1913 a transphenoidal operation was carried out with no particular difficulty. The sella floor was almost completely eroded, and the tumor was found to be eosinophilic adenoma. After the operation, he found some relief from his mild headaches as well as a decrease in the swelling of his hands and feet.

One year later, March 13, 1914, a very cyanotic, dyspnoeic, orthopnoeic and irrational man was admitted to the hospital. He was edemotous. He died twelve hours later (the autopsy results are presented in Appendix 4). An additional finding was that the calvarium was thinner than that of other acromegalics (in the opinion of W.T. Councilman, who performed the autopsy) with few frontal endostoses. The greatest thickness of the skull was measured as 6mm. Pacchionian digitations (thin areas) were marked and a few perforated the skull. Prognathism was extreme, and the lower jaw was significantly wider "across" than the lower jaw. A goiter was present, and the testes had atrophied.

Cushing and Davidoff (1927) provided a comparative study of Case II and Case III to illustrate the skeletal differences between an acromegalic-hyperpituitary giant

individual and an acromegalic individual. Both individuals displayed tufting of the terminal phalanges and enlargement of the sella turcica. Case II, although a hyperpituitary giant, had evidence of severe vertebral exostoses. Cases II and III both had mandibular lengthening and prognathism. Case II shows a greater increase in the mandibular angle.

An enlarged sella turcica is not always inevitable, as the cases in this section will exemplify. It is only when the enlarging lesion remains long confined within the sellar envelopes that the fossa becomes hugely distended. When, as in Case III, the growth had broken through the envelopes early in its progress the sella may remain relatively small, or when the adenoma never attains any considerable size the fossa as in Case I, may not appear enlarged at all (Cushing and Davidoff 1927:85).

Transphenoidal surgery can also modify the acromegalic skull. Within the Cushing and Davidoff (1927) article, it is mentioned that the maxillary spur and the vomer can be removed in such a surgery. These missing structures (and possibly others) in a skull diagnosed with acromegaly can imply that transphenoidal surgeries were preformed.

Case IV

Individual number four (Cushing and Davidoff 1927) was a woman who was diagnosed with acromegaly when she was 51 years of age. She entered the hospital at that time due to headaches. Her family history showed no indications of potential diagnosis, with her personal history being unremarkable as well. This might have been

due to "the patient's want of observation and inaccuracies of memory" (Cushing and Davidoff 1927:67).

Menstruation began at 15 years of age and continued regularly until an abrupt menopause occurred at 40 years of age. She married at 18 to a man of her own age. She had nó miscarriages nor were any children born to the couple. She had surgery to cure glaucoma, in 1903.

Numbness of her hands and feet following began when she was about thirty years old. At around forty years of age, she noted increasing drowsiness, lethargy and lack of ambition. Restlessness, inability to concentrate and dull, diffuse pains in her abdomen and back were also noted at this time. About 1905, the headaches, usually located in the temporo-frontal region, became more severe. At age 43, friends noticed that her fingers were increasingly stubby and pudgy. She noticed that her nose was enlarged, and her dentist noted a change in the palate and alveolar arches conformation. He diagnosed her with acromegaly.

At this time, she was 5 feet 2 inches (157.48 cm) and weighed 151 pounds. Physical examination indicated that she had tufting of the terminal phalanges, prognathism, and that the sella turcica was greatly enlarged. On July 16, 1915 a surgery was performed. The headaches stopped, but two months later she was readmitted. She had numb feeling in her hands, but her drowsiness had decreased. She was readmitted on Jan 21, 1916, when she became comatose and died.

Case V.

Geddes (1911) describes the case history of a woman with acromegaly in "Report Upon An Acromegalic Skeleton". A brief clinical history is presented with a series of photographs as well as a description of the skeleton.

For individual number five, age of onset of acromegaly was given as 25 years of age, at which time the woman, a lady's maid, sought medical treatment for a sore throat. A photograph of the woman was presented to show her appearance before the onset of the acromegalic symptoms. She has a narrow nose and fine lips, and her skin was fair and clear. A few weeks after this episode, her hands started to grow and were painful. Menstruation stopped shortly after, and only occurred again once, five years after onset. Extreme lassitude was the next recorded symptom to appear. Growth of the feet and the coarsening of facial features were noted some short time later. Coarsening of hair and a "marked " increase in tongue size were documented as appearing in the same time-period. A photograph of the woman at 26 years of age, during the first year with the disease, documents the thickening of the lips, the enlargement of the nose and ears and the coarsening of the hair.

The next new symptom, increase in the thyroid, was stated as occurring at about the twelfth year after onset. At age 40, the fifteenth year of the disease, she became blind in her right eye. At forty-two, her boot size was recorded as size 7 (she had previously worn a size 3). A photograph recorded her appearance in this, the seventeenth year of living with acromegaly. Her right eye diverges due to its blindness, and freckles were apparent, although none were noted in earlier photographs. She was neatly dressed with well-groomed hair.

She lived for eight more years during which time her "condition gradually progressed" (Geddes 1911:258). A photograph records her appearance at 49 years of age, after living with acromegaly for 24 years. Continued progression of facial changes is noted in the text as well as the increased divergence of her right eye. Again, she is well groomed and neatly dressed; she wears a lace collar pinned in the middle with a broach.

Death occurred at the age of 50, 25 of those years she had lived with acromegaly. A post-mortem photograph of the woman is presented: "To show especially the hair" (Geddes 1911:261). A pituitary tumor was found at autopsy, when her skeleton was described in detail. In general, there was increased vascularization of the bone, especially in the bones of the cranial vault. Rheumatoid arthritis was noted in every movable joint. Every bone was abnormal in shape and appearance. The femoral length (head to internal condyle) was Right, 421 centimeters, Left, 423 centimeters.

Most striking were the length of her face, the "buccal gap", the great height of the maxilla, and the prominent nasal bones. There also was asymmetry of the skull, a thick cranium, an enlarged pituitary fossa, the foramen magnum was reduced to a slit, and the maxillary sinuses were enormously expanded. The length of the individual's face versus stature (according to Cushing and Davidoff 1927) was enough to distinguish acromegaly from giantism. She also had enlargement of the anterior ends of ribs, marked cervico-dorsal kyphosis, a type of osteomalacia, and reduction of the spinal foramina. Her pelvis had a flat sub-pubic angle; she had a great width of sacrum, which was rugged but atrophic (quite thin), and growth at the pubic symphysis and the sacral alae.

Case VI.

Thomson (1890) gives another description of acromegaly in "Acromegaly, With The Description of a Skeleton," published four years after M. Pierre Marie's original description of acromegaly. Cunningham originally presented the autopsy information on this individual in 1879. Individual number six was a male fireman, 36 years of age. Due to his great size and distinctive features, his condition was of interest to the medical community of the time. Dr. C Muirhead provided care during this man's two-month hospital stay. His height was recorded as 6 feet 0.5 inches (184.15 cm) post-mortem. Muirhead's 1878 analysis was written about 8 years before M. Pierre Marie's original description of acromegaly. For this reason, a diagnosis of acromegaly would have been impossible at that time. Thomson (1890) makes the diagnosis of acromegaly years later.

Notes of the case were from the hospital ward-book were presented by Thomson and Cunnigham. The diagnosis of the hospital admission was "a case of strongly-pronounced *diabetes mellitus*".

They quote from the hospital ward book as follows:

> "The whole aspect and general configuration was so peculiar as at once to arrest the attention of any observant person. His frame was so huge, his movements so ungainly, his expression so unpleasing, the brow so overhanging, and the feet and hands so enormously large and flat as to suggest the idea to some in the ward of a resemblance to a gorilla, and by this epithet he was spoken of among the other patients. I was not aware of this till after he left the hospital; and, on thinking of his appearance, I cannot say that I recognize the likeness. His voice was as remarkable as, and in unison with, his otherwise large development: it was strong, deep, and hoarse—in fact, the patients used to speak of the gorilla roaring when he called for anything he wanted.
>
> "He had no symptom whatever of paralysis or paresis. So far from this he was in the habit, when he first came into hospital, of going to the kitchen to help the nurse to carry up the breakfast and dinner. ...

> Farther this act of his, a purely voluntary one, showed that he was not insensible to kindness, and a willing to oblige. But while saying this much, I must allow that his expression indicated a low type of intellect—it was heavy, stupid, dull, utterly devoid of anything like active intelligence. He was quite uneducated; I believe that he could neither read nor write. He was easily irritated, and though sometimes he gave vent to this in a fit of passion, more commonly he exhibited it by hysterical weeping, and in this way his fits of anger invariably terminated" (Thompson 1890:515).

The sight and hearing of this individual were unimpaired, notwithstanding that the optic tracts, commissure, and nerves were rendered perfectly flat by pressure. This was also the second case in which general progressive hypertrophy has been associated with enlargement of the pituitary body.

The individual's head and thorax were peculiarly large; his limbs were spare, though his hands and feet were enormous. Diabetes was the only cause of death specified on the certificate of death. His stomach was 4 to 5 times normal size, and the bones were very large and out of proportion to the muscular development of the subject. Enlargement of the bone was uniform and symmetrical. A distinct depression of the inner surface of the skull-cap was visible where a prominent fluctuating bulging of the dura mater over the parietal lobe of the right cerebral hemisphere was observed during dissection. The pituitary body was found to be enlarged to about four or five times its usual size, as was the pituitary fossa in which it lay.

Thompson's (1890:484) article gave a detailed description of erosion of his pituitary fossa. Other findings included that the optic groove was obliterated, and the optic foramina was flattened. The anterior fossa was shallower than usual due to the large size of the frontal sinuses and by the encroachment of the cranial cavity of the

orbital plates of the frontal bone. This individual had no mastoid, sphenoidal, and maxillary sinus dilitation, and no evidence of abnormal curvature of the spine

There were projecting processes along the superior and inferior margins of vertebral bodies, dorsally and ventrally. These projecting processes tended to continue over the intervertebral disc in the area of the anterior ligament. His ribs were long, and the sternum was reported to be "gigantic". Costal cartilage ossification was affected.

Thompson (1890:486) additionally reported that, "Such an extensive of the cartilages , and connective tissues generally, exactly corresponding to what is seen in cases of osteo-arthritis, viz., the development of large masses of bone in the substance of muscles and tendons in parts of the body distant from those affected by the arthritis itself". There was also unusual vascularity of the periosteum, deformity of the sterno-clavicular articulations, which suggested osteoarthritis, and partial ossification of the glenoid ligament. All the phalanges were broader and thicker.

CHAPTER 5

ANALYSIS AND DISCUSSION

Analysis of the Skeletal Case Studies

Upon reading the literature regarding acromegaly and giantism, it became apparent that more than one definition of "giant" was in use. While the medical differential diagnosis of acromegaly and hyperpituitary giantism is the focus of this work, it is necessary to acknowledge that anthropology and western culture also have definitions of what makes someone a "giant".

In those skeletal cases of giantism where height was mentioned, 100% of the cases were taller than 6 feet 6 inches (198.12 cm). Some were described in the reports as giants as they related to the height of others in their population. Others were described as giants by people in their own population. Medical diagnosis of the disease as we know it came only after Cushing's 1912 discovery of the pituitary (Bergland 1965:268). It was at that time that the conditions of acromegaly and giantism were found to result from an overproduction by the pituitary.

Although the number of individuals presented in this study is not large, trends in diagnostic criteria can be inferred from the number of times a characteristic was used in a diagnosis (this concept will elaborated on in the discussion section). The raw data presented in Appendix 3 is organized by individual and by characteristic. If a specific characteristic was noted as being present in an individual case study diagnosis, then a "Yes" was placed in the corresponding cell. If the characteristic was not noted as being present or was noted as being "not present," then a "No" was placed in the cell.

Differentiating between whether a characteristic was diagnosed as being "not present" or was simply not mentioned is not dealt with in this study.

Following the raw data for the observed characteristics are percentage analyses for each characteristic. Percentages afford a simple method with which to observe the frequency certain characteristics were noted in each of the diagnoses given in the literature: "giant", hyperpituitary giant and acromegaly, and acromegaly. The percentage data for each characteristic are also found in Appendix 3. The percentages represent the array of features that were reported by the authors of the individual cases and will be presented and analyzed next.

The acromegalic/giantism characteristic most commonly referred to in the skeletal case study literature was "tall height," which was ascribed to 100% of the "giant" cases, 83.33%, hyperpituitary giant and acromegalic and 14.28% of the acromegalic individuals. Elongation of mandible was mentioned in 100% of acromegalic diagnoses, 67% of hyperpituitary and acromegalic cases and 25% of those cases designated "giant". Elongation of the mandible is a characteristic associated with acromegaly (Ortner and Putschar 1981, Jaffe 1972).

The Tegernsee Giant was described as having an elongated mandible (Nerhlich 1991 and Pirsig 1994). As he was 25 years of age, it is possible that he was entering the acromegalic stage even though he had an epipyhseal age of 17. Growth in height was often documented in other individuals even at the age of 28. Acromegalic characteristics were noted in those individuals who grew into their late twenties (Cushing and Davidoff 1927). Prognathism was noted in 42.857% of acromegalics, 33.33% of giantism with acromegaly, and 0% of the "giants". This relates to the bony

overgrowth occurring in the jaw. Individuals with giantism would not be expected to exhibit this characteristic.

Given the cultural and anthropological definitions of the disease, the characteristic percentage results are not surprising. Even medical books indicate tall stature as a characteristic. People who suffer from a pituitary adenoma of the GH secreting type can be extremely tall, but they do not have to be tall or over 6 foot 6 inches (198.12 cm) or not necessarily in the top third of height of their population! In theory, a dwarf can be a medical hyperpituitary giant. As Brothwell (1981:162) described giantism, "Height says it all." Height does not say it all, it does not account nor describe the other lesions that can exist. Roberts and Manchester (1983) suggest that extreme height is characteristic of acromegaly. Acromegaly by definition occurs after epiphyseal closure, therefore acromegalics do not exhibit extreme height (Jaffe 1972:332). Rhine (1985) and Hosovski (1991) give lists of characteristics where height is not mentioned.

In regard to bone size, 66.67% of giants with acromegaly, 42.857% of acromegalics and 25% of giants were described as having all bones enlarged and elongated. This result seems off since one would expect to have all giants described in this matter. This result is probably due to the fact that two of the giants of the Ptolemaic cemetery were described only as having no pathological features. No other descriptions were available regarding these individuals. The lack of reporting for these two individuals is probably skewing the results. These results also confirm that "elongated" and "enlarged" were commonly used to define giantism. One would not expect acromegalics to have elongated bones unless they had giantism.

Arthritis of the vertebral column is described in 57.143% of those with acromegaly, 33.33% of those listed as giants with acromegaly and 0% of giants. Giants often did not live long enough to develop many skeletal lesions related to their condition (Aufderheide and Rodriguez-martin 1998:327).

The frequency of other characteristics are found in Table 21:

Table 21: The Frequency of Other Selected Characteristics.

Characteristic	Acromegalics Only %	Acromegaly and Giantism %	Giantism Only %
Cranial Vault Thickened	28.57	66.667	25
Enlarged Frontal Sinuses	57.143	50	25
Enlarged Sella Turcica	28.571	50	25
Proportional	14.286	50	0
Kyphoscoliosis	14.286	33.33	0
Robust Skeleton	14.286	33.33	0
Bony Obliteration	0	16.67	25
Fractures	0	16.67	50

The severity of acromegaly has been linked with the severity of the lesions presented. In other words, the more characteristics of acromegaly and/or giantism that are presented, the more severe the case the longer the assumed duration of the disease within the individual. One would not expect to see severe acromegaly in a hyperpituitary giant of extreme height. With the accompanying physiological stresses, death would be likely before acromegaly would become too pronounced (Aufderheide and Rodriguez-Martin 1998:327).

The presence of the enlarged sella turcica with other features is the most convincing of diagnostic criteria. However, a series of lesions with the characteristic

distribution defined previously is also suggestive. Unlike working with living individuals, there are no further tests available at this time to confirm diagnosis.

If we compare these results with data from living individuals, we see that a variable presentation and severity of lesions is not uncommon. In an example presented by Cushing and Davidoff (1927), the sella turcica showed no enlargement, though a diagnosis of acromegaly was made.

T-test Results and Analysis for the Skeletal Case Studies

Mean height of the skeletal case studies will be compared with the mean height of the modern U.S. population using parameters collected by the United States Department of Health and Human Services (DHHS) (1987: 27). Height is examined because it is one of the primary markers associated with giantism. This characteristic has been described in the literature as "... the subjects become extremely tall..." (Jaffe 1972:333). This section will look at how "extremely tall" compares with the average height of the modern United States population, since those making the diagnoses tend to be operating from within the context of Western populations.

For the purpose of this analysis, the mean of the skeletal case study heights will be compared with the mean of the U.S. population (DHHS 1987:27). The case studies will further be divided to examine how those individuals diagnosed as being "giant" [17], "acromegalic-hyperpituitary giant", and "acromegalic" compare with the mean height of the US population. "Giants," as defined in the literature, should demonstrate heights

[17] The placement in categories is based upon the diagnoses of the skeletal case studies as determined in the literature.

greater than the mean height. Acromegalics, as defined medically, should show a mean height similar to the individuals' population of origin (or the mean of the modern U.S. population, in this case). An acromegalic population should also follow a normal curve for "height," since acromegaly affects adult individuals randomly and regardless of their pre-onset height.

The small number of individuals in this sample precludes any convincing conclusions about these issues, but the results are interesting and set the stage for further inquiry. Heights derived from skeletal material were used unless they were not available, in which case, heights attributed to the living individual were used. The important factor for diagnosis was the *perceived height* of the individual being diagnosed.

Since it is expected that the mean height of this sample population will be higher than the US mean height, a one–tailed t-test will be employed. One-tailed t-tests are used when there is strong evidence to suggest that the given difference between the sample and the population mean lies entirely within only one tail of the population distribution. A test statistic that falls in the region of rejection in a one-tailed test may not fall in the region of rejection of a two-tailed test. In other words, it takes a more extreme test statistic to reject the null hypothesis in a two-tailed test (Earickson and Harlin 1994:169-175).

In this case, it was suspected that the mean height of the skeletal case studies was not representative of the US population in 1977-80. The mean height in the modern U.S. population was 175.5 cm (DHHS 1987:27). The hypotheses to be tested were that the mean height of the "giant" skeletal case study sub-group, the "acromegalic

giants" sub-group, the "acromegalics" sub-group, and the skeletal case study "total" population each had heights that were significantly greater than 175.5 cm (Earickson and Harlin 1994:153).. The null hypotheses were that the mean height of the "giant", "acromegalic giants", and "acromegalics" sub-groups and the "total" population each had heights equal to or less than 175.5 cm, or that there was no difference between these groups and the modern United States population (Earickson and Harlin 1994:151).

A t-score is calculated to standardize a value so that it can be used to compare two means from two normally distributed but independent populations. When a value is converted to a t-score, the value is expressed in terms of the deviation of the sample mean from the actual mean of the population from which the sample was drawn (Earickson and Harlin 1994:163). The calculated t-score is then located on a standard table to find its equivalent probability. The t-test formula for comparing means is:

$$t = \frac{X(1) - X(2) - \text{Delta}}{\text{Square Root of } (S(1)\text{ Squared}/N(1) + S(2)\text{ Squared}/N(2))}$$

where X (1) is the sample mean from population (1), X (2) is the sample mean from population (2), Delta is the specified value to be tested (in this case, the hypothesized difference between the population means which is 0), S (1) is the standard deviation of population (1), S (2) is the standard deviation of population (2), N (1) is the size of population (1), and N (2) is the size of population (2)[18]. The number of degrees of freedom for the problem is the smaller of N (1) – 1 and N (2) – 1 (Earickson and Harlin 1994:169-170).

[18] The standard deviation in this case is found in the U.S. Department of Health and Human Services document, *Anthropometric Reference Data and Prevalence of Overweight: United States, 1976-80. Data From the National Health Survey, Series 11, No. 238.*

The critical t-score is read from a standard table using degrees of freedom and the level of significance or alpha level. The probability level was set at 95%. Since this was a one-tailed t-test the region of rejection is less than 5% or equivalent to an alpha level

of .05(Earickson and Harlin 1994:169-175). Degrees of freedom, which are calculated by the equation n-1, are calculated for each sample being compared. The smaller value is used to determine the critical t-score for each pair of samples tested. These values can be found in Table 23. If the calculated t-score was equal to or less than the critical t-score, the null hypothesis of "there is no difference between the mean of the sample and that of the population mean height" was rejected.

Table 22 Heights (in centimeters) Used for T-test Analysis

The Mutter Giant	235.60 cm	Acromegaly and Giantism
The Norfolk Giant	232.52 cm	Giantism
Charles O'Brien	231.00 cm	Acromegaly and Giantism
The Persian Giant	220.00 cm	Acromegaly and Giantism
The Polish Giant	215.50 cm	Acromegaly and Giantism
The Tergenesse Giant	210.00 cm	Giantism
Marushia/Sauer Individual	193.04 cm	Acromegaly and Giantism
Smithsonian Individual #2	189.75 cm	Acromegaly
The Archaeology of Nubia #1	189.00 cm	"Giant"
The Archaeology of Nubia #2	189.00 cm	"Giant"
Hosovski Individual	173.00 cm	Acromegaly
Rhine's New Mexico Acromegalic	165.00 cm	Acromegaly

Table 23 Basic Statistics for Skeletal Case Studies with Heights

	Giantism Only	A. and G.	Acromegaly Only	Total Group
Number	4	5	3	12
Sum	820.52 cm	1095.14 cm	527.75 cm	2443.41 cm
Mean Height	205.130 cm	219.03 cm	175.913 cm	203.617 cm
Range	43.52 cm	42.56 cm	24.75 cm	70.6 cm
Standard Deviation	20.771	16.634	12.625	23.777
Degrees of Freedom	3	4	2	11
Critical t-score*	2.353	2.132	2.920	1.796
Calculated t-score	62.105	5.847	0.05666	4.096

*(at 95% confidence level, p is less than 0.05)

Table 24 U.S. Population Statistics 1977-1980, All Races, Male, Age 18-74

Number	5916
Mean	175.5 cm
Standard Deviation	7.2

The calculated t-scores for the groups "giant", "acromegalic giants" and "total" all were well above the critical t-score values of 2.353, 2.132, and 1.796, which led to the rejection of the null hypothesis (acceptance of the alternative hypothesis) at a 95% confidence level. This meant that the mean heights for these groups significantly exceeded the mean height for the 1977-1980 US population. The calculated t-score for the acromegalic individuals did not exceed the critical t-score of 2.920. Therefore the null hypothesis was not rejected; there was not a significant difference between the mean height of the "acromegalics" group and that of the US population from 1977-1980.

It was expected that giants and acromegalic giants would be taller than the average height of their contemporaneous population. They were also taller than the mean height of a modern US population. For more comprehensive studies, the scale of giantism should be balanced by two factors: the mean height of the contextual population (not the observer's), and the presence of other markers.

As a group, acromegalics were shown to have the same mean height as the US population, but two of the three individuals in the distribution had heights above the mean height for their populations, and the third individual was taller than the mean height of the US 1977-1980 survey[19]. As mentioned throughout this work, acromegaly is an adult onset disease, so a normal distribution of height would be expected. In theory, one would expect acromegalics of all heights. Granted, the sample examined was extremely small, but this study suggests that a height bias might exist that hampers the identification of acromeglics, or perhaps the distribution of height of acromegalics is

[19] Rhine's acromegalic was 1 in. or 2 cm. above average, the Hosovski Individual was 1 in. or 1.7 cm. Above average, and the Smithsonian Individual #2 was 5.5 in. or 14.25 cm. above average.

not normally distributed. The distribution of height for a much larger sample of acromegalics and giants would be an interesting topic for further research.

Analysis of Soft-Tissue Cases and Life Histories

The above case histories are presented to allow for examination of the changes in the skeletal system, as a function of the duration of giantism and acromegaly as a single disease that varies by age of onset. This allows an understanding of the timing of appearance of lesions and their severity. Variability of the presentation of giantism and aromegaly is widely recognized, but there is a recognizable pattern of progression (Cushing and Davidoff 1927, and Geddes 1911). These life histories allow a more reality-based interpretation of the life of an individual's skeleton in forensic investigations or in archaeological contexts. We therefore have a better idea of what was going on in the life of someone diagnosed with this disease posthumously. Timelines of clinical and skeletal changes are presented in Appendix 4.

Information from the clinical histories of the people presented above allows a chronology of appearance of symptoms to be generated. It is evident that the characteristics associated with acromegaly develop insidiously for 14-22 years and then "all of a sudden" become quite apparent. This has been validated by the medical literature's description of the course of the disease as well (Nabarro 1987). These characteristics include increased skeletal frame, rounded shoulders, larger thorax, increased size of facial bones, phalangeal tufting, larger head, prominent supraorbital ridges, prognathism, closed epiphyses, enlarged sella turcica, increased height, spinal curvature, larger hands and feet. If present, it is during this time period of 14-22 years

after the onset of the disease process, that these characteristics become blatantly discernable.

Increased height is described in two of the cases (Case I and Case II). Case I describes a man whose onset of the disease was thought to occur at about 23 years of age. Case II describes a man whose condition was thought to have occurred during his 13th year. However, both males experienced a "second period of growth" near the same age, 23-31 and 25-27. Epiphyseal closure of the femur in the male according to McKern and Stewart (1957) observations occurs between 18 and 22 years of age. This implies increased pituitary function could have been present earlier than suspected in the individual in Case I.

Delayed epiphyseal closure has been noted in individuals with giantism, namely O'Brien (Landolt and Zachmann 1980:1311-1312), the Hosovski Individual (1991:273-279) the Tergeness Giant (Nerhlich et al. 1991 and 1994, and Pirsig et al. 1994). This can be due to the influence of the pituitary, both through the physical presence of the tumor and through changes in hormone secretion, on puberty. Following out this line of reasoning, a characteristic of giantism could be open epiphyses in an individual whose chronological age would suggest that epiphyses would be closed. The chronology of the soft-tissue case studies demonstrate that a second period of growth can occur in individuals from 23-28 years of age so that the acromegalic features would not become marked until epiphyseal closure occurred.

Case V and Case VI, both noted growth at the costal cartilages. "Such an extensive ossification of the cartilages is very unusual at the age of thirty-six..." was noted in autopsy report of the man's history described in Case VI (Thompson 1890).

Since the rib ends are used in the determination of age in the Iscan Method (Iscan et al. 1984), age should be estimated from a variety of methods when a pituitary condition is suspected.

Case VI also noted that the woman's pubic symphysis and sacral alae showed overgrowth upon autopsy. Like the rib ends, the pubic symphysis is used in estimating the age of an individual. Determination of sex is also based upon observation of this area. Again, methods that use areas of potential growth (areas of cartilage) should not be used when pituitary function might be affected.

Duration of the disease varied in each instance between 15 and 30 years. A summary of the soft-tissue case studies and the duration of each case of giantism and acromegaly is presented in Table 22.

Table 25: Summary of Giantism and Acromegaly Duration in Soft-Tissue Case Studies.

I	male	from about 29 years from age 23 to 52
II	male	from about 27 years from age 13 to 40
VI	female	from about 25 years from age 25 to 50
IV	female	from about 21 years from age 30 to 51
III	male	from about 15 years from age 20 to 35
V	male	from Unknown to age 36

None of the individuals was mentioned as having children. If there is any genetic component to acromegaly, there might be a reduced transmission due to a decreased ability of hyperpituitary individuals to procreate.

Some conclusions can be drawn from the data presented above and in Appendix 4, which are useful in diagnosing and analyzing acromegalic and hyperpituitary giant skeletons. Enlargement of the sella turcica does not occur in all cases of hyperpituitarism as Case I illustrates. Hyperpituitarism can occur due to the hyperproliferation of cells or due to the hypersecretion of cells. The latter would not necessarily be associated with a tumor of the pituitary or its enlargement.

One purpose of this thesis is to give a method of differential diagnosis to recognize more instances of acromegaly and giantism. Pituitary tumors were found in 25% of the population at autopsy (Harrison 1981:1899). An eroded or enlarged sella turcica is, therefore, not necessarily an indication of acromegaly/giantism by itself. A series of other characteristics must be considered to accurately identify acromegaly and giantism. It is a constellation of characteristics that defines acromegaly and giantism, and not a single characteristic.

Conversely, if there is no sella turcica enlargement, but there are other characteristic lesions, acromegaly and giantism cannot be excluded. Cushing and Davidoff's (1927) skeletal autopsy of two clinically documented individuals diagnosed with acromegaly and acromegaly/giantism showed that sella turcica enlargement was not necessary for diagnosis. In these cases, the tumor may have grown intracranially, with no remodeling of the sella turcica. It has been documented (see Robbins and Cotran 1979) that a tumor need not occur at all, if the cells that are responsible for GH production increase production to abnormal levels.

The timelines presented in Appendix 3 were based upon each individual's observation of the changes in their bodies, and the changes noted by the medical

observers. Comparing the individual's observation of their own body changes with those of friends, as in Case IV, it is possible to see that changes are missed by the person afflicted. The man in Case III was unaware of the changes in his body, much to the astonishment of the medical / physicians since they considered his bodily changes quite extreme. However, the man in Case I became quite attuned to changes occurring in his body and noted them readily to the physicians. These differences in perception will, of course, affect the notation of body changes. Perceptions of the physicians would also vary depending upon the relationship with the patient, the focus of interest, and their knowledge of acromegaly.

One of the purposes of this project was to examine the inconsistencies in the diagnosis criteria used to identify individuals with acromegaly and giantism. Individuals in this study were chosen because they were used as examples of giantism, acromegaly, or giantism and acromegaly in the paleopathological literature. These are examples which observers will potentially be using to diagnose these diseases in future individuals. Many of the examples that are commonly used have not been reassessed for over 100 years.

Few, if any, of the individual's skeletons were diagnosed during life since acromegaly and giantism were not recognized as disease entities until Marie's work in 1886. As the accession of many of these individuals was shrouded in mystery due to the passage of time or the unorthodox methods of collection or both, little is known of their life history. This is not to say that posthumous diagnosis is invalid, but a living diagnosis with a history of skeletal changes would help to identify those skeletal feature exhibited in people with acromegaly.

Another purpose of this project was to point out that the two primary characteristics used to identify acromegaly, "height" and "elongation of the mandible" are not sufficient criteria by themselves. Giants were diagnosed primarily by tall stature, "elongated and enlarged bone growth". Those individuals diagnosed as "giant" were all over 6 foot 6 inches tall. Does this mean that there are no giants under this height? It depends on which giants you are discussing. Medically, a hyperpituitary giant is someone who has a pituitary adenoma that secretes GH and produces greater than usual growth. "Giant", as defined in this study, will be an individual with giantism, as defined medically, who also has associated lesions as detailed in Table 3.

Above average height would be contingent upon populational genetics, individual genetics as well as environmental factors including available nutritional resources and stress (Weinreb 1984:299, and Wells 1969). The period of greater growth can also vary. For instance, a person who develops a secreting tumor at birth, such as Robert Wadlow (Hayles 1980:168), would be taller than an individual who developed the disease at 12 years of age. Considering the above information, those individuals with giantism can be of variable height.

As stated previously, the height of acromegalics should follow a normal population statistical curve, since acromegaly is defined as occurring after epiphyseal closure is completed (i.e. adulthood) (Robbins and Cotran 1979:1340). However, some authors (Brothwell 1981:162, and Roberts and Manchester 1997:181) have incorrectly defined acromegaly as being associated with increased height, which could cause confusion in diagnosis.

Aging the Acromegalic/Hyperpituitary giant Skeleton

Aging an individual with acromegaly and or giantism from skeletal material would present some difficulties. In particular, there are two aspects of the disease, which potentially could introduce error in the assessment of age. First, giantism presents variability in the fusion of the epiphyseal plates. In the reassessment of O'Brien's skeleton by Nerlich et al., they found that his epiphyses were not fused. O'Brien was 22 years old at death, while epiphyseal closure showed 17 years of age (Landolt and Zachmann 1980:1311-1312). The Mutter Giant's age was also based on epiphyseal closure (Humberd, Mutter Museum Archives). This information is supported by clinical evidence presented by Cushing and Davidoff (1927) and Geddes (1911) that many individuals with giantism have a second period of growth in height often around 27-28 years of age. Most long bone epiphyses in persons without giantism are fused by that time.

Second, aging in acromegalic individuals might prove to be even more problematic. Bone overgrowth occurs in areas where hyaline cartilage is associated with bone surfaces, such as the pubic symphysis, the costo-chondral junction and the vertebral column. Epiphyseal closure may or may not have occurred depending upon the age of onset of the disease. Arthritis is also common in individuals with giantism, especially in the vertebral region. There would be more weight-bearing stress indicators than would normally be found in an individual without giantism or acromegaly of the same age.

Todd's (1920) and McKern and Stewart's (1957) methods use the pubic symphysis as an indicator of age. Iscan's (1989:1094-1104) method uses the distal rib

ends to determine age ranges. Arthritic changes in the vertebral column are associated with physical stress and increasing age (Stewart 1979). These points were made apparent by the Marushia and Sauer (1997) case, Humberd's personal correspondence regarding the Mutter Museum Giant (Mutter Museum Archives), and the article regarding the reassessment of O'Brien (Landolt and Zachmann 1980).

It is possible that the individual from Persia described in Ortner and Putchar's (1981) *Identification of Pathological Conditions in Human Skeletal Remains* represents an example of this difficulty. Documentary evidence suggests that the individual designated as 42 years old is actually only 19 years old. The diagnosis is also in question due to clinical information collected for medical treatment. Documentary evidence collected from personal collections and medical journals suggested that the individual was not suffering from giantism alone. Von Recklinghausen's Disease and HOA are also possible diagnoses (Fuchs 1935:490).

The age of the Mutter Museum's Giant is questionable as well. A personal communication from Humberd discussing the Mutter Museum Giant reads, "I find myself disagreeing, too, with my good friend, Dr. Hinsdale, about the age of your specimen at death. Dr. Hinsdale's estimate was 22 to 24 years; your own placard reads "23 years." I am led by a number of reasons to believe... he was only about 17 or 18 years old..." (Dr. Charles Humberd to Dr. Joseph McFarland, June 26th, 1938, Mutter Museum Archives). The age based on epiphyseal closure for O'Brien was very similar, although he was known to be 22 years of age at death. (see skeletal Case Study Number 8).

Observer Height Bias in Differential Diagnosis of Acromegaly and Giantism

The stature of each individual case study was compared with a normal height distribution for the individual's population or a population closest in time and space. Individual population-normal curves were estimated using the mean given for the population and the 5 – 8 cm standard deviation range quoted by Wells (1969:454). Individuals without means for their population were examined in relation to populations in the same time period and the closest in geographical region as possible with the information available.

At first, this may seem to be of little value, but upon inspection, one point becomes clear: that all the individuals with documented heights are above the mean height in their contextual populations. One would expect a normal distribution of height given the fact that acromegaly is defined as occurring in adulthood after epiphyseal closure. Giantism can apparently occur in a pure form, but it seems to be more common in the literature to have acromegalic giants or hyperpituitarism that spans from childhood to adulthood.

In reassessing the diagnoses of the cases, one must also assess the criteria originally used for diagnosis. Above average height (in Western and populational contexts) was found in 100 % of the skeletal case studies. From the data, a possible sampling bias in diagnosis is height. Because these are sample cases, this bias can be carried into further diagnoses of acromegaly and giantism.

The Role of the Mandible in the Differential Diagnosis of Acromegaly

Acromegaly was defined by an elongated mandible in all acromegaly cases, including cases diagnosed as "giantism with acromegaly". Enlarged frontal sinuses, vertebral arthritis, prominent chin and increased bone deposition at points of muscle insertion were cited in over half of the acromegalic cases. Enlarged frontal sinuses were not mentioned in any of the hyperpituitary giant cases, but were described in both individuals designated acromegalic and hyperpituitary giant.

Giants with acromegaly were diagnosed with acromegaly by virtue of their elongated mandible. Smithsonian Individual #2 was diagnosed as acromegalic, but was supposed to have increased pituitary "action" before puberty. His height was estimated to be 6 foot 3 inches (189.75 cm). Under the criteria presented in this work, this individual would have been designated hyperpituitary giant and acromegaly. This individual probably had a producing tumor before puberty; the levels, while above normal, were low. This is consistent with the case presented by Sauer and Marushia (1997). The individual was just at the limit for "giant" in the anthropological sense. Interestingly, neither individual expressed severe manifestations of the disease. This reaffirms the possibility of slight elevations in GH levels, which might explain the variability found in the occurrence and severity of skeletal lesions.

In dealing with remains from about 1970 onward, there is the added possibility of human growth hormone excess being deliberately introduced from external sources, as in cases of body building or medical treatments. The sella turcica would not necessarily be affected. How a differential diagnosis of an individual taking exogenous

human GH would differ from acromegaly and giantism is a question in need of further research ("Anabolic Steroids.com", 1997).

This implies that skeletal remains diagnosed with acromegaly and giantism could have come from two things; hyperpituitarism or voluntary introduction of exogeneous human GH. The first case would be a medical disease state, the second would result in a medical disease state, but would also imply cultural body modification, not unlike head-shaping and tooth-filing.

CHAPTER 6

SUMMARY AND CONCLUSIONS

The differential diagnosis of the individuals as presented in the literature were not always convincing. Nine of the skeletal cases were compelling in the authors' diagnosis, eight of the cases were unconvincing. None of the cases were complete enough to allow for a confident, independent assessment of diagnosis, though several of the cases were more thorough than others. This finding is in accord with conclusions made by Ortner and Aufderheide (1991:1) in their introduction to *Human Paleopathology*. They stated that:

> "To what extent does current medical knowledge relate to the interpretation of paleopathological specimens? Clearly our descriptive methodology and classificatory system are currently major barriers to comparative research. In many published reports it is virtually impossible to evaluate the evidence presented because the descriptions are vague and imprecise. Worse still, some authors provide a medically based diagnostic opinion with insufficient data to permit independent evaluation" (Ortner and Aufderheide 1991:1).

The medical and anthropological literature used for this project, in general, either did not have complete skeletal analyses or presented incomplete skeletal information. Photographs, which can be extremely helpful in the visual recognition of acromegalic characteristics, were often not available. Most of the literature also relied on secondary sources, which can introduce new error or transmit outdated or incorrect information. As has previously been stated, the terms "acromegaly" and "hyperpituitary giant" are also inconsistently defined. In addition, many individuals

used as models for the affects of acromgegaly/giantism on the skeletal system predate the medical recognition of these diseases.

Ortner suggests a solution to this dilemma of diagnosis. He states that, "The emphasis would be on careful description of abnormal conditions rather than reaching a diagnostic conclusion" (1991:10). This thesis supports Ortner's resolution to the problem of differential diagnosis in the paleopathology literature. A differential diagnosis can be suggested, but should never be considered absolute.

This work also provides information on a number of additional levels. It provides a compendium of cases of giantism and acromegaly in the anthropological literature. A foundation is provided for examination of the disease process of acromegaly and giantism using medical literature as well. Anthropology and medicine have also been used together to forward human understanding of past and present disease processes with an eye to the future as well.

Differential diagnosis, a tool borrowed from medicine, may be influenced by other bodies of thought. "Giant" has been shown to have a different definition in the cultural, anthropological, and medical bodies. This can lead to confusion. A pathological "giant" would not necessarily be the same as a "giant" in the cultural or anthropological sense. This work suggests that medical practitioners as well as anthropologists must be aware of the interaction of cultural, anthropological, and medical spheres in the practice of their professions.

Giantism, for all definitions, was shown to be defined by increased/extreme height. Defined medically, giantism is primarily based upon a GH producing tumor that occurs before epiphyseal closure. Extreme height is not a certainty. Nutritional stress,

a common condition of many populations, can decrease the height of an individual lower than their genetic potential. This possibility could affect how giants would be discovered in a group with low nutritional standards. Because discerning medical giants would be hampered by the perception that height defines giantism. The incidence of the disease would appear lower than normal. The statistic is quoted that 25% of autopsies have evidence of pituitary adenomas (Harrison 1981:1899). It would be interesting to investigate the impact nutritional levels have on giantism. Perhaps, a reduced calorie diet might be suggested to individuals with acromegaly/giantism as a means to decrease growth for those not responding to present-day medical interventions.

Diagnoses can carry with them assumptions based upon the ability to diagnose a disease process in human remains. It is the familiar caveat, be aware that analysis of skeletal remains is at best an estimate, not an absolute. Skeletal lesions suggest a disease process; they do not prove it. An enlarged sella turcica was present in less than half of the described cases with other characteristic lesions present. The same disease process can present with different lesions in different individuals due to the length of time the disease was present and the differences between individual responses to disease. More case studies would allow for a greater understanding of the variability of the disease.

An account of the lesions associated with acromegaly and giantism are presented here as a guide in diagnosis specifically for acromegaly and giantism. However, this work also provides the rationale of differential diagnosis especially for the non-medical reader. Differential diagnosis is most accurate when the user has a

large foundation of information from which to draw. To diagnose a disease, many diseases presenting lesions must be contemplated to provide a starting point for comparison, as pointed out by Bouchier and Morris (1982: 31). In short, to attempt differential diagnosis in skeletal remains as well as in living individuals, one should have a working knowledge of the medical literature as well as osteology.

Buikstra in her 1976 paper "Differential Diagnosis: An Epidemiological Model" makes a strong case for a contextual examination of disease. She suggests that not only the individual lesions be examined but that they be placed within a much broader concept of mortality, morbidity and the ecology of the disease. Tuberculosis is the disease to which this methodology is applied. Her study provided the next step for this study of acromegaly. Applying the model of differential diagnosis to a population to determine the number of occurrences and the presenting characteristics of the disease within that specific population would make an excellent Ph.D. study. First it is necessary to define the characteristics of the disease then examine a population to determine incidence, mortality rates, and possible etiologies.

Disease can be examined qualitatively and quantitatively. Both are necessary, but are rarely examined in tandem in the present. Descartes is purported to be the founder of the mind and body dichotomy still found in today's cultural framework. Study can be made of the physical characteristics of the disease, with little attention given to the individual who possessed it. Anthropology can act as a representative of the individual. Bioarchaeologists use this information to reconstruct past life histories from human physical remains and artifacts. Forensic anthropologists use this information to match physical and cultural profiles of missing persons with unidentified

human remains. Implicit in this research is the notion that disease is not only a physical process borne by the individual, but also a process defined by culture, medicine and anthropology.

Appendix 1

Characteristics of Specific Diseases

Characteristics of Specific Diseases[20]

Acromegaly
- Enlarged Sinuses
- Thick Calvarium
- Prominent Supercilliary Ridges – Supraorbital Ridges
- Prognathism
- Prominent Muscle Markings (Origins/Insertions)
- Phalangeal Tufting
- Kyphosis/Scoliosis
- Enlarged Sella Turcica
- Arthritis

Giantism
- Excessive Height
- Enlarged Sella Turcica
- Normal Body Proportions
- Scoliosis
- Weight Stress Lesions
- Arthritis
- Fractures of Weight Bearing Bones

Marfan's
- Excessive Height
- Height Disproportionate to Arms and Legs
- Arachnodactyl – Spider Fingers
- Long-Headed – Dolicocephalic
- Bossed Frontal
- Pronounced Supraorbital Ridges
- Kyphosis/Scoliosis
- Pectus Excavatum – Pigeon Breast Deformity
- Underbite

Paget's
- Primarily Occurs in One Bone or a Few, Not all
- Normal Height
- Thickened Skull, but very Porous with Nodules
- Bowing of Weight-Bearing Bones

[20] These disease criteria are synthesized from a variety of sources, the most complete being: Fairbank (1976), Ortner and Putschar (1981), Robbins and Cotran (1979), Bouchier and Morris (1982), Nabarro (1987), Aufderheide and Rodriguez-Martin (1997), Cushing and Davidoff (1927), Aegerter and Kirkpatrick (1975), McKusick (1986a), Jaffe (1972), and Hamdy (1981).

HOA
- Thickening of Calvarium/ Skull Base
- Enlargement of Sinuses
- Height Within Normal Limits
- Periosteal Reaction in Mid Distal Ends of Radius, Ulna, Tibia and Fibula
- Increased Diameter of Long Bones
- Spinal Ligaments Ossified
- Bone is Consistently Thick, Rough, and Irregular

Secondary HOA
- Thickening of Calvarium/ Skull Base
- Enlargement of Sinuses
- Height Within Normal Limits
- Periosteal Reaction in Mid Distal Ends of Radius, Ulna, Tibia and Fibula
- Increased Diameter of Long Bones
- Spinal Ligaments Ossified
- Bone is Consistently Thick, Rough, and Irregular
- Associated with Pulmonary and Systemic Diseases

A-G Syndrome/ Hypogonadism (Can Happen in Giantism)
- Gracile Skeleton
- Castration
- Excessive Height
- Disproportionate Limb Length to Body
- In Adults – Stocky Build, Thick Boned, Short
- In Childhood – Tall

Greater Than Average Height
- Excessive Height
- Proportionate Height

Neanderthal
- Thick Cranium
- Prominent Supraorbital Ridges
- Average Height
- Robust Features
- Enlarged Occipital Bun
- No Foot-Shaped Vault
- Robust Skeleton

Appendix 2

Characteristics of Skeletal Case Studies

Characteristics of Skeletal Case Studies

1. The Polish Giant

Male/Female	Female
Age	25 to 30
Height	215.5 cm (7 feet 2 inches)
Documented Diagnosis	Both Acromegaly and Giantism
Cranial Vault Thickened	
Enlarged Frontal Sinuses	
Prognathism	
Kyphoscoliosis	
Vertebral Arthritis	
Bony Obliteration of Skull Structures	
Tall Height	
Osteoma	
Fusion of Vertebrae	
Degenerative Changes in Epiphyses	
Fan-Shaped Position of Anterior Teeth	
Proportional Growth	
Enlarged Sella Turcica	
Length and Diameter of All Bones Enlarged	
Fractures	
Enlarged Mandible	
Enlarged Maxillary Sinuses	
Increased Pneumatization of Mastoid Cells	
Evidence of Weight Loading in Vertebrae	

2. The Tergensee Giant

Male/Female	Male
Age	25
Height	235.0 (7 feet 8.75 inches)
Documented Diagnosis	Giant
Cranial Vault Thickened	
Cystic Bone Lesions	
Bony Obliteration of Skull Structures	
Spondylosis	
Tall Height	
Robust Skull	
Enlarged Sella Turcica	
Length and Diameter of All Bones Enlarged	
Fractures	
Elongation of Mandible	
Epiphyses Not Closed	

3. The Mutter Giant

Male/Female	Male
Age	17 to 24
Height	235.6 (7 feet 8.75 inches)
Documented Diagnosis	Both Acromegaly and Giantism
Enlarged Frontal Sinuses	
Prognathism	
Kyphoscoliosis	
Tall Height	
Blunt Mandible Angle	
Proportional Growth	
Length and Diameter of All Bones Enlarged	
Elongation of Ribs	
Elongation of Mandible	
Enlarged Mandible	
Arthritis-Not Vertebral	
Large Face	
Epiphyses Not Closed	
Pigeon Breast	
Enlarged Maxillary Sinuses	
Dolichocephalic	
Evidence of Weight Loading in Vertebrae	

4. Persian Giant

Male/Female	Male
Age	Either 19 or 42
Height	220.00 (7 feet 2.6 inches)
Documented Diagnosis	Both Acromegaly and Giantism
Cranial Vault Thickened	
Tall Height	
Length and Diameter of All Bones Enlarged	
Enlarged Supraorbital Ridges	

5. Smithsonian Individual #2

Male/Female	Male
Age	35 to 45
Height	189.75 (6 feet 3 inches)
Documented Diagnosis	Acromegaly
Prognathism	
Robust Skeleton	
Tall Height	
Robust Skull	
High Temporalis Origin Markings	
Blunt Mandible Angle	
Proportional Growth	
Length and Diameter of All Bones Enlarged	
Elongation of Ribs	
Tufting of Terminal Phalanges	
Elongation of Mandible	
Prominent Chin	

6. Smithsonian Individual #3

Male/Female	Male
Age	39
Height	Unknown
Documented Diagnosis	Acromegaly
Malocclusion	
Enlarged Frontal Sinuses	
Prognathism	
Vertebral Arthritis	
Hypertrophied Nose Bones	
Enlarged Sella Turcica	
Tufting of Terminal Phalanges	
Elongation of Mandible	
Prominent Chin	
Increased Bone Deposition at Insertions	

7. Gardarene Skull

Male/Female	Male
Age	40 to 50
Height	Unknown
Documented Diagnosis	Both Acromegaly and Giantism
Robust Skull	
High Temporalis Origin Markings	
Enlarged Supraorbital Ridges	
Elongation of Mandible	
Enlarged Mandible	
Enlarged Occipital Protuberance	
Increased Bone Deposition at Insertions	

8. Charles O'Brien

Male/Female	Male
Age	22
Height	231.00 (7 feet 8.4 inches)
Documented Diagnosis	Both Acromegaly and Giantism
Cranial Vault Thickened	
Tall Height	
Robust Skull	
Enlarged Sella Turcica	
Elongation of Mandible	
Enlarged Mandible	
Prominent Chin	
Epiphyses Not Closed	
Enlarged Sinuses	

9. Rhine's New Mexico Acromegalic

Male/Female	Male
Age	30 to 40
Height	165.00 (5 feet 5 inches)
Population Mean	163.00 (5 feet 4 inches)
Documented Diagnosis	Acromegaly
Cranial Vault Thickened	
Enlarged Frontal Sinuses	
Kyphoscoliosis	
Vertebral Arthritis	
Scalloping of Vertebral Bodies	
Robust Skeleton	
Rugged Face	
Enlarged Supraorbital Ridges	
Tufting of Terminal Phalanges	
Elongation of Mandible	
Prominent Chin	
Increased Bone Deposition at Insertions	
Postcranial Exostoses	
Enlarged Maxillary Sinuses	
Increased Pneumatization of Mastoid Cells	
Narrowing of Phalangeal Shafts, Broad Bases and Heads	

10. Egyptian Skull

Male/Female	Female
Age	Unknown
Height	N/A
Documented Diagnosis	Acromegaly
Elongation of Mandible	

11. Marushia/Sauer Individual

Male/Female	Male
Age	30 to 50
Height	193.04 (6 feet 5 inches)
Documented Diagnosis	Both Acromegaly and Giantism
Cranial Vault Thickened	
Enlarged Frontal Sinuses	
Vertebral Arthritis	
Robust Skeleton	
Tall Height	
Robust Skull	
Robust Zygoma	
Proportional Growth	
Enlarged Sella Turcica	
Length and Diameter of All Bones Enlarged	
Enlarged Supraorbital Ridges	
Elongation of Mandible	
Enlarged Mandible	
Enlarged Occipital Protuberance	
Arthritis-Not Vertebral	
Enlarged Maxillary Sinuses	
Dolichocephalic	

12. San Cristobal Individual

Male/Female	Female
Age	"Adult"
Height	Unknown
Documented Diagnosis	Acromegaly
Enlarged Frontal Sinuses	
Vertebral Arthritis	
Enlarged Sella Turcica	
Elongation of Mandible	
Enlarged Mandible	
Osteoporosis	
Arthritis-Not Vertebral	
Prominent Chin	
Increased Bone Deposition at Insertions	

13. Dick's Mound Skull

Male/Female	Male
Age	Unknown
Height	Unknown
Documented Diagnosis	Acromegaly
Length and Diameter of All Bones Enlarged	
Elongation of Mandible	

14. Hosovski Individual

Male/Female	Male
Age	30
Height	173.00 (5 feet 8 inches)
Population Mean	171.3 (5 feet 7 inches)
Documented Diagnosis	Acromegaly
Periosteal Reaction	
Cranial Vault Thickened	
All Sinuses Enlarged	
Prognathism	
Vertebral Arthritis	
Robust Skeleton	
Rugged Face	
Robust Skull	
Robust Zygoma	
Hypertrophied Nose Bones	
Osteoporosis	
Blunt Mandible Angle	
Length and Diameter of All Bones Enlarged	
Enlarged Supraorbital Ridges	
Elongation of Mandible	
Enlarged Occipital Protuberance	
Increased Bone Deposition at Insertions	
Postcranial Exostoses	

15. The Norfolk Giant

Male/Female	Male
Age	Unknown
Height	232.52 (7 feet 7.5 inches)
Documented Diagnosis	Giant
Rugged Face	
Tall Height	
Fractures	

16. The Archaeology of Nubia #1.

Male/Female	Male
Age	Unknown
Height	189.0 (6 feet 2.5 inches)
Documented Diagnosis	Giant
Rugged Face	
Tall Height	

17. The Archaeology of Nubia #2

Male/Female	Male
Age	Unknown
Height	189.00 (6 feet 2.5 inches)
Documented Diagnosis	Giant
Tall Height	

Appendix 3

Data and Percentages for the Analysis of the Skeletal Case Studies

Individual	Male/Female	Age	Height
Pottery Pueblo	Male	30 to 40	165
Hosovski Individual	Male	30	173
NMNH 227508	Male	35 to 45	189.75
Ancient Egyptian in British Museum	Female	Unknown	.
San Cristobal	Female	Adult	.
Vienna	Male	39	.
Dick's Mound Individual	Male	Unknown	.
Giant From Ostrow Lednicki	Female	25 to 30	208.5
Persian Giant	Male	Either 19 or 42	220
Charles Byrne	Male	22	231
Mutter Giant	Male	17 to 24	235.6
Marushia/Sauer	Male	30 to 50	193.04
Gardar Skull	Male	40 to 50	.
Ptolemaic Cemetery at Meris	Male	Unknown	189
Tegernsee Giant	Male	25	235
Ptolemaic Cemetery at Meris	Male	Unknown	189
Burgh Castle, Suffolk	Male	Unknown	232.52

Documented Diagnosis	Malocclusion	Periosteal Reaction	Cranial Vault Thickened
Acromegaly	No	No	Yes
Acromegaly	No	Yes	Yes
Acromegaly	No	No	No
Acromegaly	No	No	No
Acromegaly	No	No	No
Acromegaly	Yes	No	No
Acromegaly	No	No	No
Both A and G	No	No	Yes
Both A and G	No	No	Yes
Both A and G	No	No	Yes
Both A and G	No	No	No
Both A and G	No	No	Yes
Both A and G	No	No	No
Giant	No	No	No
Giant	No	No	Yes
Giant	No	No	No
Giant	No	No	No

Individual	Enlarged Frontal Sinuses	Prognathism	Kyphoscoliosis
Pottery Pueblo	Yes	No	Yes
Hosovski Individual	Yes	Yes	No
NMNH 227508	No	Yes	No
Ancient Egyptian in British Museum	No	No	No
San Cristobal	Yes	No	No
Vienna	Yes	Yes	No
Dick's Mound Individual	No	No	No
Giant From Ostrow Lednicki	Yes	Yes	Yes
Persian Giant	No	No	No
Charles Byrne	No	No	No
Mutter Giant	Yes	Yes	Yes
Marushia/Sauer	Yes	No	No
Gardar Skull	No	No	No
Ptolemaic Cemetery at Meris	No	No	No
Tegernsee Giant	No	No	No
Ptolemaic Cemetery at Meris	No	No	No
Burgh Castle, Suffolk	No	No	No

Vertebral Arthritis	Scalloping of Vertebral Bodies	Robust Skeleton	Cystic Bone Lesions
Yes	Yes	Yes	No
Yes	No	Yes	No
No	No	Yes	No
No	No	No	No
Yes	No	No	No
Yes	No	No	No
No	No	No	No
Yes	No	No	No
No	No	No	No
No	No	No	No
No	No	No	No
Yes	No	Yes	No
No	No	No	No
No	No	No	No
No	No	No	Yes
No	No	No	No
No	No	No	No

Individual	Rugged Face	Bony Obliteration of Skull Structures	Spondylosis	Tall Height
Pottery Pueblo	Yes	No	No	No
Hosovski Individual	Yes	No	No	No
NMNH 227508	No	No	No	Yes
Ancient Egyptian in British Museum	No	No	No	No
San Cristobal	No	No	No	No
Vienna	No	No	No	No
Dick's Mound Individual	No	No	No	No
Giant From Ostrow Lednicki	No	Yes	No	Yes
Persian Giant	No	No	No	Yes
Charles Byrne	No	No	No	Yes
Mutter Giant	No	No	No	Yes
Marushia/Sauer	No	No	No	Yes
Gardar Skull	No	No	No	No
Ptolemaic Cemetery at Meris	No	No	No	Yes
Tegernsee Giant	No	Yes	Yes	Yes
Ptolemaic Cemetery at Meris	No	No	No	Yes
Burgh Castle, Suffolk	No	No	No	Yes

Robust Skull	High Temporalis Origin Markings	Robust Zygoma	Hypertrophied Nose Bones
No	No	No	No
Yes	No	Yes	Yes
Yes	Yes	No	No
No	No	No	No
No	No	No	No
No	No	No	Yes
No	No	No	No
No	No	No	No
No	No	No	No
Yes	No	No	No
No	No	No	No
Yes	No	Yes	No
Yes	Yes	No	No
No	No	No	No
Yes	No	No	No
No	No	No	No
No	No	No	No

Individual	Osteoporosis in Skull	Blunt Mandible Angle	Osteoma
Pottery Pueblo	No	No	No
Hosovski Individual	Yes	Yes	No
NMNH 227508	No	Yes	No
Ancient Egyptian in British Museum	No	No	No
San Cristobal	No	No	No
Vienna	No	No	No
Dick's Mound Individual	No	No	No
Giant From Ostrow Lednicki	No	No	Yes
Persian Giant	No	No	No
Charles Byrne	No	No	No
Mutter Giant	No	Yes	No
Marushia/Sauer	No	No	No
Gardar Skull	No	No	No
Ptolemaic Cemetery at Meris	No	No	No
Tegernsee Giant	No	No	No
Ptolemaic Cemetery at Meris	No	No	No
Burgh Castle, Suffolk	No	No	No

Fusion of Vertebrae	Degenerative Changes in Epiphyses	Fan-Shaped Position of Anterior Teeth
No	No	No
No	No	No
No	No	No
No	No	No
No	No	No
No	No	No
No	No	No
Yes	Yes	Yes
No	No	No
No	No	No
No	No	No
No	No	No
No	No	No
No	No	No
No	No	No
No	No	No
No	No	No

Individual	Proportional Growth	Enlarged Sella Turcica
Pottery Pueblo	No	No
Hosovski Individual	No	No
NMNH 227508	Yes	No
Ancient Egyptian in British Museum	No	No
San Cristobal	No	Yes
Vienna	No	Yes
Dick's Mound Individual	No	No
Giant From Ostrow Lednicki	Yes	Yes
Persian Giant	No	No
Charles Byrne	No	Yes
Mutter Giant	Yes	No
Marushia/Sauer	Yes	Yes
Gardar Skull	No	No
Ptolemaic Cemetery at Meris	No	No
Tegernsee Giant	No	Yes
Ptolemaic Cemetery at Meris	No	No
Burgh Castle, Suffolk	No	No

Length and Diameter of all Bones Enlarged	Elongation of Ribs	Fractures	Enlarged Supraorbital Ridges
No	No	No	Yes
Yes	No	No	Yes
Yes	Yes	No	No
No	No	No	No
No	No	No	No
No	No	No	No
Yes	No	No	No
Yes	No	Yes	No
Yes	No	No	Yes
No	No	No	No
Yes	Yes	No	No
Yes	No	No	Yes
No	No	No	Yes
No	No	No	No
Yes	No	Yes	No
No	No	No	No
No	No	Yes	No

Individual	Tufting of Terminal Phalanges	Elongation of Mandible	Enlarged Mandible
Pottery Pueblo	Yes	Yes	No
Hosovski Individual	No	Yes	No
NMNH 227508	Yes	Yes	No
Ancient Egyptian in British Museum	No	Yes	No
San Cristobal	No	Yes	Yes
Vienna	Yes	Yes	No
Dick's Mound Individual	No	Yes	No
Giant From Ostrow Lednicki	No	No	Yes
Persian Giant	No	No	No
Charles Byrne	No	Yes	Yes
Mutter Giant	No	Yes	Yes
Marushia/Sauer	No	Yes	Yes
Gardar Skull	No	Yes	Yes
Ptolemaic Cemetery at Meris	No	No	No
Tegernsee Giant	No	Yes	No
Ptolemaic Cemetery at Meris	No	No	No
Burgh Castle, Suffolk	No	No	No

Enlarged Occipital Protuberance	Osteoporosis	Arthritis- Not Vertebral	Prominent Chin
No	No	No	Yes
Yes	No	No	No
No	No	No	Yes
No	No	No	No
No	Yes	Yes	Yes
No	No	No	Yes
No	No	No	No
No	No	No	No
No	No	No	No
No	No	No	Yes
No	No	Yes	No
Yes	No	Yes	No
Yes	No	No	No
No	No	No	No
No	No	No	No
No	No	No	No
No	No	No	No

Individual	Increaseased Bone Deposition at Insertions	Large Face	Epiphyses Not Closed
Pottery Pueblo	Yes	No	No
Hosovski Individual	Yes	No	No
NMNH 227508	No	No	No
Ancient Egyptian in British Museum	No	No	No
San Cristobal	Yes	No	No
Vienna	Yes	No	No
Dick's Mound Individual	No	No	No
Giant From Ostrow Lednicki	No	No	No
Persian Giant	No	No	No
Charles Byrne	No	No	Yes
Mutter Giant	No	Yes	Yes
Marushia/Sauer	No	No	No
Gardar Skull	Yes	No	No
Ptolemaic Cemetery at Meris	No	No	No
Tegernsee Giant	No	No	Yes
Ptolemaic Cemetery at Meris	No	No	No
Burgh Castle, Suffolk	No	No	No

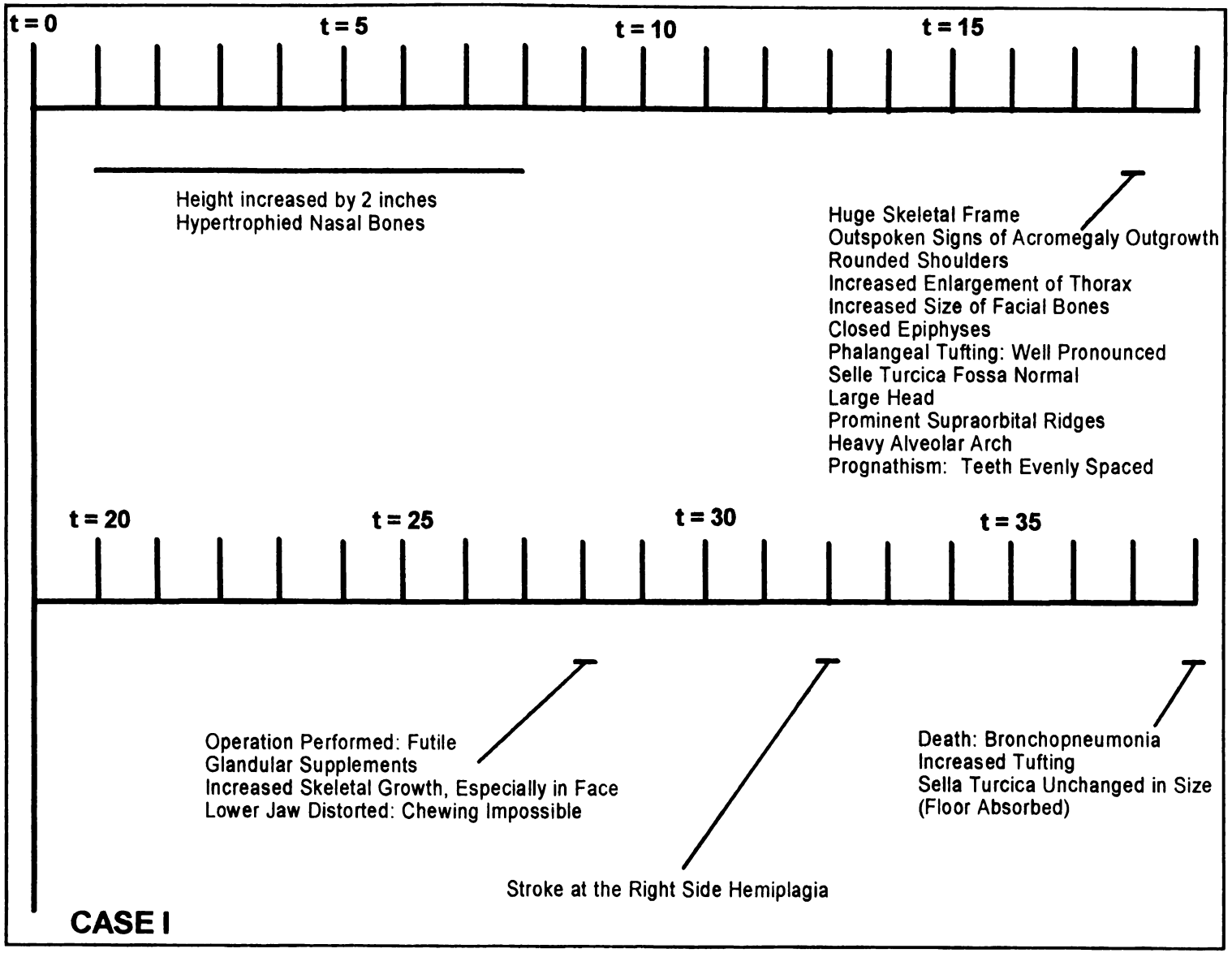
Pigeon Breast	Postcranial Exostoses	Enlarged Maxillary Sinuses	Increased Pneumatization of Mastoid Cells
No	Yes	Yes	Yes
No	Yes	No	No
No	No	No	No
No	No	No	No
No	No	No	No
No	No	No	No
No	No	No	No
No	No	Yes	Yes
No	No	No	No
No	No	No	No
Yes	No	Yes	No
No	No	Yes	No
No	No	No	No
No	No	No	No
No	No	No	No
No	No	No	No
No	No	No	No

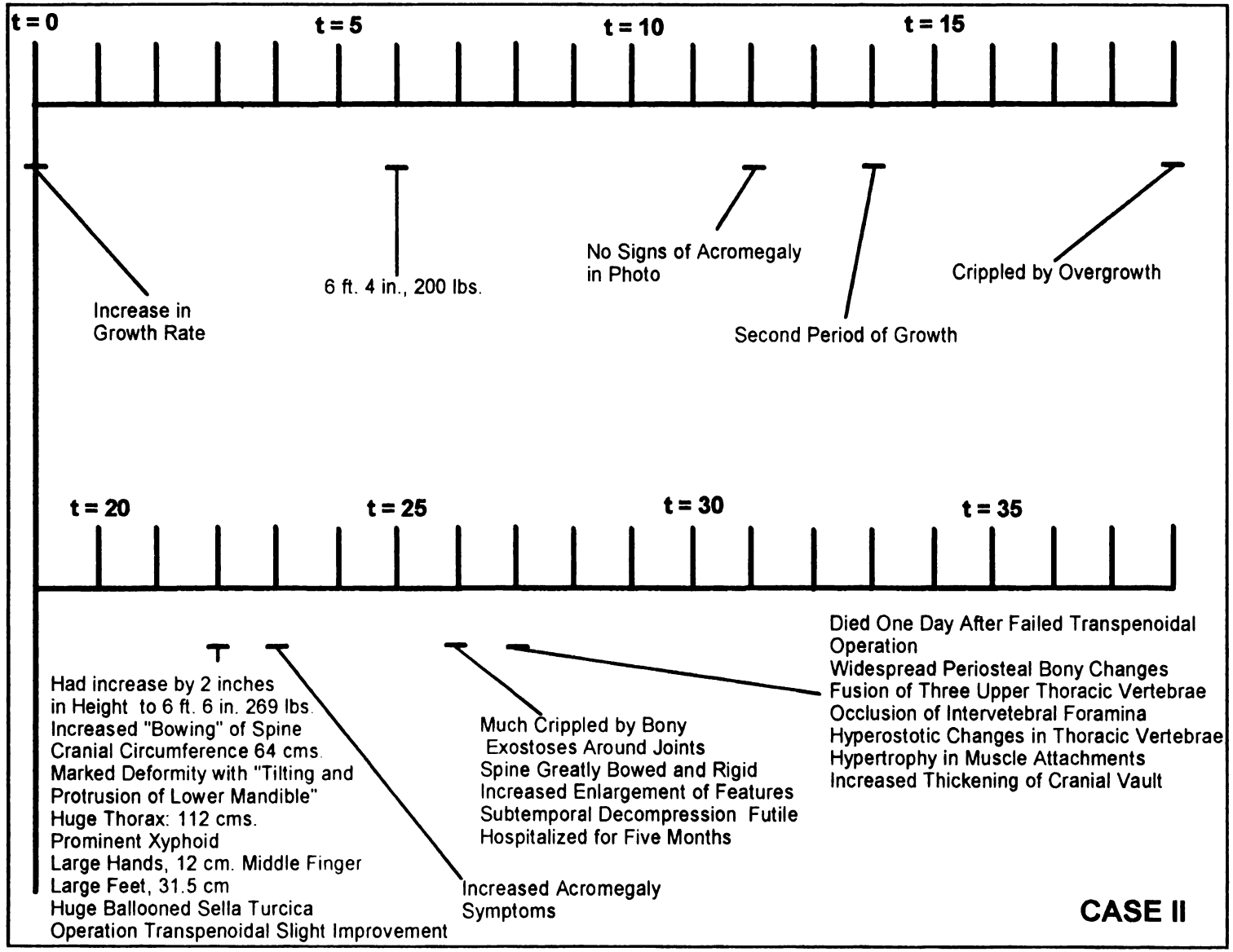
Individual	Narrowing of Phalangeal Shafts, Broad Bases and Heads	Enlarged Sinuses
Pottery Pueblo	Yes	No
Hosovski Individual	No	No
NMNH 227508	No	No
Ancient Egyptian in British Museum	No	No
San Cristobal	No	No
Vienna	No	No
Dick's Mound Individual	No	No
Giant From Ostrow Lednicki	No	No
Persian Giant	No	No
Charles Byrne	No	Yes
Mutter Giant	No	No
Marushia/Sauer	No	No
Gardar Skull	No	No
Ptolemaic Cemetery at Meris	No	No
Tegernsee Giant	No	No
Ptolemaic Cemetery at Meris	No	No
Burgh Castle, Suffolk	No	No

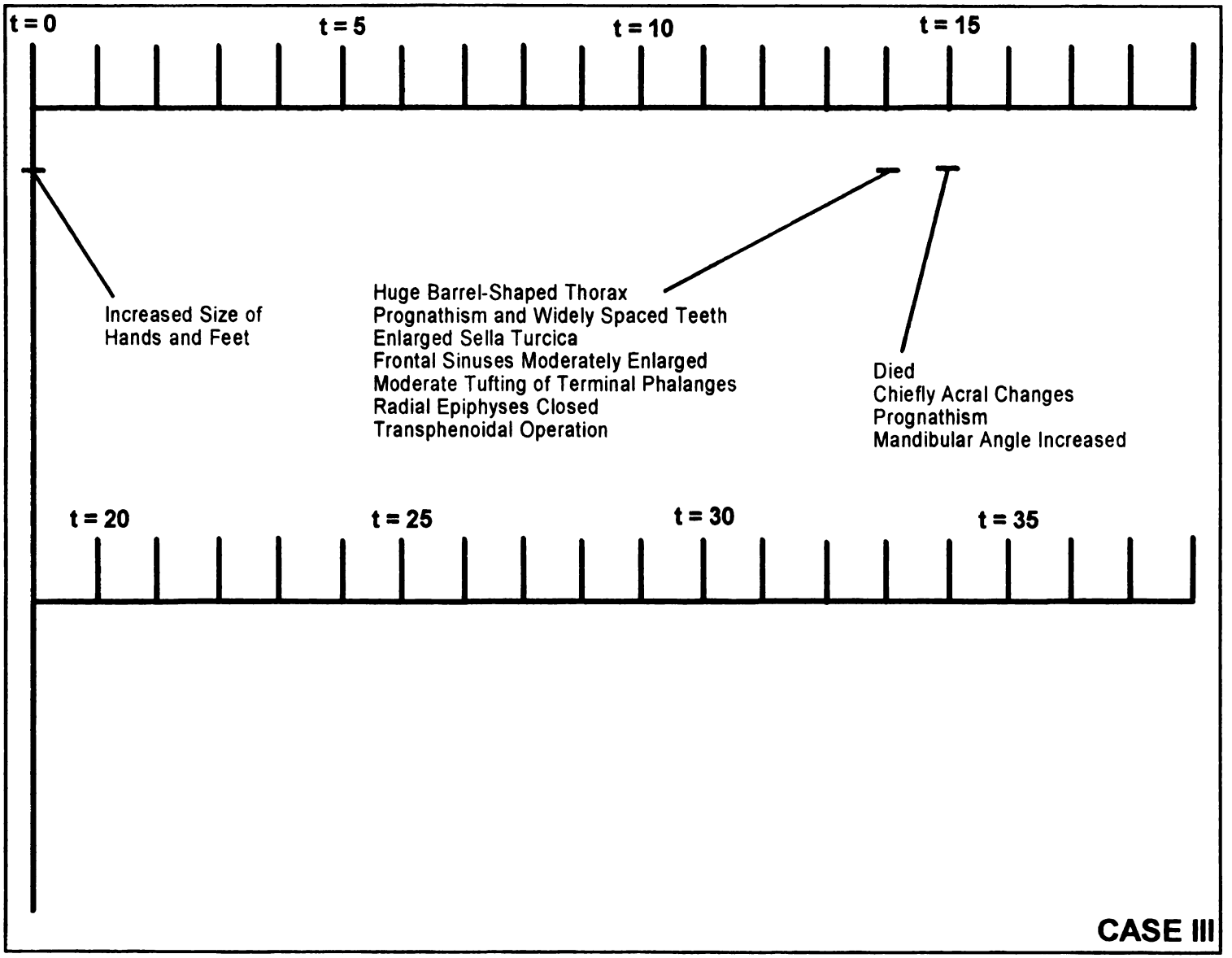
Dolichocephalic	Evidence of Weight Loading in Vertebrae
No	No
No	No
No	No
No	No
No	No
No	No
No	No
No	Yes
No	No
No	No
Yes	Yes
Yes	No
No	No
No	No
No	No
No	No
No	No

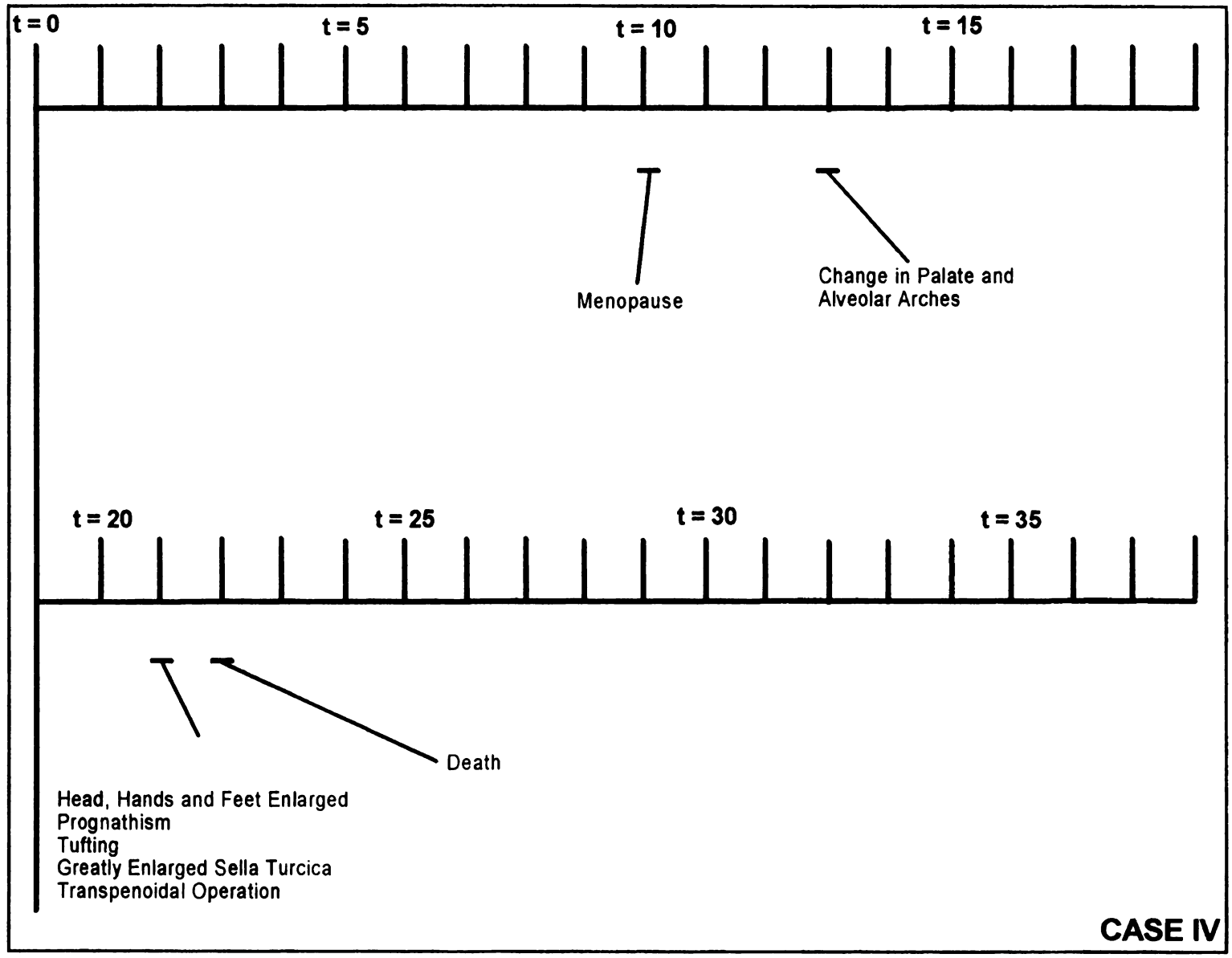
Appendix 4

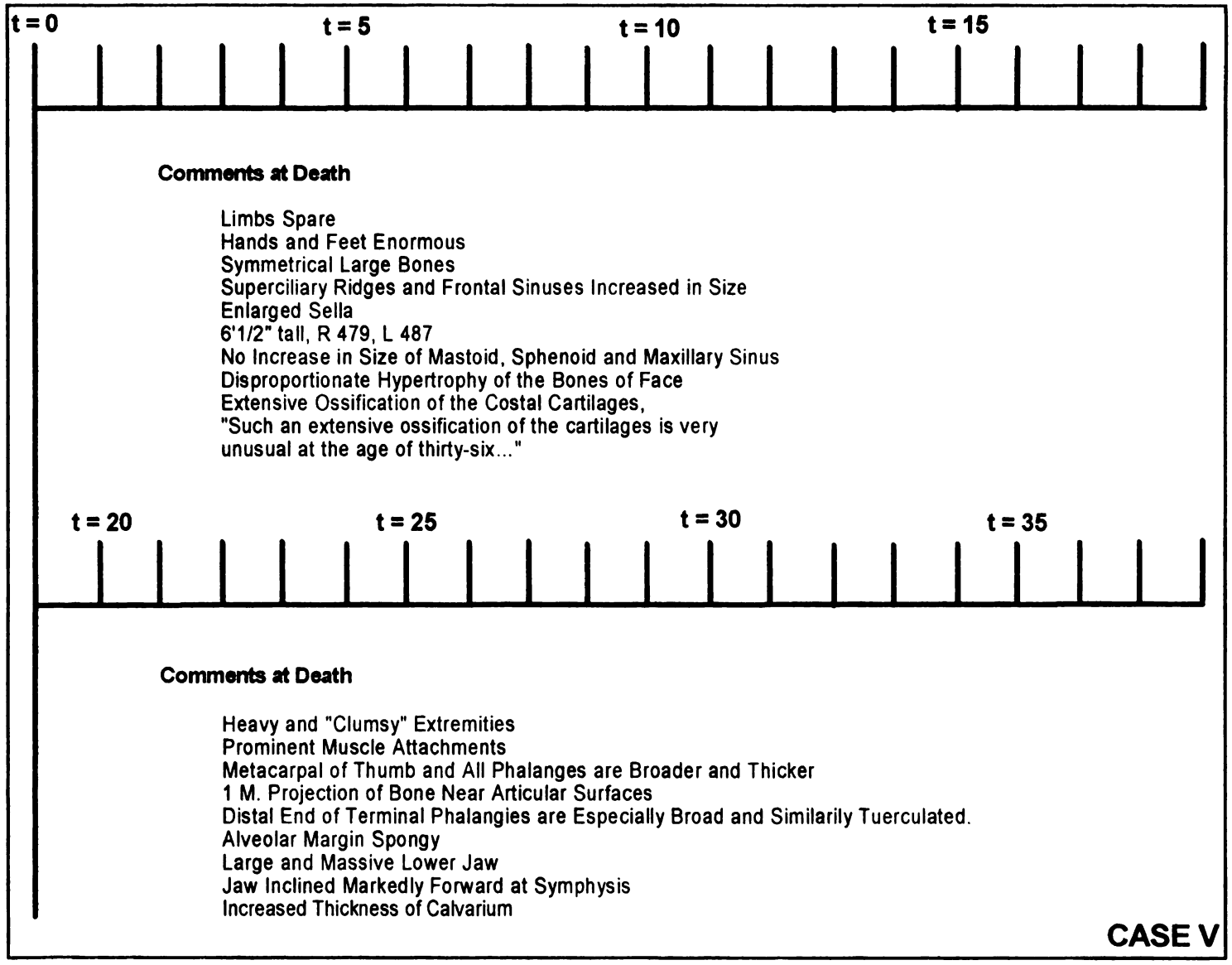
Time Lines and Data for the Soft-Tissue Case Studies

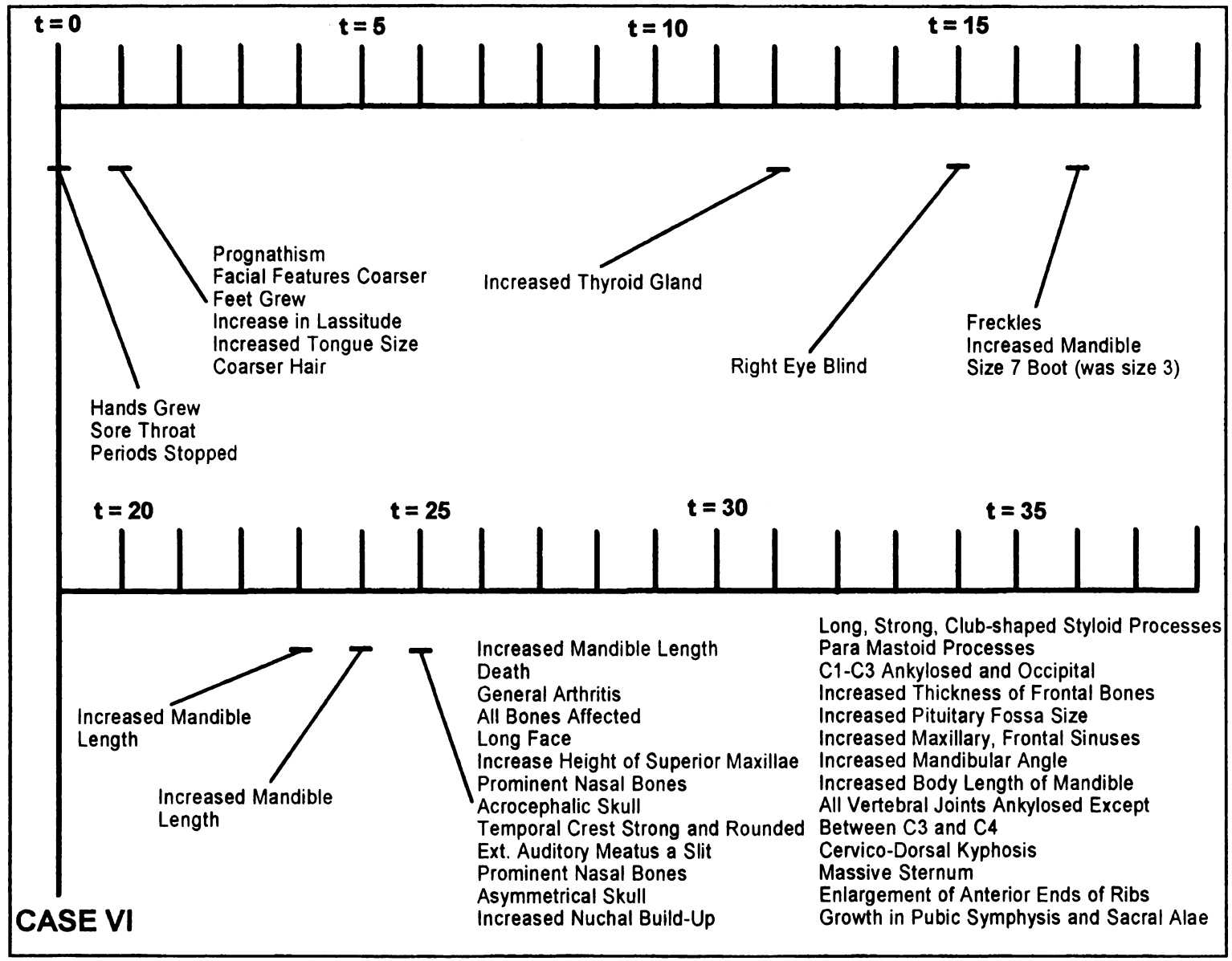

t = 0
t = 5
t = 10
t = 15
Height increased by 2 inches
Hypertrophied Nasal Bones
Huge Skeletal Frame
Outspoken Signs of Acromegaly Outgrowth
Rounded Shoulders
Increased Enlargement of Thorax
Increased Size of Facial Bones
Closed Epiphyses
Phalangeal Tufting: Well Pronounced
Selle Turcica Fossa Normal
Large Head
Prominent Supraorbital Ridges
Heavy Alveolar Arch
Prognathism: Teeth Evenly Spaced
t = 20
t = 25
t = 30
t = 35
Operation Performed: Futile
Glandular Supplements
Increased Skeletal Growth, Especially in Face
Lower Jaw Distorted: Chewing Impossible
Stroke at the Right Side Hemiplagia
Death: Bronchopneumonia
Increased Tufting
Sella Turcica Unchanged in Size
(Floor Absorbed)
CASE I


t = 0
t = 5
t = 10
t = 15
Increase in Growth Rate
6 ft. 4 in., 200 lbs.
No Signs of Acromegaly in Photo
Second Period of Growth
Crippled by Overgrowth
t = 20
t = 25
t = 30
t = 35
Had increase by 2 inches in Height to 6 ft. 6 in. 269 lbs.
Increased "Bowing" of Spine
Cranial Circumference 64 cms.
Marked Deformity with "Tilting and Protrusion of Lower Mandible"
Huge Thorax: 112 cms.
Prominent Xyphoid
Large Hands, 12 cm. Middle Finger
Large Feet, 31.5 cm
Huge Ballooned Sella Turcica
Operation Transpenoidal Slight Improvement
Increased Acromegaly Symptoms
Much Crippled by Bony Exostoses Around Joints
Spine Greatly Bowed and Rigid
Increased Enlargement of Features
Subtemporal Decompression Futile
Hospitalized for Five Months
Died One Day After Failed Transpenoidal Operation
Widespread Periosteal Bony Changes
Fusion of Three Upper Thoracic Vertebrae
Occlusion of Intervetebral Foramina
Hyperostotic Changes in Thoracic Vertebrae
Hypertrophy in Muscle Attachments
Increased Thickening of Cranial Vault
CASE II


t = 0
t = 5
t = 10
t = 15
Increased Size of
Hands and Feet
Huge Barrel-Shaped Thorax
Prognathism and Widely Spaced Teeth
Enlarged Sella Turcica
Frontal Sinuses Moderately Enlarged
Moderate Tufting of Terminal Phalanges
Radial Epiphyses Closed
Transphenoidal Operation
Died
Chiefly Acral Changes
Prognathism
Mandibular Angle Increased
t = 20
t = 25
t = 30
t = 35
CASE III


t = 0
t = 5
t = 10
t = 15
Menopause
Change in Palate and
Alveolar Arches
t = 20
t = 25
t = 30
t = 35
Death
Head, Hands and Feet Enlarged
Prognathism
Tufting
Greatly Enlarged Sella Turcica
Transpenoidal Operation
CASE IV


t = 0
t = 5
t = 10
t = 15
Comments at Death
Limbs Spare
Hands and Feet Enormous
Symmetrical Large Bones
Superciliary Ridges and Frontal Sinuses Increased in Size
Enlarged Sella
6'1/2" tall, R 479, L 487
No Increase in Size of Mastoid, Sphenoid and Maxillary Sinus
Disproportionate Hypertrophy of the Bones of Face
Extensive Ossification of the Costal Cartilages,
"Such an extensive ossification of the cartilages is very
unusual at the age of thirty-six..."
t = 20
t = 25
t = 30
t = 35
Comments at Death
Heavy and "Clumsy" Extremities
Prominent Muscle Attachments
Metacarpal of Thumb and All Phalanges are Broader and Thicker
1 M. Projection of Bone Near Articular Surfaces
Distal End of Terminal Phalangies are Especially Broad and Similarily Tuerculated.
Alveolar Margin Spongy
Large and Massive Lower Jaw
Jaw Inclined Markedly Forward at Symphysis
Increased Thickness of Calvarium
CASE V


t = 0
t = 5
t = 10
t = 15
Prognathism
Facial Features Coarser
Feet Grew
Increase in Lassitude
Increased Tongue Size
Coarser Hair
Increased Thyroid Gland
Right Eye Blind
Freckles
Increased Mandible
Size 7 Boot (was size 3)
Hands Grew
Sore Throat
Periods Stopped
t = 20
t = 25
t = 30
t = 35
Increased Mandible
Length
Increased Mandible
Length
Increased Mandible Length
Death
General Arthritis
All Bones Affected
Long Face
Increase Height of Superior Maxillae
Prominent Nasal Bones
Acrocephalic Skull
Temporal Crest Strong and Rounded
Ext. Auditory Meatus a Slit
Prominent Nasal Bones
Asymmetrical Skull
Increased Nuchal Build-Up
Long, Strong, Club-shaped Styloid Processes
Para Mastoid Processes
C1-C3 Ankylosed and Occipital
Increased Thickness of Frontal Bones
Increased Pituitary Fossa Size
Increased Maxillary, Frontal Sinuses
Increased Mandibular Angle
Increased Body Length of Mandible
All Vertebral Joints Ankylosed Except
Between C3 and C4
Cervico-Dorsal Kyphosis
Massive Sternum
Enlargement of Anterior Ends of Ribs
Growth in Pubic Symphysis and Sacral Alae
CASE VI

REFERENCES

Aegerter, Ernest and Kirkpatrick, John A. Jr.
1975 *Orthopedic Diseases.* W.B. Saunders Company, Philadelphia.

Anderson, W.A.D. and John M. Kissane
1977 *Pathology* (Volume Two). C.V. Mosby Company, Saint Lousi, MO.

Aufderheide, A.C. and Rodriguez-Martin, C.
1998 *The Cambridge Encyclopedia of Human Pathology.* Cambridge University Press.

Barkan, Ariel
1997 Controversies in the Diagnosis and Therapy of Acromegaly. *Endocrinology* 7(5):300-307.

Barry, Hugh C.
1969 *Paget's Disease of Bone.* E. & S. Livingstone LTD., London.

Bassoe, Peter.
1903 Giantism and Leontiasis Ossea, with Report of the Case of the Giant Wilkins. *The Journal of Nervous and Mental Disease* 30(9): 513-532.

Beighton, P. et al.
1993 Genetic Skeletal Dysplasias in the Museum of Pathological Anatomy, Vienna. *American Journal of Medical Genetics* 47:843-847.

Bennike, Pia
1985 *Paleopathology of Danish Skeletons: A Comparative Study of Demography, Disease and Injury.* Akademisk Forlag, Denmark.

Bergland, Richard M.
1965 New Information Concerning the Irish Giant. *Journal of Neurosurgery* 23(3): 265-269.

Brauer, J.L.
1991 A Case of Acromegaly in a Pre-historic Skeleton from the San Cristobal Ruins, New Mexico. (Paper presented at the 18th meeting of the Paleopathology Association held in Milwaukee, Wisconsin, April 2-3, 1991). *Paleopathology Newsletter 74* (June: Supplement: 2 (Abstract).

Bouchier, Ian A. D. and Morris, John S.
1982 *Clinical Skills: A System of Clinical Examination.* W.B. Saunders Company, Ltd., London.

Brothwell, D.
1967 *Diseases in Antiquity: A Survey of the Diseases, Injuries, and Surgery of Early Populations.* Charles C. Thomas, Pub., Springfield, Illinois.

1981 *Digging up Bones.* Cornell University Press, Ithaca, New York.

Buikstra, Jane E.
1976 Differential Diagnosis: An Epidemiological Model. *Yearbook of Physical Anthropology*, 20:316-328.

Byock, Jesse L.
1995 Egil's Bones. *Scientific American* January, 1995: 82-97.

Carcassi, U.
1992 History of Hypertrophic Osteoarthropathy (HOA). *Clinical and Experimental Rheumatology*, 10:3-7, Suppl. 7 May-Jun 1992.

Collins, R. Douglas.
1981 *Dynamic Differential Diagnosis.* J.B. Lippincott Company, Philadelphia.

Cummins, Richard O. and Mickey S. Eisenberg.
1986 *Blue Book of Medical Diagnosis.* W.B. Saunders Company, Philadelphia.

Cunningham, D.J.
1879 A Large Sub-Arachnoid Cyst Involving the Greater Part of the Parietal Lobe of the Brain. *Journal of Anatomy and Physiology: Normal and Patholog*ical, 13(4) :508-517.

Cushing, Harvey and Davidoff, Leo M.
1927 *The Pathological Findings in Four Autopsied Cases of Acromegaly with a Discussion of their Significance.* The Rockefeller Institute for Medical Research, New York.

Earickson, Robert and Harlin, John
1994 *Geographic Measurement and Quantitative Anlysis.* Macmillan College Publishing Company, New York.

Erdheim, J.
1931 Uber Wirbelsaulenveranderungen bei Akromegalie (Concerning vertebral column changes in acromegaly). *Virchow's Archiv fur Pathologische Anatomie und Klinische Medizin* 281:197-296.

Fairbank, T.J.
1976 *Fairbank's Atlas of General Affections of the Skeleton.* Churchill Livingstone, London.

Ferembach, D., Schwidertzky, I., and Stloukal, M.
1980 Recommendations for Age and Sex Diagnosis of Skeletons. *Journal of Human Evolution* 9:517-549.

Fuchs, D.H.
1935 Pictures of a Giant – Presentation given to the Society of Physicians, Vienna. Reported in *The Journal of the American Medical Association*, 104(1):490.

Geddes, A.C.
1911 Report upon an Acromegalic Skeleton. *Journal of Anatomy and Physiology* 45:256-292.

Gladykowska-Rzeczycka, J.J.
1998 A Giant from Ostrow Lednicki (XII-XIII c), Dist. Lednogora, Poland. *The Mankind Quarterly*, XXXIX(2):147-172.

Gray, H.
1937 The Minneapolis Giant. *(Unknown Publication)*. 1669-1682.

Hacking, Peter
1995 A Pituitary Tumour in a Medieval Skull. *International Journal of Osteoarchaeology* 5:390-393.

Hamdy, R.C.
1981 *Paget's Disease of Bone: Assessment and Management.* Praeger Publishers, East Sussex, UK.

Hamwi et al.
1960 Acromegaly. *American Journal of Medicine*, 29(4):690-9.

Harrison, T.R.
1981 *Harrison's Principles of Internal Medicine* (9th Edition). McGraw-Hill, New York.

Hawkins, Desmond
1992 The Diagnosis of Pituitary Disease from the Human Skeletal Remains. *International Journal of Osteoarchaeology* 2:51-64.

Hayles, M.D.
1980 Gigantism. *Pediatric Annales*, 9(4):163-169.

Hinsdale, Guy
1898 *Acromegaly.* Mutter Museum Document, Philadelphia.

Hosovski, E.
1991 A Case of Acromegaly in the Middle Ages. *Anthrop. Anz.*, Jg. 49, 3:273-279.

Humberd, Charles D.
1939 The Mutter Museum Skeleton of the Kentucky Giant. *Kentucky Medical Journal* (1939).

Huxley, T.H.
1959 *Man's Place in Nature* (translated). University of Michigan Press, Ann Arbor.

Iscan, M.Y. and Kennedy, K.A.R.
1989 *Reconstruction of Life From The Skeleton*, Alan R. Liss, Inc., New York.

Iscan, M.Y. Loth, S.R., and Wright R.K..
1984 Age Estimation from the Rib by Phase Analysis: White Males. *Journal of Forensic Science*, 29(4):1094-1104.

Ivanhoe, Francis
1985 On the Neandertal Pubis and Acromegaly. *Current Anthropology*. 26(4):526-529

Jaffe, Henry L.
1972 *Metabolic, Degenerative, and Inflammatory Diseases of Bones and Joints*. Lea and Febiger, Philadelphia.

Jarco, Saul (ed.)
1966 *Human Palaeopathology*. Yale University Press, London.

Keith, A.
1913 Abnormal Crania – Achondroplastic and Acrocephalic. *Journal of Anatomy and Physiology*, 47:189-206.
1931 *New Discoveries Relating to the Antiquity of Man*. Norton, New York.

Lackey, W.J. and Fallston, N.C.
1934 Giantism and Acromegaly. Southern Medicine and Surgery 96(6):275-277.

Landolt, A.M. and Zachmann, M.
1980 The Irish Giant: New Observations Concerning the Nature of His Ailment. The Lancet (June 14, 1980).

Lang, E. and Bessler, W.T.
1961 The Roentgenologic Features of Acromegaly. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* 86:321-328.

Leri-Paris, Andre
1913 Akromegalie. From *Handbuch Der Neurologie*. Verlag Von Julius Springer, Berlin.

Littlejohn, G.O., et al.
1986 New Bone Formation in Acromegaly: Pathogentic Implications for Diffuse Idiopathic Skeletal Hyperostosis. *Clinical and Experimental Rheumatology* 4:99-104.

Long, Esmond R.
1935 From Pathology to Epidemiology in Tuberculosis. *American Medical Association Journal*, 104 (21): 1883-1888.

Matovinovic, J. and Kicic, M.
1967 Akromegalija (Acromegaly). *Medicinska Enciklopedija* (Medical Encyclopedia), Band I:62-65. Jugoslavenski Leksikografski Zavod, Zagreb.

McAlister, Neil H.
1974 John Hunter and the Irish Giant. Canadian Medical Association Journal 3:256-257.

McFarland, Joseph
1938 Notes on the Mutter American Giant. *Transactions & Studies of the College of Physicians of Philadelphia*, 4 Ser., Vol. 6, No. 2.

McKern T. W. and Stewart, T.W.
1957 *Skeletal Age Changes in Young American Males. Analyzed from the Standpoint of Age Identification.* Environmental Protection Research Division (Quartermaster Research and Development Center, U.S. Army, Natick, MA), Technical Report No. EP-45.

Moore, Keith L.
1992 *Clinically Oriented Anatomy* (Third Edition). Williams & Wilkins, Baltimore, MD.

Morse, D.
1969 *Ancient Disease in the Midwest.* Springfield, IL: Illinois State Museum Reports of Investigations, no. 15.

Nabarro, J.D.N.
1987 Acromegaly. From *Clinical Endocrinology*, Jenkins, J.S. and Clayton, R.N. (eds.). Blackwell Scientific Publications, London.

Nerhlich, A., Peschel, Ol, Lohrs, U., Parsche, F. & Betz, P.
1991 Juvenile gigantism plus polyostotic fibrous dysplasia in the Tegernsee giant. *Lancet* 338(8771): 886-7 (Letter).

Nerhlich, A., Parsche, F., Wiest, I., and Lohrs, U.
1994 The Skeleton on the Tegernsee Giant: Macroscopic and Histologic Findings. *Homo* 45/Suppl: S90.

Ontell, F.K., Moore, E.H., Shepard, J.O. and Shelton, D.K.
1997 The costal cartilages in health and disease.
Radiographics 17: (3) 571-577 May-June 1997.

Ortner, Donald J. and Putschar, Walter G.J.
1981 *Identification of Pathological Conditions in Human Skeletal Remains.* Smithsonian Institution Press, Washington D.C.

Osler, William (ed.)
1909 *Modern Medicine: Its Theory and Practice.* Lea and Febiger, Philadelphia.
1915 *Modern Medicine: Its Theory and Practice.* Lea and Febiger, Philadelphia.

Perkins, Michael
1931 Acromegaly in the Far North. *Nature* 128 (3229): 491-492.

Pirsig, W., Merkle, E., Nerlich, A., Parsche, F., and Lohrs, U.
1994 The Skeleton on the Tegernsee Giant: Radiological and Endoscopic Findings. *Homo* 45/Suppl: S102.

Rhine, Stanley
1985 A possible case of acromegaly from New Mexico. *Health and Disease in the Prehistoric Southwest*, ed. C.F. Merbs & R.J. Miller, pp. 210-19. Anthropological Research Papers no. 34. Tempe, AZ: Arizona State University.

Robbins, Stanley L., and Cotran, Ramzi S.
1979 *Pathologic Basis of Disease.* W.B. Saunders Company, Philadelphia.

Roberts, C.
1986 Leprosy and Leprosaria in Medieval Britain. *MASCA Journal* 4(1):15-21.

Roberts, C and Manchester, K
1983 The Archaeology of Disease. Sutton Publishing Limited, Cornell University Press, Ithaca, New York.

Sauer, N.J. and Marushia, M.M.
1997 Differential Diagnosis of Hyperpituitarism. Paper presented at *the American Academy of Forensic Sciences*, January, 1997.

Seligman, C.G.
1931 Acromegaly among the Old Northmen. *Nature* 128 (3223):221

Schereschewsky, N.A.
1926 Giantism. *Endocrinology* 10:17-28

Singh, Gurmeet and Menon, P.S.N.
1995 Pachydermoperiostosis in a 13 Year-Old Boy Presenting as an Acromegaly-Like Syndrome. *Journal of Pediatric Endocrinology and Metabolism* 8(1):51-54.

Stedman, Thomas L. (ed.)
1897 *Twentieth Century Practice: An International Encyclopedia of Modern Medical Science by Leading Authorities of Europe and America.* William Wood and Company, New York.

Stratton, R.F.
1998 Tall stature, microcephaly, hypotonia, advanced bone age, and unusual infra-auricular creases. *American Journal of Medical Genetics* 75-3: 261-262
Jan 23 1998.

Swedlund, Alan C. and Armelagos, George J.
1976 *Demographic Anthropology.* Wm. C. Brown Co. Pub., Dubuque, Iowa.

Tibaldi, Joseph M. and Resta, Christina A.
1998 Unusual Presentation of a Case of Acromegaly. *The Endocrinologist* 8:44-45.

Thompson, Henry Alexis
1890 Acromegaly, with the Description of a Skeleton. Journal of Anatomy and Physiology, 24:475-492.

Todd, T.W.
1920 Age Changes in the Pubic Bone: I. The Male White Pubis. *American Journal of Physical Anthropology* 3:285-334.

Trinkaus, Erik
1985 On the Neandertal Pubis and Acromegaly. *Current Anthropology.* 26(4):526-529

Uehlinger, E.
1960 Osteofibrosis Deformans Juvenilis (Polyostotische Fibrose Dysplasie Jaffe-Lichtenstein). *Virchow's Archiv fur Pathologische Anatomie* 306:255-299.

Weinreb, Eva Lurie
1984 Anatomy and Physiology. Addison-Wesley Publishing Company, Reading, MA

Wells, C.
1964 Bones, Bodies and Disease. Fredrick A. Praeger Inc., New York.

Wells, L.H.
1969 Stature in Early Races of Mankind. From *Science in Archaeology: A Survey of Progress and Research* (Brothwell, Don and Higgs, Eric, eds.). Praeger Publishers, New York.

Zivanovic, Srboljub
1982 Ancient Diseases. Meuthen & Co. LTD, London.

Government Documents

1987 *Anthropometric Reference Data and Prevalence of Overweight: United States, 1976-80. Data From the National Health Survey, Series 11, No. 238.* DHHS Publication No. (PHS) 87-1688. United States Department of Health and Human Services (DHHS), Public Health Service, National Center for Health Statistics, Hyattsville, Md.

Egypt Government Document: Maoslaohat al-Misaaohah
1907 *The Archaeological Survey of Nubia.* National Printing Department, Cairo, Egypt.

Internet Resources

Victor A. McKusick (a). *#154700 Marfan Syndrome; MFS.* Online Mendelian Inheritance in Man, OMIM ™: Developed by McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD). [Online] Available: http://www.ncbi.nlm.nih.gov/omim/, 6/23/1986

Victor A. McKusick (b). *167250 Paget Disease of Bone 1; PDB1.* Online Mendelian Inheritance in Man, OMIM ™. [Online] Available: http://www.ncbi.nlm.nih.gov/omim/, 6/2/1986

Victor A. McKusick (c). *102200 Acromegaly.* Online Mendelian Inheritance in Man, OMIM ™. [Online] Available: http://www.ncbi.nlm.nih.gov/omim/, 6/4/1986

"Anabolic Steroids.com" publication. *We Started Noticing That His Toes And Fingers, As Well As His Ears, Began Growing And So Was His Head.* [Online] Available: http://anabolicsteroids.com/acromegaly.html, 1997.

"National Institutes of Health" publication. *Acromegaly: Publication No. 95-3924.* MGH Pituitary Center Homepage. [Online] Available: http://brain.mgh.harvard.edu:100/acromeg.htm, February 1995

Collections

The Collection of Warren Raymond

The Documentary Archives of the Mutter Museum