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Differential diagnosis of vertebral lytic lesions from an Ohlone cemetery site CA-SCL-038

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Differential Diagnosis of Vertebral Lytic Lesions from an Ohlone Cemetery Site

CA-SCL-038

A Thesis

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by

Victoria M. Wu

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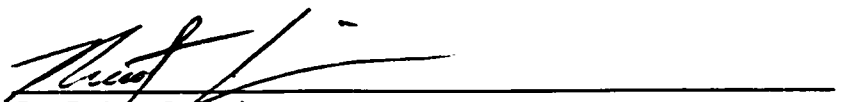

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Abstract

Differential Diagnosis of Vertebral Lytic Lesions from an
Ohlone Cemetery Site CA-SCL-38

by Victoria M. Wu

Six individuals excavated from CA-SCL-38, an archaeological site located at Elmwood Correctional Facility in Milpitas, California, presented with vertebral lytic lesions previously unseen in California. To discern the possible disease processes which may have been involved in producing the pathological lesions, a differential diagnosis was performed. Disease processes included in the differential diagnosis were neoplastic disese, fungal infections, non-tuberculous mycobacteriosis, tuberculosis and other conditions such as actinomycosis, brown tumor of hyperparathyroidism, brucellosis, Gorham's Disease, Paget's Disease, rheumatoid arthritis, sarcoidosis and vertebral osteomyelitis. Comparison between the clinical manifestations of bone involvement in each of these diseases and the skeletal remains of the individuals from SCL-38 resulted in localization of two possible disease processes which may have been the cause of the lytic lesions. It was determined that tuberculosis, either due to *M. bovis* or *M. tuberculosis*, or coccidiodomycosis were the most likely pathogen which produced the lytic lesions.

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1. INTRODUCTION

All patients are living puzzles. The conglomeration of signs and symptoms that they present are only the smallest of clues in the search for the answer, yet in the end, it is these fragments that are necessary for the proper placement of all clues, and in turn, a proper diagnosis. For the paleopathologist though, the puzzle will perpetually be incomplete, for few diseases can be identified wholly through the study of bone alone.

Yet despite the inability of skeletal remains to provide a comprehensive record of disease and health in prehistoric populations, they do provide the only glimpse that is presently available of the morbidity and mortality of these populations.

1.1. Objective

The objective of this present analysis is to describe and analyze vertebral lytic lesions from six individuals from the CA-SCL-38 site. This analysis is an attempt to determine the probable pathogenic agents or disease processes which are responsible for the production of these lesions. The motivation for undertaking this analysis is two-fold: 1) it is only through the study of skeletal pathology that the biological history of disease in humanity can be discerned; 2) the unusual nature of these lesions. Lytic lesions due to inflammatory disease are uncommon in paleopathology; in California, the type of lytic lesion, as seen in these individuals, has never be documented previously.

1.2 Lytic Lesions in Paleopathology

Clinically, the number of disease processes and pathogens known to cause lytic lesions in bone is impressive. From sarcomas to carcinomas, bacterial infections and autoimmune disease, the literature is a seemingly endless stream of diagnoses and case reports. This is not the case in the paleopathological literature however. In cases which lytic lesions are documented, there are only a handful of disease processes which can be linked to the lesions as a possible causative agent. The disease processes found in the paleopathological literature that have been associated with prehistoric skeletal remains, afflicted by lytic lesions, are treponematosis, osteoarthritis, rheumatoid arthritis, tuberculosis and metastatic cancer.

1.2.1 Tuberculosis

Tuberculosis has been a plague upon humanity for an extensive period of human history. The oldest possible case of tuberculosis in the Old World was reported in 1907 by Bartels on a Neolithic skeleton of a young man found near Heidelberg, Germany, dated to approximately 5000 B.C.E (Ortner & Putschar, 1981). There is collapse of the fourth and fifth thoracic vertebrae which is fused with the sixth vertebrae, creating an angulation, often, but not exclusively, seen in tuberculosis (Ortner & Putschar, 1981). In the Old World, tuberculosis is an established entity, with a myriad of cases describing skeletal lesions attributed to tuberculosis. The dates of these skeletal remains are between 4000 and 1000 B.C.E and the remains have a geographic distribution of Italy, France, Denmark, Jordan and Egypt.

Many of the reports of tuberculous-like lesions from skeletal remains come from Egypt. One of the earliest reports comes from Elliot-Smith and Ruffer, who in 1910, reported on a probable case of tuberculosis from an Egyptian mummy from the Twenty-first dynasty (as cited in Ortner & Putschar, 1981). There is extensive destruction of the last four thoracic vertebrae and the first lumbar. There is also a swelling inferior to the lesion on the first lumbar which the authors postulated to be a psoas abscess. Other authors, Morse, Brothwell, and Ucko (1964) and Williams (1929), have also concluded that the case for tuberculosis in the Old World, particularly Egypt, is strong.

In the New World, the opposite case applies. Hrdlicka in 1909 stated that "tuberculosis was rare, if it did exist." in pre-Columbian America (as cited in Buikstra & Cook, 1981, 3). This conclusion was based on observations that: 1) there were no references to the disease among Native Americans; 2) there was a lack of remedies for the disease among Native groups; 3) Native Americans were more susceptible to the disease than Europeans; 4) there were no skeletal remains of undoubtedly pre-Columbian origin which had tuberculous lesions; and 5) the elderly of the tribe were free of any signs of tuberculosis of the lymph nodes and bones (Buikstra & Cook, 1981). There is now, however, a growing body of evidence to suggest that, at least in South America, tuberculosis was present and widespread. Allison, Mednoza and Pezzia (1973) described the mummified remains of a child from the Nazca culture dated to 200 to 800 C.E who had evidence of Pott's disease, tuberculosis of the lung, pleura, liver and the right kidney, as well as evidence of a psoas abscess. Acid fast bacilli were also detected. Recent molecular evidence also points to the existence of tuberculosis in South America. Salo, Aufderheide, Buikstra and Holcomb (1994) and Arriaza, Salo, Aufderheide and Holcomb.

(1995) both detected DNA from an organism belonging to the *Mycobacterium tuberculosis* complex using Polymerase Chain Reaction (PCR) from mummies in Peru and Chile. In North America, evidence of tuberculosis has been limited to a handful of sites mostly from the midwest and southwest. Three possible cases of skeletal tuberculosis come from Pueblo Bonito, New Mexico. The date of the site is 828-1130 C.E (Ortner & Putschar, 1981).

1.2.2 Treponemal Disease

If the case for tuberculosis is tenuous in the North America, then the opposite can be said of treponemal disease. Rather, it is in the Old World that pre-Columbian evidence for the existence of treponemal disease, particularly venereal syphilis, is inconclusive. At present, there are three different lines of thought on the origin and presence of pre-Columbian treponemal disease, with the emphasis on venereal syphilis, in the Old World.

The first suggests that syphilis did not exist in the Old World previous to its introduction by Columbus and his crew after their voyages to the New World. The second possibility suggests that syphilis did exist in the Old World previous to Columbus' voyages and it was Columbus who introduced it into the New World and its virgin population. The last possibility is that the disease existed in both the New and Old World previous to Columbus but perhaps in a different form than what we recognize today as venereal syphilis.

The existence of some form of Pre-Columbian treponemal disease is fairly well documented in the New World. The earliest report of possible treponemal disease from a New World site came from Jones, who in 1876, reported on the presence of syphilitic

lesions on individuals in a prehistoric Tennessee population (as cited in Hutchinson, 1993; Ortner & Putchar, 1981). The same type of lesion was also reported later by Haltom and Shands, in 1938, from a prehistoric Moundville population in Alabama; Hrdlicka in 1922 from a Florida population; and Williams in 1932 and 1936 on populations in Ohio, Tennessee and Florida (as cited in Hutchinson, 1993). Skeletal evidence for the presence of treponemal disease has since then been found in a number of different states such as Illinois, Alabama, Arkansas, Mississippi, Georgia, Florida, New York, North Carolina and Louisiana. It has been argued, based on the wealth of skeletal evidence for treponemal disease in the New World, that treponemal disease, in some form or another, was endemic in the New World long before the arrival of Columbus.

The evidence for the presence of treponemal disease in the Old World previous to the voyages of Columbus is far less extensive. Bloch, in 1901 and 1911, noted that, previous to the fifteenth century, there was no evidence to show that syphilis existed in Europe (as cited in Ortner & Putschar, 1981). It was only during the last decade of the fifteenth century that evidence of syphilis in Europe appeared (Ortner & Putschar, 1981). Dennie in 1962 also concurred with this opinion. He believed that the initial virulence of syphilis, upon its introduction to Europe, was a clear sign that the disease did not exist previously in this population. As the disease became subsequently milder and eventually endemic in the population, Dennie argues that it is evident that syphilis was an introduced disease from the New World (as cited in Ortner & Putschar, 1981).

Not all authorities agreed, however, with the opinion that syphilis and other treponemal diseases did not exist in the Old World previous to Columbus's voyages. Holcomb (1941) believed that the earlier descriptions of certain conditions attributed to

leprosy by medieval writers were in fact cases of syphilis. He attributes this conclusion to the descriptions, not only of the lesions themselves, but of the mode of transmission, which was venereal. Other authors, however, dispute this claim. Crobsy (1969) declared that there is no unequivocal description of syphilis in the ancient medical literature. Wong and Wu, in 1936, state that there has never been a description of syphilis by ancient Chinese writers, and Bloch, in 1908, states that, given the social conditions of the Roman Empire and Middle ages, where the presence of moral excesses should have led to the widespread prevalence of syphilis, there is a lack of skeletal evidence for syphilis among the pre-Columbian remains (as cited in Ortner & Putschar, 1981).

There is also a third view among the arguments on the origin of treponemal disease. This third view is espoused, in different forms, by Hudson (1968), Hackett (1963) and Cockburn (1961), as well as Stewart and Spoehr (1952). This third view is an attempt to develop an evolution-based theory for the origin of treponemal disease. In this view, it is thought that the original treponeme organism migrated with humans and was endemic in both New and Old Worlds long before Columbus. In variations upon this theme, Stewart and Spoehr (1952) suggested that, while both continents had endemic treponemal disease, the strain of organism responsible differed between the two continents. Therefore, neither population had immunity to the other's disease and thus the increase in bony lesions seen after Columbus's initial voyage, in both New and Old World, can be attributed to the lack of immunity.

Hudson (1968) suggests that the original treponeme was an environmental saprophyte which was introduced accidentally to humans cutaneously and later evolved to a disease similar to yaws. Hudson proposed that, as humans moved into different, dryer,

more temperate environments, the organism, adapted to surviving in moist conditions, moved into different regions of the body, eventually resulting in the evolution of venereal syphilis.

Hackett (1963), on the other hand, proposed that the original treponemal organism mutated into different forms as humans ventured out of the rainforest. As the organism encountered new environmental conditions, mutational events would occur, producing a new organism. Hackett also proposed that at the end of the fifteenth century a mutation occurred in the European organism, resulting in a rampant epidemic of venereal syphilis, which then spread throughout the world due to colonial expansion.

1.2.3 Metastatic Disease

Metastatic diseases, either primary or secondary, are a rare entity in paleopathology. Of the two conditions, primary neoplasms are rare, not only in the paleopathological literature, but in clinical practice as well. One of the earliest examples of a possible osteosarcoma, reported by Ruffer and Willimore, in 1914, was of a tumor afflicting a right os coxa from Egypt, dated to about 250 C.E (as cited in Ortner & Putschar, 1981). Ortner and Putschar report on three more cases of probable malignancies. Two of the cases, one reported by Dastugue (1965) and the other by Kelln, McMichael and Zimmerman (1967) are considered by the authors to be questionable cases of bone tumors. In the former case, the authors propose that the origin of the lesion is likely due to trauma and in the latter, the authors propose that the lesion seen can be explained by conditions other than osteosarcoma.

The only case of primary malignant tumor presented by Ortner and Putschar (1981) that appears to be an unambiguous case of osteosarcoma is found in the remains of a Celtic warrior, specimen, NHMB A95, stored at the National History Museum in Bern, Switzerland, dated to approximately 800-600 B.C.E. Suzuki (1987) also reported on a probable case of osteosarcoma from pre-contact Hawaii. The young adult female presented with an osteoblastic lesion on the distal metaphyseal area of the left femur. Examination of the lesion determined that the diagnosis of osteosarcoma was compatible with the characteristics presented by the lesion.

Secondary tumors of bone, metastatic carcinomas, are far more common, both in the clinical literature as well as the paleopathological literature. Even so, the paleopathological literature pertaining to metastatic carcinomas is, at best, limited. The majority of cases attributed to metastatic carcinoma are of individuals displaying clear and distinct osteolytic lesions. Grevin, Lagier and Baud (1997), discuss the case of a cremated pelvis dating to the first century A.D. Using microradiology, the authors proposed that the osteosclerotic lesion seen in the pelvis was the result of metastasis of prostate carcinoma. Anderson, Wakely and Carter (1992), discuss the skeletal remains of an elderly male from medieval Canterbury. Based on gross examination of the lesions as well as SEM (scanning electron microscopy) and plain film radiographs, the authors conclude the source of the lesion to be the dissemination of prostate carcinoma. Tkocz and Bierring (1984), also discuss a case of probable prostate carcinoma. The skeletal remains, from Svendborg, Denmark, are of a mature male dated to the middle ages. The individual presents with multiple osteosclerotic, osteolytic lesions.

A case of possible metastatic carcinoma of the breast was presented by Strouhal (1993). The skeletal remains are of a 35-45 year old female from Sayala, Egyptian Nubia during the Christian period. The individual presented with multiple lesions scattered throughout the skeleton. Lesions were mostly lytic with slight osteoblastic activity. A case of possible bronchogenetic carcinoma was presented by Grupe (1988) in skeletal remains of a male 40-50 years of age. The remains were excavated from Schleswig, Germany and are dated to approximately the 11th or 12th century. Multiple lytic lesions were found on lumbar vertebrae, pelvis, ribs and sternum. Trace element analysis of the bone revealed high levels of cesium and antimony present. The author speculates that while the high levels of antimony itself are not carcinogenic, its presence may indicate that the individual was a metal worker and thus could have been exposed to other metals which are carcinogenic.

1.2.4 Septic Arthritis

References to cases of septic arthritis in the paleopathological literature are rare. Septic arthritis is a condition in which the bones of the joints are infected by a bacterium, either disseminating from a remote site of infection, infection through a direct wound, or an extension of an infection in bone. In cases of septic arthritis, all joints can be affected, but one-third of cases involve the knee and one-third the hip (Ortner & Putschar, 1981). Unrelieved septic arthritis terminates in bony ankylosis with the acute and final stages of bone involvement similar to that of tuberculous arthritis in dry bone, though there is generally less bone destruction and concomitant shortening than in tuberculosis (Ortner & Putschar, 1981). There are only a few cases of probable septic arthritis described in the

literature. A fairly definitive case of septic arthritis comes from Peru. The fused left femur and tibia was an isolated surface find near Chancay. There is no date associated with the remains; however, the bones reflect a considerable amount of periosteal reaction, sclerosis and cloaca which are indicative of infection and inflammation (Ortner & Putschar,1981). Wells in 1962, attributes a degenerated left humeral head from a young female from an Early Saxon cemetery to septic arthritis (as cited in Ortner & Putschar, 1981). In the Americas, cases of probable septic arthritis have been discussed by Jarco, Simon and Bick (1963), Moodie (1928), Morse (1969) and Aceves-Avila, Baez-Molgado, Medina and Fraga (1998). Of these four cases, the cases described by Jarco et al. and Moodie can possibly be attributed to other causes such as congenital abnormality or degenerative arthritis due to trauma (Ortner & Putschar, 1981).

1.2.5 Degenerative Disease

Degenerative disease is one of the most common ailments seen in paleopathology. Degenerative arthritis is a non-inflammatory disease which develops in response to the changes in joints and articular surfaces due to aging and degeneration of cartilage. This condition is progressive with age and the general wear and tear that occurs with the aging process. Secondary degenerative arthritis can often develop in joints following primary degenerative arthritis. Secondary degenerative arthritis tends to develop in structurally or functionally abnormal joints and can be the end stage of various inflammatory, traumatic, metabolic, congenital or acquired joint disease (Ortner & Putschar, 1981).

Degenerative arthritis of the vertebrae is seen, in varying degrees of severity, in almost all archaeological populations. Degenerative arthritis of the diarthrodial joints is

associated with porosity, eburnation and marginal lipping on the vertebra. Degenerative change of the vertebral body is associated with erosion and development of marginal osteophytes; porosity and eburnation are rarely seen and lytic lesions are never seen (Ortner & Putschar, 1981).

1.2.6 Paleopathology in California

In California, there is a remarkable lack of skeletal lesions relating to disease among the pre-historic population. There are only a few diseases recognized, paleopathologically, in California. Degenerative disease, dental disease, inflammatory processes such as osteomyelitis and periostitis, trauma, porotic hyperostosis, a case study of a hydrocephalic child and one of a microcephalic child, are the only pathological conditions which have been documented. Jurmain (1990a, b) reported on degenerative disease and dental disease among a pre-historic population from CA-ALA-329. He determined that individuals in this hunting-gathering population suffered from more degenerative disease than settled agriculturists from Pecos Pueblo, but had far less involvement than Alaskan Eskimos. Among this population, dental disease is the most common pathological process seen. Jurmain observed that tooth wear began at a very young age and, in permanent dentition, wear was observed on all elements by the second decade. By the end of the third decade, most individuals had no enamel remaining (Jurmain, 1990a). It is thought that the high level of dental attrition and the subsequently high incidence of periodontal remodeling, socket resorption and dental abscesses is the result of a diet high in abrasive material. The extreme degree of attrition, found in this population, is the most severe for any population described (Jurmain, 1990a). Also, from

ALA-329, Pierce (1982), determined that there was a 13% incidence of periosteal reaction among this population in the form of periostitis. In the same work Pierce also describes three cases of systemic hematogenous osteomyelitis in one female and two male individuals.

Walker (1989) examined a population from the Channel Island area of Southern California for evidence of cranial trauma. He determined that individuals from the northern Channel Islands suffer a higher rate of depression fractures than individuals from the mainland coast. Walker speculated that the prevalence of cranial trauma among the islanders was possibly due to competition for limited resources in a geographically circumscribed environment (Walker, 1989). Also from the Channel Islands, Walker (1986) analyzed 432 crania from a non-agricultural fishing population and determined that individuals from the northern Channel Islands have a higher incidence of porotic hyperostosis than individuals on the mainland. Among the islanders, those residing on the smaller islands, which have limited resources, have a higher incidence of porotic hyperostosis than those living on the larger islands. Walker explained the difference in incidence between the mainlanders and islanders as due to differences in water contamination, exposure to fish-borne parasites and nutrition rather than the usual explanation of a diet lacking in iron and protein.

Richards (1985) diagnosed a case of possible microcephaly from the remains of a three year old child from a site in San Jose, CA. The individual exhibited cranial capacity comparable to a six month old infant with a reduced stature and a facial skeleton equivalent to a nine month old individual. From the cranial endocast, the individual was determined to have severe malformation of the orbital aspect of the frontal lobes and

significant reduction of the size of the cerebral cortex and left temporal lobe (Richards, 1985).

A case of possible hydrocephalus in a child from central California was described by Richards and Anton (1991). The child's partial skeleton exhibit abnormal craniofacial configuration as well as malformed postcranial elements.

1.3 Purpose of Differential Diagnosis

The purpose of the differential diagnosis is an attempt to sort through all possible conditions which can cause vertebral lytic lesions by comparing all the disease conditions and their physical manifestations. Many different conditions and pathogens can produce skeletal lytic lesions. A great number of these conditions also can produce lesions in the vertebrae. The differential diagnosis will detail the types of lesions produced by the different diseases (lytic, blastic or mixed), any predilections the various diseases have for certain individuals, skeletal sites, age groups, or sexes. With the production of a detailed differential diagnosis of the conditions which can produce vertebral lytic lesions, it becomes possible to compare the vital statistics of the individuals, along with the descriptions of their particular skeletal lesions, to each of the possible diseases and therefore discount or accept that disease as a possibility.

The criteria used to determine which disease processes and pathogens would be considered in this differential diagnosis is straightforward. Disease processes such as neoplasms, both primary and metastatic, will be considered if the tumors produce lytic lesions and the lytic lesions could be situated to the vertebrae. For pathogenic organisms, the criteria is as follows: all pathogens which commonly produce lytic lesions in the

vertebrae will be discussed. Diseases caused by common bacteria, even if the disease itself is rare, will be considered. This is the case for nontuberculous mycobacterosis (NTM). While the diseases produced by NTM's are uncommon, the organisms themselves are fairly ubiquitous in the environment. It would not be difficult for individuals to come across such organisms and possibly become infected though casual contact. Other disease processes which clinically manifest lytic lesions in the spine will also be included in the discussion. The diseases may be rare, but if their sole manifestation is in the spine, then they cannot be excluded.

2. MATERIALS AND METHODS

2.1 Site Description

CA-SCL-38 is a site located within the Elmwood Correctional Facility in the city of Milpitas, California. The site is historically known as the Alms House Mound and was described by C.W. Meighan in 1952 as an "extensive habitational site marked by a low, almost not discernible mound" (Bellifemine, 1997, 46). The site had been previously disturbed by plowing activities associated with the County Alms farm and the burial context had been disrupted (Bellifemine, 1997). The site is located in the northern part of the Santa Clara Valley on a flood plain between two local creeks, the Coyote Creek and Lower Penitencia Creek, to which the Coyote Creek is adjacent. The climate of the Valley is considered Mediterranean with wet winters and dry summers (Bellifemine, 1997). The Valley is also affected by various high and low pressure systems off the coast which create within the Valley a series of micro-climates. Within San Francisco Bay, towards the northern end, the level of precipitation increases inland. The variability in

weather conditions has also created a series of distinct ecological environments such as marshland, mountains, temperate rain forest and arid chaparral, among others, to allow the support of a diverse mix of plants and wildlife.

CA-SCL-38 was excavated due to the expansion of Elmwood Correctional Facility to build barracks. Initial subsurface testing in April 1993, consisting of eight excavated units and 16 auger bore holes (Bellifemine, 1997), determined the presence of buried human remains on the site, though the site had been previously excavated briefly. The first excavation was performed by U.C. Berkeley in 1950 and resulted in the recovery of six burials (Bellifemine, 1997). The second was performed by San Jose State University in 1952. A large group of burials, approximately 228 individuals (Jurmain, in preparation), were documented and excavated by the Ohlone Families Consulting Services from August 1993 to October 1993 and removed to San Jose State University under the care of the Department of Anthropology, where elements were inventoried, washed, cataloged and submitted for analysis. The analysis consisted of determining age of death for each individual, when possible; determining the probable sex of the individual; metric and non-metric analysis and determination of possible pathological conditions which may have been present in the individual. Skeletal elements possessing unusual pathological or traumatic conditions were photographed and radiographs of the affected elements taken. A single rib was also taken from each individual for possible future molecular analysis. At the end of the analysis the remains were reburied back on site in accordance with NAGPRA regulations.

2.2 Ethnographic Overview

The Ohlone linguistic groups occupied the area ranging from the San Francisco Peninsula, on the west, to both sides of the Carquinez straits in Contra Costa County and south to Monterey Bay (Bellifemine, 1997). This linguistic group forms part of the Utian family (Miwok-Coastanoan), within the Penutian stock. Cultural information of the Ohlone Tribe is derived from ethnographic and ethnohistoric sources such as the diaries of early Spanish and European expeditions into the San Francisco Bay Area, mission records, and ethnographic work done in the first part of the 1900's. From the data gathered, it appears that the Ohlone were organized into tribal associations with control of a certain amount of territory, varying from 60 to 150 square miles (Bellifemine, 1997). The Ohlone were dependent upon the ecological conditions of the land for resources. This in turn determined the population density of the various groups living in the region. Social structure also varied between groups. Some were organized into a single community while others were divided into smaller groups among several different sites. There did not appear to be any higher permanent political organization among the Ohlone. Rather, the "tribelets" were associated with one another by alliances through marriage, conflicts and the ecological conditions under which each group subsisted (Bellifemine, 1997).

2.3 Osteological Analysis

The analysis performed on the six individuals from SCL-38 with vertebral lytic lesions included aging, sexing, gross examination of all elements, as well as the affected vertebra, and radiographic analysis of the vertebral lesions. Aging and sexing were done using standard osteological techniques. The particular criteria used to age and sex each

individual will be included in the information provided on the skeletal material from each of the six burials.

The affected vertebra(e) from each individual was washed, allowed to air dry, and the lytic lesions were examined by the naked eye and though the use of a large magnifying glass. The lytic lesions were examined for signs of healing and remodeling of the bone, production of sclerotic bone around the lesion, the extent of the damage to the element from the lesion and the extent to which the lesion had spread to adjacent elements. Edges of each lesion were examined by magnifying glass, as well as a dissecting microscope to determine if the damage was produced through a disease process or perhaps was a result of post-mortem damage during excavation. Measurements of each lesion were also taken. Measurements were obtained utilizing a digital caliper. The measurements obtained by the calipers is accurate to the nearest 0.1mm.

Radiographs were also taken of the major skeletal elements of all six individuals, along with the affected vertebra, when the elements were available. The radiography was performed at the Jose State University Health Center, department of radiology. Along with the affected vertebra(e), the other elements examined radiographically were the skull, all major long bones, the os coxa and all other unaffected vertebrae. The elements examined radiographically varied between individuals depending upon the completeness of the burial.

2.4 Molecular Analysis

2.4.1 DNA Extraction

A small amount of affected bony material, < 1 gram, was removed from burial 6, burial 33 and burial 62. The bone was removed from areas of the vertebra directly adjacent and in contact with the lesion, using a diamond bladed GEM saw, in the Anthropology Laboratory at San Jose State University. The saw was washed with 100% bleach and sterile water between each usage to prevent cross contamination between the samples. Bone samples were not exposed to UV light or sterilized by immersion in bleach, since any mycobacterial DNA present would be adherent to the surface of the bone. UV irradiation would cross-link all DNA on the surface of the bone and thus render it useless for analysis. The bone samples were wrapped in several layers of sterile foil and crushed with a hammer into fine fragments. The fragments were ground further using a sterile mortar and pestle in a UV sterilized laminar flow hood. DNA was extracted from each of the ground samples using the BIO101 GENECLEAN kit for Ancient DNA (BIO101, Vista, CA) using the expanded protocol. Extracted DNA was eluted using 100µl of sterile TE (25mM Tris-HCL, pH. 7.6, 10mM EDTA, pH. 8.0) and stored at 4°C in a sterile microfuge tube. Along with the bone samples, a blank sample containing all of the extraction reagents, but no bone, was processed. This is the negative control and will determine if any of the samples become contaminated by an outside source of mycobacterial DNA. The DNA used as a positive control in this experiment come from an attenuated strain of *Mycobacterium tuberculosis* from the American Tissue Culture Collection (ATCC). This strain was kindly grown up and DNA extracted by Christina Ivy at the Peter Small Laboratory, Stanford University, Palo Alto, California

2.4.2 Polymerase Chain Reaction (PCR) for *Mycobacterium* DNA

PCR amplification was performed on the extracted DNA, one positive control, two negative controls, and a reagent control using the protocol described in Espinosa de los Monteros et al. (1998). There are two sets of protocols described in this paper. The first is the amplification of the pcnA sequence and the second is of the oxyR sequence. These genetic polymorphisms are found in both *Mycobacterium tuberculosis* and *Mycobacterium bovis*. The technique is based on the difference found at position 169 of the pncA genes between the two species and a difference at position 285 in the oxyR gene. In this experiment, the primers ordered were specific for the oxyR gene of the mycobacterium. The selection of the oxyR gene instead of the pncA gene for amplification was due to the size of the PCR product produced. Amplification of the oxyR gene produced a product of 185 base pairs in length, while amplification of the pncA gene produced a product 290 base pairs in length. Given the degenerated nature of any template DNA which may be present, the chances of amplifying a smaller product is greater.

Briefly, for the PCR amplification, two master mix tubes, final volume of each tube 264µl, 24µl per PCR reaction plus 10% extra, were made with the final concentration of reagents as follows: 2mM MgCl, 1X PCR reaction buffer without $MgCl_2$ (Promega, Madison, WI), 0.2mM dNTP mix, 1 Unit *Taq* DNA polymerase, 20 pmol of each primer (Operon Technologies, Alameda, CA) and 0.01% gelatin. One master mix tube was labeled *Mycobacterium tuberculosis* and contained the PCR reagents in the above concentrations and contained the primers OxyRTB-1 (20 pmol) and OxyRMT (20 pmol). The other master mix tube was labeled *Mycobacterium bovis* and contained the PCR

reagents in the above concentrations but contained the primers OxyRTB-1 (20 pmol) and OxyRMB-1 (20 pmol). The PCR amplification was performed in 0.5ul thin walled PCR tubes. Six PCR reactions were set up for each master mix. For the *Mycobacteria tuberculosis* master mix, three PCR tubes labeled *M. tuberculosis* were aliquoited with 20µl of extracted DNA. One PCR tube was labeled positive control and contained a final concentration of 1µg of *M. tuberculosis* DNA, in 20µl of TE, which was obtained from Stanford University. One tube was labeled negative blank control and contained 20µl of the blank extraction and the last tube contained no template DNA, only PCR reagent plus 20µl of sterile deionized water. For the *M. bovis* master mix, three PCR tubes were labeled *M.bovis* into which 20µl of the extracted DNA was aliquoted. Two PCR tubes were labeled negative control, with one containing a final concentration of 1µg of *M. tuberculosis* DNA, in 20µl of TE, and the other containing 20µl of blank extraction. The last tube was labeled reagent blank and contained no template DNA, only PCR reagent plus 20µl sterile deionized water. Twenty-four microliters of the appropriate master mix was then aliquoted into each labeled tube. The combined 44µl reaction was then subjected to 30 cycles of PCR that consisted of an initial hold at 94°C for 12 minutes, denaturing at 94°C for 45s, annealing at 70°C for 45s and elongation at 70°C for 45s. PCR products were run out on 2% agarose gels and stained with ethidium bromide (0.5µg/ml).

3. THE SKELETAL MATERIAL

3.1 SCL38-6

SCL38-6 is a female individual and was 21-25 years of age at the time of death. The remains are extremely poorly preserved and friable to touch. The majority of elements are incomplete and fragmentary. Sex was determined using Loth's methods (Loth & Henneberg, 1996) and age was estimated from the degree of fusion of epiphyses.

In addition to the vertebral lytic changes seen, SCL38-6 showed evidence of enamel hypoplasia. Multiple transverse hypoplastic lines are present on the upper right and left canines, right and left lower canines and right lower lateral incisor and left lateral incisor. Also, SCL38-6 had a congenital malformation of the right upper lateral and central incisors. Incisors are malformed and misshapen.

On the articular surface of the sternal end of both left and right clavicles there is hypertrophic growth covering the surface as well as evidence of pitting and hyperostosis on the coracoid process of the right scapula. There are no other pathological processes seen due to the extremely fragmented state of the remains.

3.2 SCL38-33

SCL38-33 is male and was 27-37 years of age at the time of death. The remains are moderately well preserved with most elements present, though the margins of most articular surfaces have been eroded, with some broken postmortem. Sex was determined using the morphological characteristics taken from the os coxa and age was determined using the Suchey-Brooks method (Suchey, 1985).

In addition to the lytic vertebral changes, SCL38-33 showed evidence of enamel hypoplasia. Multiple transverse hypoplastic lines are present on the lower right lateral and central incisors as well as the left lower canine, lateral and central incisors.

There is evidence for slight porotic hyperostosis in this individual. There is a porous reaction across the bone of both brow ridges and across outer surface of both parietals. The lesions consist of slightly porous, reactive bone scattered lightly across the surface of affected areas.

3.3 SCL38-62

SCL38-62 is male and was 17-21 years of age at the time of death. The remains are poorly preserved and most of the available elements are incomplete and fragmentary. This individual has moderate mastoids and chin. The ilium presented with a narrow sciatic notch and a flat sacro-iliac articular surface. The os coxa of this individual was incomplete and sex was determined using the criteria mentioned above. Age was determined by examining the fusion of epiphyses of various elements.

In addition to the lytic changes, there is evidence of enamel hypoplasia in this individual. Multiple transverse hypoplastic lines are present on the right lower canine, right upper lateral incisor and the right upper central incisor.

There is also a small lesion 4 millimeters (mm) in width and 3 mm in height near the top of the distal surface of the left 3rd cuneiform with a corresponding lesion on the individuals 3rd left metatarsal. The right foot also has a similar lesion in approximately the same position, 3mm in height by 5mm in width.

3.4 SCL38-107

SCL38-107 is female and was 35-45 years of age at the time of death. Sex was determined using the morphological characteristics taken from the os coxa and age was determined using the Suchey-Brooks method (Suchey, 1985). The remains are well preserved and in excellent condition with the majority of elements present and complete.

In addition to the vertebral lytic changes, SCL38-107 showed evidence of enamel hypoplasia. Multiple transverse hypoplastic lines are present on the lower right canine, lateral incisor and central incisor. Hypoplastic lines are also present on the lower left canine, lateral incisor and central incisor. There is a small amount of tartar build up in the form of calculus on the teeth present, mainly around the gumline.

The only other major evidence of pathological lesions seen in SCL38-107 was moderate osteoarthitis. A description of the elements involved, starting with the axial skeleton, follows. The sternal end of the left clavicle has a great deal of hypertrophic growth covering the majority of the articular surface. The new bone is rough in appearance and somewhat ragged looking in detail. The hypertrophic bone appears to have been somewhat remodeled but still highly porous. The right clavicle also has hypertrophic growth on the articular surface of the sternal end. The new bone growth is not as extensive as that on the left clavicle, but still covers the majority of the articular surface. The hypertrophic growth is smoother, more remodeled than that of the left clavicle, although its texture is still porous.

The glenoid fossa of the right scapula has a small patch of eburnation located to the left of the supraglenoid tubercle. In the center of the glenoid cavity there is evidence of pitting and erosion of the cortex. There is slight lipping around the margins of the head

of the left humerus. Slight lipping is present around the edges of the trochlear notch of the right ulna and the head of the left ulna. There is also slight lipping around the radial tuberosity of the left radius where some periostitis is evident.

T5-T8 have hypertrophic growth around the margins of both the superior and inferior costal facets. L1, L3 and L5 all have mild lipping around the margins of both superior and inferior articular processes as well as lipping around the margins of the vertebral body.

There is an irregular patch of eburnation and pitted erosion in the middle of the right sacral auricular surface at the superior margin. On the medial margin of the lateral condyle of the right femur there is an area of eburnation extending along the entire length of the medial condylar margin. On the anterior surface of the lateral condyle of the left tibia there is also a small patch of eburnation.

3.5 SCL38-109

SCL38-109 is male and was 21-30 years of age at the time of death. The sex of the individual was determined from the morphological characteristics taken from the os coxa. Age was determined using the Suchey-Brooks method (Suchey, 1985). The remains are well preserved and in good condition with the majority of elements present and complete.

The majority of pathological lesions other than the vertebral lytic lesions in this individual are congenital in nature. The right transverse process of the 7th cervical vertebrae is unfused.

On the 1st and 2nd lumbar vertebrae there is the presence of extraneous bone growth on both superior articular facets. The extraneous bone is irregular in appearance but well remodeled and protrudes from the margins of the articular facets. The presence of this bone is likely evidence for the beginning of primary degenerative joint disease (DJD).

3.6 SCL38-229

The individual is male and was 25-35 years of age at the time of death. The remains are fairly fragmentary, although the surface preservation of recognizable elements is good when available. Sex was determined from the morphological characteristics of the os coxa and age was determined using the Suchey-Brooks method (Suchey, 1985).

In addition to the lytic vertebral changes, the tip of the acromion of the right scapula had at one point been broken and separated from the rest of the bone, most likely due to trauma. The break was healed and the tip had been fused to the rest of the acromion but the fusion and remodeling were incomplete at the time of death. Stirland (1997) states this condition as os acrominale.

A cervical vertebrae, C3-7 (it cannot be identified more precisely), has the right foramen closed due to the presence of new bone growth in the area. This bone is well remodeled and the foramen is completely obstructed and filled with the hypertrophic growth. The right superior articular process has a patch of eburnation on its surface with moderate lipping around the margins of the articular surface. The vertebral body has osteophytes surrounding the margins of both the superior and inferior surfaces. The right inferior transverse process has slight lipping around the margins and small patches of

eburnation across the articular surface. The inferior surface of the body appears slightly compressed and is pitted. There is also the right side of a cervical fragment which shows compression of the body and osteophytes present along the margins of both the inferior and superior surfaces. There is lipping on the right superior transverse process with patches of eburnation present on the articular surface. The inferior transverse process was broken postmortem. On what appears to be C7, there is slight lipping on the right side of the superior surface of the body with a patch of eburnation on the right superior transverse process.

There is compression of the left side of the body of L1, extending to the midline. There is also lipping on the margins of both superior and inferior articular processes.

Only the left half of the mandible is present with three teeth *in situ*: left lower canine, 1st premolar and 1st molar. The 2nd lower left molar was lost antemortem. All remaining teeth were heavily covered with calculus.

3.7 The Lytic Changes

3.7.1 SCL38-6

The pathological lesion is located on what appears to be L5. There is only partial preservation of the body of this vertebra . The lesion is located on the superior surface of the vertebra body. The body itself is badly damaged postmortem but the dimensions of the lesion appear to be ~12.9 mm in width and ~17.5 mm in length. The lesion is situated towards the anterior surface of the superior body on the right side and extends deeply into the trabecular bone, giving it a hollowed out, scalloped appearance. The lesion is completely lytic in nature with no sign of reactive bone or remodeling (i.e., the external

edges of the lesion are sharp). There are also two sinus openings extending from the lesion and perforating the wall of the vertebral body. Both are located near the upper margin of the anterior body and to the right side of the midline. The two sinuses are situated next to one another. The first, on the lateral side, is 6.5 mm in width and 8.5 mm in length. The edges are rounded and remodeled. The second sinus is 7.2 mm in width and 7.9 mm in length. Its edges are also rounded and remodeled.

There is the presence of moderate new bone growth around the body and the presence of a moderately sized osteophyte descending from the right hand side of the body past the inferior margin. The new bone is rough, porous and fairly disorganized. There is little to no remodeling of the hypertrophic growth surrounding the body. The hypertrophic bone is coarse woven in appearance and is rough to the touch.

3.7.2 SCL38-33

The pathological lesions affect T12 and L1. On T12 the main lesion is located in the center of the inferior surface of the body of the vertebrae. The lesion is 20.8 mm in width and 20.5 mm in length. Most of the surface and interior of the body has been resorbed due to the lesion. The exposed trabecular bone is scalloped in appearance and has perforated the vertebra on the posterior surface of the body. There is no sign of remodeling of the edges of the lesion although there is the presence of hypertropic bone growth on the lower right and left side margins of the inferior body surface. The new bone is rough and porous in appearance. The osteophyte on the right side is larger and the bone is more porous than that of the left side. Growth of new bone on both sides extends inferiorly towards L1. There is another, smaller lesion located on this element. This lytic

lesion is located on the left superior articular process near the margin of the articular surface on the right side. The lesion is 2.5 mm in width and 1.3 mm in length. The lesion is associated with some porous, reactive bone around the margins of the lesion but with no signs of remodeling or appreciable healing.

On L1 the lytic lesion is located in the center of the superior surface of the vertebral body. Most of the body and the interior of the body have been resorbed, leaving the vertebral body hollowed out with exposed trabeculae scalloped in appearance. The lesion measures 26.2 mm in width and ~19.0 mm in length. The approximate measurement of length reflects the fact that the posterior aspect of the vertebral body has been resorbed, and thus it is not definite where the lesion ended. There are also three sinus openings perforating the body of the vertebra.

Two sinuses are located near the superior margin of the body. Both sinus openings are perfectly circular and the edges are somewhat rounded and remodeled. The first is on the right side and is 7.9 mm in width and 8.7 mm in length. There is a rough patch of porous bone growth on the side of the body in this area. The growth is quite severe and covers most of the wall of the body on the right side next to the sinus opening and has spread to a small degree around the sinus. The second sinus opening is more to the left side of the body. The defect is 5.8 mm in width and 6.4 mm in length. It is smaller than the other sinus cavity. There is also new bone growth on this side of the body. The growth is most severe at the uppermost margin of the left superior body surface but becomes smoother as it extends down the side of the vertebra.

The third sinus is located in the middle of the anterior surface of the body, to the right of the midline. The sinus is 3.8 mm in width and 4.3 mm in length. The edges of the

cavity are rounded and there is new bone growth encircling both the right and left sides. The new bone growth adjacent to and surrounding the sinuses covers practically the entirety of the body surface on both sides, but is more severe on the right side. The hypertrophic growth on L1 corresponds to the new growth seen on T12.

3.7.3 SCL38-62

The pathological lesions encompass T12-L2. Only the dorsal aspects of the vertebrae remain. The bodies of all the involved vertebrae have been completely destroyed leaving only the spinous processes and associated articular processes intact. The spinous processes of all the affected vertebrae are also eroded. Only one third of the original length of the spinous processes remain intact. The edges of the spinous processes are well rounded and remodeled. There is no evidence of periosteal bone growth around the remainder of the spinous processes. Both transverse processes of T12 have been eroded away. What remains is a small nub of bone a few millimeters in length protruding from the pedicle. The edges of the remains of the transverse processes are remodeled. The edges are smooth and rounded. The transverse processes of L1-L2 do not appear to have undergone any erosive destruction. The remaining dorsal portions of these elements are fused together though the production of a large amount of hypertrophic bone growth due to the inflammatory reaction occurring in the area. Reactive new bone formation is rampant, the remaining aspects of the vertebrae are all encased within the new bone growth, as if set in plaster. The reactive bone is coarse and extremely disorganized. There is no appreciable remodeling of the new bone around the affected elements. However, the superior and inferior articular processes are not fused to one another. While

the remainder of the dorsal elements of the three vertebrae are immobilized within the hypertrophic bone matrix, there is no fusion of the joints between the vertebrae.

3.7.4 SCL38-107

The pathological lesion is located on the inferior surface of the body of L4 on the right side margin. The lesion is 15.4 mm in length and 9.6 mm in width. The lesion is completely lytic in nature with no signs of healing or remodeling. There is no reactive bone growth near or around the lesion. The exposed trabecular bone appears scalloped away with only the slightest shell of the cortex remaining on the right margin delineating the lesion. The scalloping of the trabecular bone gives the internal surface of the lesion the appearance of having been scooped out repeatedly. The corresponding area on L5 has been damaged post-mortem; therefore it is not possible to determine if the lesion was localized to only L4 or had spread.

3.7.5 SCL38-109

The pathological lesions affect T6 and T7. In T6 the lytic lesion is 4.58 mm in diameter with smooth edges. The lesion is located near the end of the spinous process and covers approximately one-third of the spinous process from the end. The inferior third of the spinous process is covered by hypertrophic growth. The hypertrophic growth is somewhat porous but has been fairly well remodeled and the edges are smooth. There is a perforation of the cortical bone at the tip of the spinous process which extends into the spinous process. There is also a second lesion on the inferior dorsal aspect of the left inferior articular facet. It is a small perforation extending into the trabecular bone. There

is no new bone growth around the lesion, although there is some porous reaction of the cortical bone around the lesion.

The lesion on T7 is located on the superior dorsal aspect of the vertebra directly below the right superior articular facet and extends onto the right transverse process. The edges of the lesion are smooth and thickened in certain areas. The lytic cavity extends into the right transverse process and is continuous with two sinus cavities. The first sinus cavity perforates the right transverse process directly distal to the articular facet . The edges of the sinus are sharp. The second sinus is located inferior to the first sinus opening. The edges of this sinus are somewhat rounded. The lytic lesion also extends beyond the midline of the spinous process. There is some reactive bone around the left side of the lesion but very little elsewhere. The extra bone growth in that area has been remodeled extensively. It is smooth and only slightly porous. To the left of the spinous process, just past the midline, there are two sinus openings. Both are almost directly on the midline and show no signs of healing, although the edges are somewhat rounded. The lesion has almost perforated though the anterior wall of the neural arch between the two inferior articular facets. There is only a thin layer of cortical bone remaining. Pinpricks of light can be seen though the bone where the cortex has been eroded away. The remaining cortical bone resembles lace in appearance. The lesion on T6 corresponds to the lesion on T7. It appears that the infectious process started in T7, as evidenced by the large lytic lesions and draining sinuses. The location of the lesion on T7 conforms well to the site of infection on T6, thus inferring that the infectious process from T7 spread from T7 up to the spinous process of T6.

3.7.6 SCL38-229

The pathological lesion is located on the right transverse process of T12. The process has been expanded and ballooned along the cortex, but the trabecular bone has mostly been resorbed leaving an expanded cortical shell. There is very little reactive bone in the area. The margins of the lesion are smooth and the internal surface of the lesion is smooth as well. The lesion is completely lytic in nature with no clear sign of healing. The lesion extends from the right transverse process to almost the midline of the vertebra right immediately adjacent to the right interior articular facet. The lesion encompasses more or less the entire transverse process. The area affected is ~29.5 mm across. The original bone remaining in the area has a woven, lacy appearance due to the erosion of trabecular bone. There is expansion of cortex along with the lack of new bone growth.

4. Differential Diagnosis

The purpose of this section is to provide a complete listing and review of all possible disorders and conditions which may cause the production of lytic lesions in the spine. The material is organized as follows: outline of possible conditions inducing lytic lesions of the spine; discussion of conditions unlikely to have caused the lesions seen at SCL-38 and why these conditions should not be given as much consideration in the final diagnosis; and a detailed discussion of the most likely causes of the vertebral lytic lesions seen in this population.

CONDITIONS CAPABLE OF PRODUCING LYTIC LESIONS IN THE SPINE

I. Neoplastic Disease
    A. Benign Tumors
        1. Aggressive Osteoblastoma
        2. Aneurysmal Bone Cyst
        3. Benign fibrous Histocytoma
        4. Chondroblastoma
        5. Chondromyxoid fibroma
        6. Cystic Angiomatosis
        7. Desmoplatic Fibroma
        8. Giant Cell Tumor
        9. Hemangioma of Bone
        10. Reparative Giant Cell Granuloma
    B. Malignant Tumors (Primary)
        1. Chordoma
        2. Clear Cell Chondrosarcoma
        3. Conventional Chondrosarcoma
        4. Conventional Osteosarcoma
        5. Ewing's Sarcoma
        6. Fibrosarcoma
        7. Langerhans Cell Histocytosis
            a. Eosinophilic Granuloma
        8. Hodgkin's Disease
        9. Non-Hodgkin's Lymphoma
        10. Lymphoma
            a. Multiple myeloma

b. Solitary myeloma

C. Metastastic Carcinomas
1. Breast
2. Gastrointestinal
3. Lung
4. Pancreas
5. Prostate
6. Renal
7. Thyroid

II. *Mycobacterium*
A. *Mycobacterium tuberculosis* complex
1. *Mycobacterium bovis*
2. *Mycobacterium tuberculosis*
B. Atypical *Mycobacterium*
1. *Mycobacterium avium* complex
a. *Mycobacterium avium*
b. *Mycobacterium intracellulae*
c. *Mycobacterium scrofulaceum*
2. *Mycobacterium chelonei*
3. *Mycobacterium fortuitum*
4. *Mycobacterium kansasii*
5. *Mycobacterium marinum*
6. *Mycobacterium szulgai*
7. *Mycobacterium ulcerans*
8. *Mycobacterium xenopi*

III. Mycotic Infection
A. Blastomycosis
B. Coccidioidomycosis
C. *Aspergillus*

IV. Other Conditions
A. Actinomycosis
B. Brucellosis
C. Brown tumor of Hyperparathyrodism
D. Gorman's Disease of the Spine
E. Osteomyelitis (non-mycobacterial)
F. Paget's Disease
G. Rheumatoid Arthritis
H. Sarcoidosis

4.1 Neoplastic Disease: Benign Neoplasm

4.1.1 Aggressive Osteoblastoma

General Features: An aggressive osteoblastoma is a rare tumor that represents a borderline lesion between benign osteoblastoma and osteosarcoma. A benign osteoblastoma is a rare, bone forming tumor closely related to osteoid osteoma. Osteoblastomas differ from osteoid osteomas in that they have a higher growth potential and they are typically larger than 2 cm in diameter, with aggressive osteoblastomas usually exceeding 4 cm in diameter. Aggressive osteoblastomas do not metastasize, although they are likely to reoccur after intervention and are characterized microscopically by the presence of "epithelioid" osteoblasts.

Incidence and Location: The incidence and age distribution of aggressive osteoblastomas are not known exactly due to their rarity. It appears that these tumors occur in a significantly older population than conventional osteoblastoma for whom 80% of patients are between 10-30 years of age (Mirra, Picci & Gold, 1989a). In aggressive osteoblastoma the peak age incidence appears to be between the third or fourth decade of life (Dorfman, 1998). There does not appear to be any predilection for either sex, unlike conventional osteoblastoma in which the male/female ratio is 3:1 and the overall distribution pattern is similar to conventional osteoblastoma. In conventional osteoblastoma tumors have a predilection for the axial skeleton, with more than 40% of cases involving the vertebral column and sacrum (Dorfman, 1998; Mirra et al., 1989a; Coley, 1960).

Lesions Produced: The lesion produced by aggressive osteoblastoma consists of a circumscribed lytic defect sometimes surrounded by a rim of sclerosis. This is a

predominantly osteolytic condition, although reactive bone can be produced. Bone contours can be expanded. In the vertebral column and sacrum the tumor is located posteriorly within the dorsal elements of the neural arch (Dorfman, 1998). A primary tumor in the body of the vertebra is unusual. The tumor can cross joint spaces and involve adjacent bone which can then result in the production of prominent periosteal new bone formation (Dorfman, 1998). Radiologically, the osteoblastic nature of the tumor can be demonstrated by the presence of patchy cloud-like opacities.

Why this Condition is Unlikely: The lesions seen at SCL-38 are unlikely to be caused by an aggressive osteoblastoma. This is a very rare tumor, rarer than conventional osteoblastoma which represents ~0.8% of all bone tumors (Mirra et al., 1989a). The majority of lesions seen at SCL-38 are not circumscribed defects. Rather, the area of destruction is expansive and the majority of lytic lesions found are situated in the body of the vertebrae. Lesions restricted to the body of vertebrae are rare in this tumor.

4.1.2 Chondroblastoma

General features: Chondroblastoma is a rare, benign primary tumor which is characterized by a proliferation of immature cartilage cells within the epiphyseal end of long bones and predominantly occurs in skeletally immature individuals.

Incidence and Location: Chondroblastomas make up less than 1% of primary bone tumors (Dorfman, 1998; Greenspan & Remagen, 1998; Mirra et al., 1989a), with peak incidence in the second decade of life and ~50% of cases diagnosed in skeletally immature individuals (Dorfman, 1998). Males are affected more than females with a ratio of ~1.5:1, although a series reported from the AFIP (Armed Forces Institute of Pathology) indicated

that the ratio was 3:1 (Greenspan & Remagen, 1998). The majority of clinical cases involved distal femoral and proximal tibial epiphyses. Approximately 30% of cases involved the knee area, followed by the proximal humerus and proximal femur. Chondroblastomas can occur in the spine, but such involvement is considered an extreme rarity. In a Mayo Clinic series of 8,542 cases of bone tumors there were 79 cases of chondoblastoma with only 2 cases of vertebral involvement seen (Dahlin & Unni, 1986).

Lesions Produced: Radiologically, chondromblastoma generally presents as a sharply demarcated oval or round lytic defect surrounded by a ring of sclerotic bone. The lesion is small, generally 3-6 cm in diameter. Typically, the lesion is radiolucent but can, on occasion, produce fine trabeculations and sometimes irregular calcifications also can be seen.

Why this Condition is Unlikely: Chondromblastoma is considered a rare tumor and the majority of involved elements are the epiphyses of long bones. For chondroblastoma to occur in the spine is rare enough but to have occurred more than once is extremely unlikely. Also, this tumor occurs predominantly in the skeletally immature in the second decade of life which does not fit with the age and skeletal maturity of the individuals from SCL-38.

4.1.3 Chondromyxoid Fibroma

General Features: Chondromyxoid fibroma is a rare benign tumor composed of immature mesenchymal tissue with features of early primitive cartilage differentiation (Dorfman, 1998). The tumor has a predilection for the metaphyseal regions of long bones.

Incidence and Location: Chondromyxoid fibroma is a rare tumor, accounting for less than 1% of all bone tumors (Dorfman, 1998) and 0.5% of all primary bone tumors (Greenspan & Remagen, 1998). Only some 400 cases have been reported to 1985 (Mirra et al., 1989a). It is far less common than chondroblastoma. In approximately 75% of cases the lower extremities are involved (Mirra et al., 1989a). It occurs at the metaphyseal parts of the major tubular bones. Approximately one-third of cases involve the long bones around the knee, where the proximal tibial metaphysis is most frequently involved, followed by the distal femoral metaphysis. The small bones of the hands and feet are involved 25% of the time with the bones of the feet involved three times as often as the hand. The pelvis, especially the ilium, is the most frequently involved flat bone. The tumor can be found in all bones, although involvement of the bones of the upper extremity is rare. The spine is only rarely involved. There is a predilection for males over females with a ratio of ~1.5-2:1 and a preference for younger individuals under the age of 30, with majority being between 10-20 years of age (Greenspan & Remagen, 1998; Mirra et al., 1989a). In the Mayo Clinic series of 8,542 cases of bone tumors, there were 39 cases of chondromyxoid fibroma with only 1 case involving the vertebrae.

Lesions Produced: The lesions produced by chondromyxoid fibroma are usually totally lytic. Radiographically, they appear as benign-like oval, eccentric, metaphyseal lesions with long axes parallel to that of the bone (Dorfman, 1998). The tumor rarely crosses an open growth plate and does not penetrate the outer periosteal sheath. The lesion is usually defined by a well demarcated and sclerotic border. Vertebral lesions may, however, extend beyond the cortical confines of the bone and into the spinal canal.

Why this Condition is Unlikely: This is a rare condition in which the lower extremities are favored for involvement. Vertebral involvement in this condition is considered to be extremely rare, with only 1 case in 8,542 cases of bone tumors surveyed by the Mayo Clinic. Also, the peak incidence of this disease does not reflect the age brackets of the majority of afflicted individuals of SCL-38.

4.1.4 Benign Fibrous Histocytoma

General Features: This is a controversial tumor, in that there is debate over whether this is an actual benign bone neoplasm or merely a reactive lesion superimposed on a pre-existing condition (Dorfman, 1998). However, because of its atypical locations as well as unusual radiological and clinical presentations, most authors conclude that these lesions are best separated from non-ossifying fibroma of long bones, to which it is microscopically indistinguishable, and placed in its own category. Benign fibrous histiocytoma is a very rare tumor composed of fibroblast-like cells with a storiform pattern in the presence of foamy histocytes and multinucleated giant cells.

Incidence and Location: This is a very rare tumor with strict radiological and microscopic criteria (Dorfman, 1998). Affected individuals range from 5 to 75 years of age, and there does not appear to be a sex predilection, although Mirra et al. state that females are slightly selected for over males, 1.7:1 (Mirra et al., 1989a). The ilium and the ribs are the most frequently involved sites, although cases have been reported in the spine (Dorfman, 1998; Mirra et al., 1989a). Mirra et al. report three cases in the cervical vertebrae, two involving the spinous process and one in the arch of the cervical spine. In

the Mayo Clinic series of 8,542 cases of bone tumors, there were only 10 cases of fibrous histocytoma of which 1 appeared in the vertebrae (Dahlin & Unni, 1986).

Lesion Location: Radiographically, the lesion appears as a purely lytic lesion with a sharply demarcated edge which may present with a sclerotic rim and fine trabeculation. The lesion can disrupt the cortex, but is usually delineated by a thin rim of newly-formed bone (Dorfman, 1998).

Why this Condition is Unlikely: This is a very rare lesion with the ilium and ribs favored as sites of involvement. While there have been instances of vertebral involvement by this tumor, it is very uncommon. It therefore is highly improbable that all the individuals of SCL-38 were affected with this very rare tumor and, simultaneously, produced lesions in an extremely uncommon site for the tumor.

4.1.5 Desmoplastic Fibroma

General features: Desmoplastic fibroma is a rare, locally aggressive, fibroblastic tumor. It is characterized by a solitary lesion composed of differentiated myofibroblasts with abundant collagen deposition and is microscopically identical to soft tissue fibramatosis. Any bone in the skeleton can be affected, but mandibular and long bone involvement are most common.

Incidence and Location: This is a very rare tumor that accounts for less that 0.1% of all bone tumors (Dorfman, 1998). In the Mayo clinic series, desmoplastic fibroma accounted for 0.06% of all bone lesions and 0.3 % of benign bone lesions (Dahlin & Unni, 1986; Greenspan & Remagen, 1998). Lesions can appear anywhere from age 20 months to 70 years, but are most prevalent in those between 10-20 years of age. The most

characteristic site of involvement is the mental region of the mandible followed by the femur, tibia and humerus. There is no sex predilection. In the Mayo Clinic series of bone tumors, there was a total of 9 cases of desmoplastic fibroma with no cases situated in the vertebrae (Dahlin & Unni, 1986).

Lesion Location: This tumor presents a destructive growth pattern and is generally completely lytic in nature. Radiographically, the lesion has well defined margins. It is a slow growing tumor which erodes the cortex gradually, allowing the periosteum to continually lay down new bone in keeping with tumor growth. This results in the bone appearing expanded on radiographs.

Why this Condition is Unlikely: This tumor is extremely rare and its chances of occurring in five individuals in one cemetery population is extremely low. Aside from is rarity, the age of individuals which are most often affected, 10-20 years of age, are not the majority of age ranges for the individuals at SCL-38. Also, while theoretically it is possible for the tumor to affect any bone, in the Mayo Clinic series, out of 8,542 cases of cancer, with 10 cases of desmoplastic fibroma, none of the lesions were situated to the vertebrae.

4.1.6 Giant Cell Tumor

General Features: This is a benign solitary, locally aggressive tumor composed of spindled mononuclear cells and multinucleated osteoclast-like cells. The tumor frequently involves the epiphyseal regions of long bones.

Incidence and Location: This tumor accounts for ~4% (Dorfman, 1998) or 5% (Mirra et al., 1989a) of all primary bone tumors. Giant cell tumors are predominantly found in

the epiphyseal regions of long bones. In the axial skeleton the sacrum is the most common site of involvement. It is extremely rare in the vertebrae bodies. However, giant cell tumors affect the Chinese in non-western countries much more than those that live in western countries. It is estimated to account for 20% of all primary bone tumors in the Chinese population in non-western countries (Dorfman, 1998). It is not specified whether this statistic holds true for Chinese individuals living in western countries. If not, then it could be suspected that one of the causes for this tumor resides in the environment and that perhaps environment is more important that genetics in this case. Individuals affected are generally between 20-55 years of age, with the majority of cases affecting individuals between 20-40. Individuals with giant cell lesions of the vertebrae are generally younger and skeletally immature. Individuals tend to be women in their 2nd decade of life. In the Mayo Clinic series of bone tumors there were 429 cases of giant cell tumor with 16 cases in the vertebrae.

Lesion Description: Radiographically, the lesion produced by giant cell tumors are fairly characteristic and diagnostic if present in the appropriate anatomical location (Dorfman, 1998). The lesion is usually purely destructive without well defined marginal sclerosis (Greenspan & Remagen, 1998). The cortex is frequently expanded and focally destroyed. There is usually no periosteal reaction (Greenspan & Remagen, 1998). In the vertebrae, the tumor originates in the body and almost never in the posterior arch or processes.

Why this Condition is Unlikely: While not a rare tumor, it is fairly uncommon, with involvement of the vertebrae being extremely rare. The age in which individuals are most often afflicted with the tumor does match the ages of the majority of affected individuals at SCL-38, however, the ages in which the highest incidence of this tumor occurring are for

individuals who have tumors situated in typical anatomical sites. In individuals with vertebral involvement, the age of the individuals tends to be younger and still skeletally immature. Also, the tumor almost never manifests itself any part of the vertebrae except the body, which is not the case with the lesions found at SCL-38. Of the six individuals affected, three had lesions located to the body of the vertebrae, while one had a lesion located in the left transverse process and one in the spinous process.

4.1.7 Giant Cell Reparative Granuloma

General Features: This is a benign and uncommon reactive lesion, with predilection for the cranio-facial bone and the small bones of the hands and feet. It is extremely rare in the vertebrae.

Incidence and Location: The tumor tends to affect individuals between 10-25 with a peak incidence in the 2nd decade of life. Individuals with lesions of the vertebrae are generally older, the peak being in the 3rd decade of life.

Lesion Description: The lesion in the vertebrae presents as an expansile lytic lesion of the body. Expansile lesions are lesions without clearly delineated margins. The cortex of the affected bone is thin but characteristically intact, extension into the soft tissues is uncommon and periosteal reaction is usually absent (Greenspan & Remagen, 1998)

Why this Conditions is Unlikely: This is a rare tumor with an even rarer incidence of location in the vertebrae. While the majority of individuals affected at SCL-38 are within the age group which have peak incidence of this lesion in the vertebrae, the type of lesion produced by this tumor is not characteristic of the type of lesion found in the individuals of SCL-38. The lesion produced by this tumor generally does not disrupt the cortex of the

bone. It will produce lytic cavities within the bone but will not extend past the cortex and into the soft tissue. At SCL-38 all of the individuals exhibited lesions which extended past the cortical bone and would have extended into the soft tissue.

4.1.8 Hemangioma

General Features: Hemangiomas are benign solitary tumors composed of a vascular proliferation of thin walled capillary or cavernous type vessels. Hemangiomas can involve soft tissue, bone, subcutaneous tissues and skin all at the same time (Mirra, Picci & Gold, 1989b). They do not metastasize and are generally asymptomatic during life. The pathogenesis of hemangioma is that of a vascular malformation (Greenspan & Remagen, 1998).

Incidence and Location: Hemangiomas are rare lesions and account for less than 1% of all primary bone tumors (Dorfman, 1998). The tumor has a predilection for flat bones such as the skull and mandible, ~50% of cases, and ~20-30% in the spine (Dorfman, 1998; Mirra et al., 1989b). However, if asymptomatic lesions are counted, usually ascertained at autopsy, then the vertebral column is the most frequent site of involvement (Dorfman, 1998). There are no age groups exempt from this tumor; however ~70% of individuals affected are between 30-60 years of age and incidence appears to increase as age increases (Greenspan & Remagen, 1998). There is a slight predilection for females 1.6:1 (Mirra et al., 1989b). In the Mayo Clinic series there were 80 cases of hemaginoma with 20 cases located to the vertebral column.

Lesion Description: Involvement of the bodies of the lower thoracic and lumbar regions is typical. Lesions generally involve the body of the vertebrae but can extend to the lamina

and, rarely, to the spinous process (Greenspan & Remagen, 1998). Multiple vertebrae can be affected. Radiographically, the vertebrae in affected areas have thickened vertical trabeculae, giving the trabecular bone the appearance of corduroy, with thickened horizontal trabeculae. Lesions are lytic and the cortex is eroded. The vertebral body is not enlarged generally, although large lesions can expand the contour of the vertebrae. It is possible for multiple bone involvement to occur.

Why this Conditions is Unlikely: This is a lesion which tends to do little damage. The proliferating vessels can intrude into bone and expand the element and erode the cortex . However, hemanigomas do not usually present lesions as destructive as those seen in SCL-38. In SCL-38-6, 33 and 62, there is cavitiation of the body of the vertebrae, and for SCL-38-62 there is complete destruction of the bodies of three affected vertebrae.

4.1.9 Cystic Angiomatosis

General Features: This is a very rare condition characterized by multiple disseminated hemagiomas in the skeleton. The condition may be congenital.

Incidence and Location: Individuals affected are usually within the first three decades of life (Greenspan & Remagen, 1998). There is a 2:1 predilection for males (Greenspan & Remagen, 1998). A few to many bones may be involved. The disorder has a predilection for the trunk bones and sometimes cranial bones.

Lesion Description: Radiographically the lesions are lytic, often with a honeycomb or lattice-work appearance (Greenspan & Remagen, 1998). Lesions are well defined and periosteal reaction can occur. Lesions also tend to spontaneously heal or regress. The skeletal lesions are stable

Why this Condition is Unlikely: This is a very rare condition and unlike conventional hemaginomas do not have a predilection for the vertebrae, but rather the bones of the trunk and crania. The lesions produced by this tumor are not consistent with the lesions found in the individuals at SCL-38. Radiographically, the SCL-38 individuals do not have a "honeycomb" appearance to the vertebrae. The lesions are not well defined nor are they stable. At SCL-38 most of the lesions were active at the time of death of the individuals and were probably expanding further into the spinal column.

4.2 Neoplastic Disease: Malignant Neoplasms

4.2.1 Ewing's Sarcoma

General Features: Ewing's sarcoma is a highly malignant round cell sarcoma. The tumor is mainly composed of undifferentiated, round mesenchymal cells containing glycogen and exhibit a karyotypic abnormality represented by a reciprocal translocation, t(11;22)(q24;q12). This chromosomal abnormality can be documented in ~90% of tumors classified as Ewing's sarcoma (Dorfman, 1998).

Incidence and Location: Ewing's sarcoma has a predilection for the long bones of skeletally immature individuals. After major long bones, ribs and pelvis are the next favored regions. This tumor accounts for 6-8% of all primary malignant tumors of bone (Dorfman, 1998; Greenspan & Remagen, 1998; Mirra et al., 1989b). Most individuals affected are between 10-25 years. ~80% of individuals are under 20 and 50% are affected in the 2nd decade of life (Dorfman, 1998). There is a slight predilection for males, 1.4:1 (Dorfman, 1998; Mirra et al., 1989b), and any bone in the body can be affected. Ewing's sarcoma rarely affects individuals of African descent (Dorfman, 1998; Greenspan &

Remagen, 1998). In the Mayo Clinic series there were 402 cases of Ewing's sarcoma with 12 cases presenting in the vertebrae.

Lesion Description: The lesion presents radiographically as a poorly defined destructive intramedullary lesion of the diaphysis in long bones. Lesions often appear moth eaten and are permeative. The lesion is often accompanied by a prominent multi-layer periosteal reaction. The sunburst type of periosteal new bone reaction can also be present, but less commonly. In about 50% of cases there is the presence of periosteal bone reaction (Mirra et al., 1989b). Lesions can be lytic, mixed lytic/blastic and rarely, predominantly blastic.

Why this Condition is Unlikely: Ewing's sarcoma is generally a disease of children. While theoretically it can affect any bone in the body, it tends to be limited to the long bones, ribs and pelvis. Cases of spinal involvement in Ewing's sarcoma are rare. Lesions produced by Ewing's sarcoma are generally accompanied by a prominent periosteal reaction. While purely lytic lesions do occur, they are not as common as mixed lytic/blastic lesions. Ewing's sarcoma is unlikely to be the disease process leading to the production of the lesions at SCL-38 because the age of individuals affected at SCL-38 is not consistent with the age of individuals affected in the majority of Ewing's sarcoma cases. Also, the lesions produced by Ewing's sarcoma do not match with the lesions found at SCL-38.

4.2.2 Malignant Fibrous Histocytoma

General Features: Malignant fibrous histocytoma arises from meschencymal tissue or a non-hematopoietically derived histocyte with fibroblast potential (Mirra et al., 1989b).

Incidence and Location: This is a relatively rare tumor and makes up less than 2% of all primary malignant bone tumors (Dorfman, 1998). Any bone in the body can be affected. The tumor has a predilection for the metaphysis of long bones and the pelvis. The frequency of the tumor increases with age with the peak incidence occurring in individuals over 50 years old. In the Mayo Clinic series there was no differentiation between the benign fibrous histocytoma and the malignant fibrous histocytoma. The total number of cases out of 8,542 was 10.

Lesion Description: Radiographically, the lesion presents as a purely lytic and poorly defined lesion. There is typically little to no periosteal bone growth associated with the tumor. The pattern of destruction is geographic. Geographic bone destruction is characterized by a uniformly affected area within sharply defined borders.

Why this Condition is Unlikely: This is a very rare tumor as evidenced by the incidence of any type of fibrous histocytoma, either benign or malignant, in the Mayo Clinic series. While the lytic lesions produced by this tumor could easily describe the lesions seen at SCL-38, this tumor is unlikely to be the cause of the lytic lesions seen at SCL-38 for a number of reasons. The first is that this tumor is extremely rare. While theoretically any bone can be affected, the tumor has a predilection for the long bones and pelvis and even in the case of vertebral involvement, it is highly unlikely for more than one case to occur. This tumor is a tumor of the elderly with the majority of cases occurring in individuals over 50. The majority of individuals at SCL-38 were not of this age range at the time of death.

4.2.3 Multiple Myeloma

General Features: Multiple myeloma results from a neoplastic proliferation of plasma cells. It is the most common form of myeloma and most frequent malignant neoplasm presenting skeletal lesions. It is the most common neoplasm of bone and accounts for 27% of biopsied tumors (Greenspan & Remagen, 1998). The most common genetic abnormality seen in multiple myeloma are alterations in chromosomes 1, 11, and 14, with a translocation between 11 and 14 being the dominant type of abnormality.

Incidence and Location: The skull, vertebral bodies, pelvis and proximal parts of the major longs bones are most often affected. However, the tumor can localize to any part of the skeleton that contains red marrow. The majority of individuals affected are men. ~70% (Mirra et al., 1989b) and more that 90% of cases are in individuals older than 40 years of age (Dorfman, 1998). In the Mayo Clinic series, 2,932 cases of myeloma of bone were seen. Of these 556 were surgical cases of which 181 involved the vertebrae (Dahlin & Unni, 1986).

Lesion Description: Radiographically, the earliest changes are seen in the vertebrae, skull and ribs. The lesions are characterized by sharply punched out lesions that are multifoci, sharply demarcated and extremely lytic. Cortical erosion is frequently seen and periosteal bone formation is not present. In the spine, multiple myeloma may present simply as osteoporosis with no identifiable lesions. More common is the presence of numerous lytic lesions scattered throughout the vertebral column. Multiple compression fractures may be seen.

Why this Condition is Unlikely: Multiple myeloma is an extremely common tumor. According to Greenspan and Remagen (1998), it is the most common primary tumor of

bone. While the disease does have certain characteristics which could account for the lytic lesions seen at SCL-38, it is probably not the cause of the lytic lesions found at SCL-38. While multiple myeloma does favor spinal involvement and the lesions described in multiple myeloma can characterize the lesions seen at SCL-38, the majority of individual affected at SCL-38 do not fall into the age bracket of those most often affected by multiple myeloma. More important, multiple myeloma is characterized by the presence of many discrete lytic lesions scattered through out the skeletal region of involvement. The lesions seen at SCL-38, with the exception of SCL-38-62, are either single lesions on a single element or a single lesion seen on two contiguous elements due to progression of the disease. The only exception is SCL-38-62, in which the disease process has destroyed the bodies of three contiguous vertebrae, with the remaining dorsal elements having fused. The manner of destruction of the vertebral bodies in this individual is not characteristic of the discrete lytic lesions seen in multiple myeloma.

4.2.4 Non-Hodgkin's Lymphoma

General Features: This tumor is a primary lymphoma of bone that presents as an osseous mass. Its cliniopathological form is microscopically identical to its soft tissue counterpart.

Incidence and Location: This is a rare tumor and accounts for less than 0.2% of biopsy analyzed primary bone tumors (Mirra et al., 1989b). Individuals of all ages can be affected, but 50% of primary lymphomas occur in patients older than 40 (Dorfman, 1998). The femur and the pelvis are most frequently affected, accounting for ~20% of cases. The

vertebrae and humerus are next in frequency, ~10% each. There is a slight predilection for males, ~1.2-1.6:1 (Dorfman, 1998; Mirra et al., 1989b).

Lesions Description: Lesions typically present as lytic lesions with a permeative or moth eaten appearance. The cortex is frequently disrupted and prominent periosteal bone formation can be present. Lesions are generally lytic, but in certain cases bone sclerosis is present and the lesion is presented as a blastic lesion (Dorfman, 1998).

Why this Condition is Unlikely: This is an extremely rare tumor and while it has a tendency to be situated in the vertebrae it is unlikely to have occurred in all six individuals at SCL-38.

4.2.5 Hodgkin's Disease

General Features: Hodgkin's lymphoma is a malignant tumor of the lymph nodes and constitutes ~50% of malignant lymphomas. Bone involvement in Hodgkin's disease is relatively frequent (Dorfman, 1998). Bone involvement can occur early or late in the disease.

Incidence and Location: Hodgkin's disease has a predilection for the trunk bones, especially the vertebral bodies of the lower thoracic and lumbar. The pelvis, ribs and long bones are also frequently involved. Individuals affected are of all ages, but the peak incidence is 20-29 years. Males are more commonly affected than females and whites more often than blacks (Greenspan & Remagen, 1998). In children boys are affect 5:1 over girls (Dorfman, 1998).

Lesion Description: Bone lesions in Hodgkin's disease are generally multiple. The lesions can be lytic, blastic or mixed. All three forms can appear in the same individual.

The mixed lytic/blastic lesion is the most common of the three, ~58% (Mirra et al., 1989b). Periosteal new bone formation is often seen, although it is not prominent.

Why this Condition is Unlikely: The type of lesions seen at SCL-38 is not characteristic of the lesions seen in Hodgkin's disease. In Hodgkin's disease there are multiple lesions present in one individual. The type of lesion is generally a mixed lytic/blastic lesion. At SCL-38, affected individuals, with the exception of SCL-38-62, have either one lesion on one element or one lesion which has spread to the adjacent element.

4.2.6 Langerhans Cell Histiocytosis

This term replaces the term histiocytosis X and encompasses eosinophilic granuloma and two other clinical syndromes: Hand-Schiller-Christian disease and Letterer-Siwe disease. All these diseases are similar in that the proliferating cells have structural and functional features of Langerhans cells. How they differ is by their proliferation properties. For this discussion only eosinophilic granuloma will be discussed. Typically, only very young children in the first, second or third year of life are affected by the other two syndromes and are not relevant to this discussion.

4.2.6.1 Eosinophilic Granuloma

General Features: Eosinophilic granuloma produces solitary lytic lesions that are sharply demarcated with a punched out appearance. Eighty percent of affected individuals are under 30, with 50% of those individuals under 10. There is a predominance of males to females, a 2:1 ratio. Craniofacial bones are most frequently affected, with vertebrae, ribs, pelvis and femur commonly affected as well. In the vertebrae, the lesion involves the

vertebral body, frequently causing collapse. There is generally little to no periosteal bone formation.

Why this Condition is Unlikely: Eosinophilic granuloma is generally a disease of children and it is unlikely that all of the individuals at SCL-38, who were all adults at the time of death, were afflicted by this tumor. Also, the vertebral lesions produced by this tumor are located in the body of the vertebrae, not the posterior elements. At SCL-38 there are two individuals which have involvement of posterior elements only. This fact, in combination with the age of the individuals affected, reduce the possibility that eosinophilic granuloma is the agent which produced the lytic lesions seen at SCL-38.

4.2.7 Conventional Osteosarcoma

General Features: Dorfman (1998) and Mirra et al. (1989b) consider osteosarcoma to be the most common of primary malignant bone tumors, while Greenspan and Remagen (1998) consider it to be the second most common. Either way, osteosarcoma is one of the most common primary bone tumors. The tumor is composed of malignant mesenchymal tumor cells that have the ability to produce osteoid or immature bone. It is the tumor cells themselves that produce the osseous material, the newly produced bone is not reactive or metaplastic. The tumor is osteoblastic in nature. Bone production can occur throughout the tumor or it can be minimal. However, osteosarcoma is generally a tumor that is considered to be bone forming.

Incidence and Location: Osteosarcoma represents ~20-22% of all primary sarcomas of bone (Dorfman, 1998; Greenspan & Remagen, 1998; Mirra et al., 1989b). It can affect any bone, although it has a predilection for the knee, humerus, femur, pelvis and skull

bones. It is rare in the spine, ribs and phalanges. There are two major peaks of incidence for osteosarcoma. The first peak occurs during the 2nd decade of life and the 2nd peak occurs after the age of 50. Males are more likely to be affected, 1.3-1.6:1 (Dorfman, 1998). Ninety percent of osteosarcomas arise in the metaphseal, 9% in the diaphysis and 1% are epiphyseal in origin (Mirra et al., 1989b). In individuals over 60 osteosarcoma tends to present in the flat bones and vertebrae (Dorfman, 1998). In the Mayo Clinic series of bone tumors there were 1,274 cases of osteosarcoma with 25 cases located in the vertebrae.

Lesion Description: Osteosarcomas are very rare in the vertebral column, with the majority of such lesions arising from secondary osteosarcoma due to Paget's disease or radiation therapy (Dorfman, 1998). The sacrum is most frequently involved. In the vertebral column, the body of the vertebra is typically involved. The lesions present as a mixed osteolytic/osteoblastic mass which grows from the body into the spinal canal and paraspinal soft tissue (Dorfman, 1998). Osteosarcoma appears in the lower thoracic/lumbar regions most often.

Why this Condition is Unlikely: While osteosarcoma is a common bone tumor, it is unlikely to be the cause of the lytic lesions from SCL-38. This is because osteosarcomas are generally considered bone forming tumors and, even when lytic lesions are produced, it is most often a mixed lytic/blastic reaction. The lesions found at SCL-38 are all lytic with no new bone formation and, at most, some periosteal reaction. Osteosarcomas are also very rare in the vertebrae and when they do arise, it is frequently in the body of the vertebrae.

4.2.8 Conventional Chondrosarcoma

General Features: Chrondrosarcoma is the third most frequent primary malignant tumor of bone. This neoplasm is a tumor of cartilage in which the matrix is uniformly and entirely chrondroid in nature (Dorfman, 1998).

Incidence and Location: The tumor has a predilection for the ribs, sternum, scapula, humerus, pelvis and femur. It is relatively rare in the vertebrae and sacrum, ~5% (Dorfman, 1998). The incidence of individuals affected is age related, with the incidence increasing with age and peaking in individuals over 50. It is twice as common in men as in women (Greenspan & Remagen, 1998). In the Mayo Clinic series there were 545 cases of primary chondrosarcoma with 46 cases located to the vertebrae.

Lesion Location: In the vertebrae the lesion tends to arise in the vertebral bodies and extend into the soft tissue and spinal canal. The tumor prefers the lower thoracic/lumbar region of the spine and the sacrum. Radiographically, the lesion shows the presence of discrete calcified opacities with the level of mineralization in the lesion varying from lesion to lesion. Lesions can be either completely lytic or heavily calcified. Usually it is a mix of both.

Why this Condition is Unlikely: Chondrosacroma is unlikely to have been the cause of the lytic lesions seen at SCL-38. While this tumor is a common sarcoma it rarely appears in the vertebra and tends to occur in older individuals. The individuals of SCL-38 did not fit into the age categories in which the tumor appears most commonly. Also, the most common form of lesion produced by this tumor is a mixed lytic lesion with heavy deposits of calcified tissue. Lesions that are purely lytic are rare.

4.2.9 Clear Cell Chrondrosarcoma

General Features: This is a low grade, malignant, cartilaginous tumor in which the tumor cells possess a great deal of glycogen. This tumor's hallmark is that it mimics osteoblastomas (Dorfman, 1998).

Incidence and Location: Clear cell chondrosarcomas are rare tumors which account for 2% of all chondrosarcomas (Greenspan & Remagen, 1998). Mirra et al. (1989a) states that it is found in approximately 0.2% of all biopsy-analyzed primary bone tumors. The tumor has a predilection for the ends of long bones and the articular cartilage. All other skeletal elements are affected sporadically. Individuals affected can range from 14-85 years of age (Mirra et al., 1989a); however the peak incidence is between 20-40 years of age (Dorfman, 1998). There is a clear male preference of 2.4:1 (Dorfman, 1998). In the Mayo Clinic series there were 545 cases of primary chondrosarcoma, 12 were of the clear cell type. None of the affected individuals had vertebra involved.

Lesion Description: The lesions produced by clear cell chondrosarcoma are generally lytic and resemble the lesions produced by osteoblastoma. The lesion is sharply demarcated with sclerotic margins. This is a slow growing neoplasm and as a result may expand the contours of the bone.

Why this Condition is Unlikely: This is a very rare tumor which does not occur in vertebrae, except sporadically. It is unlikely that all six individuals at SCL-38 could have been afflicted by such a rare tumor, as well as afflicted in an extremely uncommon element, thus making a diagnosis of clear cell chondrosarcoma all the more improbable.

4.2.10 Fibrosarcoma

General Features: Fibrosarcoma is a fibroblastic malignancy composed of spindle cells that exhibit myofibroblastic differentiation. It does not produce bone or cartilage.

Incidence and Location: The frequency of this tumor is not well known given the different criteria used to establish diagnosis. Mirra et al. (1989a) stated that it was seen in 3-5% of all biopsy analyzed bone tumors. Dorfman in 1998 declined to state an incidence due to the problem involved in establishing a diagnosis. The skeletal distribution of this tumor is similar to that of osteosarcoma; the distal femur and proximal tibia are most often affected, but any bone can be involved. The peak incidence appears to be between the third and sixth decade (Greenspan & Remagen, 1998). Individuals 50 and older are most often affected. Males and females are equally affected. In the Mayo Clinic series there were 207 cases of fibrosarcoma with 7 cases located to the vertebrae.

Lesion Description: The lesion is completely lytic with ill defined margins and widespread destruction. There may be the formation of periosteal new bone, although it is rare. There is generally little to no reactive sclerosis. Lesions can disrupt the cortex and spread into the soft tissue.

Why this is Unlikely: While the characteristics of this tumor are similar to the lesions seen at SCL-38 it is not a likely candidate. This is an uncommon tumor which is rarely located to the vertebrae. It affects mostly older individuals, 50 years and above. Therefore, because it is uncommon, rarely located to the vertebrae and affects older individuals, the chances of it being the cause of the lytic lesions seen at SCL-38 are unlikely. Also, the lytic lesions seen at SCL-38 have well defined-margins and in all cases the cortex of the bone is disrupted.

4.2.11 Chordoma

General Features: This is a slow growing neoplasm and accounts for 3-4% of primary malignant bone tumors (Dorfman, 1998). The cells exhibit notochordal differentiation and are derived from notochordal remnants.

Incidence and Location: It is the fourth most common primary malignant tumor of bone. It is most common in the sacrococcygeal and sphenococcipital regions, ~90% of cases (Dorfman, 1998). The remaining cases are reported in the cervical and lumbar vertebrae. C2 is most often affected (Greenspan & Remagen, 1998). Thoracic vertebra are rarely affected. This tumor can affect individuals of any age, but its incidence increases as age progresses and peaks in the 5th and 6th decade of life. Males are affected twice as frequently as females (Dahlin & Unni, 1986). Like Ewing's sarcoma, it is almost never seen in individuals of African descent. In the Mayo Clinic series there were 262 cases of chordoma, of which 32 cases were located to the vertebrae.

Lesion Description: This lesion is a locally aggressive lesion. Radiographically, the tumor presents as an expansive lytic lesion with irregular scalloped borders. In the vertebrae the tumor produces lytic lesions that involve two or more adjacent vertebral bodies. Lesions in the vertebrae originate in the vertebral body and progress anteriorly.

Why this Condition is Unlikely: While chordomas are a common tumor of bone and are specifically located to the vertebrae, they does not fit the with the pattern of involvement seen at SCL-38. At SCL-38 the major assumption made is that all the lytic lesions seen in the six individuals are the result of the same disease process, no matter what that may be. For the diagnosis of chordoma to be accepted, all the lytic lesions found in the vertebrae must arise in the body and progress from that point of origin. This is not the case at SCL-

38. In two of the affected individuals at SCL-38, the vertebral lytic lesions arise in the posterior structures of the vertebrae. In one individual, SCL-109, it is the spinous process which is affected and in the other, SCL-229, it is the transverse process. Given the definition of chordoma, a tumor of notochordal remnants, it is therefore impossible to consider this tumor a possible cause of the lytic lesions found at SCL-38.

4.3 Benign Neoplasms Possibly Causing Lytic Lesions

4.3.1 Aneurysmal Bone Cyst

General Features: This is a benign lesion characterized by the presence of spongy or fibrous cystic tissue filled with blood. It is locally destructive and has a high propensity for reoccurrence.

Incidence and Location: Dorfman considers this a relatively rare lesion, ~2.5 % of all primary bone lesions, although Greenspan and Remagen state the incidence to be ~6% of primary bone lesions. It can affect any bone in the skeleton with equal frequency, although it has a slight predilection for the metaphysis of long bones, scapula and the vertebrae. The majority of individuals affected are under 20 years of age, with the peak incidence in the 2nd decade of life. In the Mayo Clinic series there were 208 cases of aneurysmal bone cysts reported with 32 cases located in the vertebrae.

Lesion Description: Radiographically, the lesion is characteristically distinctive. The periosteum is ballooned out and outlined by a thin shell of subperiosteal bone. The ballooned area overlies an area of cortical disruption. The lesion is lytic. In the vertebrae it tends to originate in the posterior neural arch and expands unilaterally but the vertebral

body may be affected. The lesion can cross joint spaces and involve several different adjacent elements.

Why this Condition is Possible: Depending on the source, the frequency of aneurysmal bone cysts tends to vary from either 2% to 6%. Nevertheless it is not a particularly common tumor but can be considered as a possible candidate as the cause of the lytic lesions seen at SCL-38. This tumor is considered to be a possible candidate, even though it is uncommon, because it does tends to occur in vertebrae, can affect any vertebral element equally and produce the type of lesions seen at SCL-38.

4.4 Malignant Neoplasms Possibly Causing Lytic Lesions

4.4.1 Solitary Myeloma

General Features: Solitary myeloma is a rare, localized form of plasma cell proliferation (Dorfman, 1998). It produces a single, destructive lytic lesion. It is considered to be a clinical variant of multiple myeloma, representing an early stage of the disease.

Incidence and Location: Solitary myelomas most often affect the vertebral bodies, with other typical sites of involvement being the pelvis, femur and humerus. Approximately 70% of solitary lesion progress within the first 3 years of diagnosis to becoming multifocal; however, there can be a latency period of 5-10 years or longer before the lesion becomes multifocal (Dahlin & Unni, 1986). The age of individuals affected is the same as multiple myeloma, with the peak incidence being in individuals older than 50. There is a predilection for males with a ratio of 2:1.

Lesion Description: The lesion presents as a single lytic, destructive lesion with little to no blastic reaction. The margins of the lesion range from sharp to moth-eaten and the cortex of the bone may be disrupted or destroyed.

Why this Condition is Possible: Solitary myelomas are a possible candidate as the cause of the lesions seen at SCL-38, despite the fact that they are rare tumors. While solitary myelomas are rare, they also affect the vertebra most often. The lesions produced by this tumor also resemble those seen at SCL-38. The lesions from SCL-38 are all lytic in nature with little to no blastic reaction. The margins of several lesions are sharp and the cortex of the bone is destroyed. All of these characteristics are commonly produced by solitary myelomas.

4.5 Neoplastic Disease: Metastatic Tumors in Bone

4.5.1 Carcinoma of the Breast

In women, breast cancer, is rarely seen before the age of 25, except in familial cases. Breast carcinomas have a high propensity for metastasizing to bone, appearing in 35-45% of advanced cases (Coley, 1960). The lesions occur in the typical skeletal sites: the vertebrae, pelvis, proximal femur and humerus (Dorfman, 1998). This tumor generally produces osteolytic lesions but can produce lesions of mixed type; less often they are purely blastic. Carcinoma in the male breast is rare with a frequency ratio to breast cancer in the female of less that 1:100 (Cotra, Kumar & Collins, 1999). Dissemination of the tumor follows the same pattern as in females.

Why this Condition is Unlikely: It is unlikely that this tumor is the cause of the lytic lesions seen in the individuals at SCL-38. While breast carcinoma tends to metastasize to

bone, specifically the vertebrae, it is not a common carcinoma seen in males. According to statistics from the American Cancer Society for 1999, ~1,300 new cases of breast cancer in males will be diagnosed and ~175,000 new cases will be diagnosed in females. The number of deaths estimated due to breast cancer in males is 400 individuals and in females, 43,300 individuals. While breast carcinoma in males does occur, it is a very rare occurrence and given that four of the six individuals afflicted at SCL-38 were male, is not very likely that they were all afflicted by a rare form of carcinoma. Also, the age of individuals generally afflicted with breast carcinoma is older, with the exception of those with the familial form of the disease. The oldest individual afflicted from SCL-38 was estimated to be 35-45 years old at the time of death. Therefore, the ages of the individuals afflicted also does not correspond well to a diagnosis of breast carcinoma.

4.5.2 Gastric Carcinoma

Gastric carcinoma is a worldwide disease with high incidences in countries such as Japan, Chile, China, Portugal and Russia. It is four-fold to six-fold less common in the United States, United Kingdom, Canada, Australia and France (Cotra et al., 1999). It is a disease of older individuals, generally 50 and above. Diet is the primary offender in cases of gastric cancer. Diets high in preservatives such as N-nitroso compounds and benzopyrne appear to be important (Cotra et al., 1999). Lack of fresh fruits and vegetables are also associated with high risk. In general, carcinomas of the gastrointestinal system are highly aggressive with a propensity for metastasis. The tumor favors the spine, ribs, pelvis, femur and skull. Skeletal metastasis tends to present as a

single solitary lesion, although the area of the gastrointestinal system in which the cancer arises determines the nature of the metastasis.

Why this Condition is Unlikely: The incidence of gastric carcinoma is closely related to the type of diet an individual consumes. Individuals consuming a diet rich in salt and preservation agents are likely candidates for gastric carcinoma. While we cannot be certain about the diets of the individuals at SCL-38, it is likely that it did not include a great deal of salt with no possibility of the presence of modern preservatives. The diets of the individuals at SCL-38 were likely to be high in fresh foods and vegetable matter which is known to reduce greatly the incidence of gastric cancer.

4.5.3 Carcinoma of the Kidney

Renal cell carcinoma represents about 1-3% of all visceral cancers (Cotra et al., 1999). This tumor occurs most frequently in older individuals in their sixth and seventh decades and has a male preponderance of approximately 2-3:1. This tumor has a tendency to metastasize widely before presenting any signs and symptoms. The skeleton is the second most common site for metastasis. This tumor frequently presents as a solitary skeletal metastasis. Skeletal lesions arise in the typical sites

Why this Condition is Unlikely: This is a rare cancer and occurs in older individuals. While it may occur in younger individuals occasionally, it is unlikely to have occurred in all of the individuals at SCL-38.

4.5.4 Carcinoma of the Lung

Bronchogenic carcinoma is one of the most common visceral cancers in industrialized nations. In men, it is the most common visceral cancer and accounts for approximately one-third of all cancer deaths (Cotra et al., 1999). The number of deaths due to lung cancer is on the increase mostly due to tobacco smoking and industrial hazards such as radiation, asbestos and air pollution. Lung cancer is the most frequently occurring human malignancy that has a high propensity for metastasis (Dorfman, 1998). Lung metastases have two major subgroups, small cell and non-small cell, both which have a high propensity for skeletal metastasis. Fifty percent of patients afflicted document skeletal manifestations in small cell carcinoma (Dorfman, 1998). The tumor generally produces lytic lesions and often presents as a solitary lesion or in unusual regions such as the acral skeleton.

Why this Condition is Unlikely: While lung cancer is considered to one of the most common visceral cancers in industrialized nations presently and thus considered to be a common disease, it must be remembered that the reason for the large number of individuals afflicted with lung carcinoma is due, in part, to hazards unique in industrialized nations. The other major reason for the large number of afflicted individuals is due to tobacco smoking. While it is not certain how greatly reduced the number of deaths would be with the removal of these carcinogens, it is conceivable that without the presence of these carcinogens the rate of lung carcinoma would decrease greatly. Therefore, given that the individuals at SCL-38 were not exposed to modern environmental hazards nor tobacco, it seems unlikely that there would be a high risk of lung cancer in this population. With the environmental risk factors removed and the fact that cancer was rare in

prehistoric populations, it does not seem probable that in lesions seen at SCL-38 were caused by lung carcinoma.

4.5.5 Carcinoma of the Pancreas

Little is known about the cause of pancreatic cancer. It is one of the fastest rising cancers in terms of new cases. Pancreatic carcinoma is now the fifth most frequent cause of cancer death in the United States, preceded by lung, colon, breast and prostate cancer (Cotra et al., 1999). This form of cancer has one of lowest survival rates. Environmental factors appear to be important in determining whether individuals develop pancreatic carcinoma. Factors such as smoking, chronic alcohol intake and a high fat diet have all been implicated. The tendency of the cancer to metastasize depends on whether the cancer arose in the body of the pancreas, the head or tail. Skeletal metastasis tend to arise as a solitary lesion

Why this Condition is Unlikely: This is another cancer which is strongly linked to environmental factors. As the risks in an individual's immediate environment rise, so does the risk of developing pancreatic cancer. The risks to the individuals at SCL-38 of developing pancreatic carcinoma is dramatically lower than those of modern day individuals. With the environmental risks removed, pancreatic carcinoma becomes a rare entity and thus is unlikely to have produced the lytic lesions seen in all of the affected individuals at SCL-38.

4.5.6 Carcinoma of the Prostate

This cancer is one of the most common human cancers and is a model for epithelial malignancy that is likely to metastasize to bone (Dorfman, 1998). The lesions produced by this tumor are typically osteoblastic and occur in the typical sites. Osteolytic lesions tend to occur in poorly differentiated carcinomas. Blastic lesions in the vertebrae and pelvis are seen most often. The osteoblastic reaction within the bone can often be so pronounced it can shadow the cancer cells radiographically.

Why this Condition is Unlikely: While prostate carcinoma is one of the most likely to metastasize to bone, it occurs only in men, due to the fact the only men have prostates. Given that two of the affected individuals at SCL-38 was female and given the assumption that all lytic lesions seen in this group are caused by the same agent, it is not possible that prostate carcinoma produced the lytic lesions seen in these individuals. Prostate carcinomas also produce blastic lesions rather than lytic ones.

4.5.7 Carcinoma of the Thyroid

Thyroid carcinoma is an uncommon cancer. In the United States it accounts for about 1.5% of all carcinomas (Cotra et al., 1999). Thyroid carcinomas tend to vary in their behavior. Tumors can be slow growing and well differentiated to highly malignant and poorly differentiated. No matter the type of tumor though, all thyroid carcinomas will eventually metastasize to bone, with the tumors containing well-differentiated cells which have a unique propensity to metastasize to bone (Dorfman, 1998). Skeletal dissemination of the tumor is most common, after metastasis to the neck lymph nodes. Lesions produced by the carcinoma present as destructive lytic lesions.

Why this Condition is Unlikely: Thyroid carcinoma is an unlikely possibility due to its rarity. It is considered a rare cancer at present, and given that cancer was a rare phenomenon in pre-historic populations, it is improbable that all six individuals of SCL-38 suffered from cases of thyroid carcinoma.

4.6 Fungal Infections

4.6.1 Coccidioidomycosis

General Features: Coccidioidomycosis is a systemic infection caused by the soil fungus *Coccidioides immitis*. This organism is restricted to the western hemisphere (Drutz & Catanzaro, 1978a) with the endemic zone for the disease extending from Northern California to Western Argentina, with the most endemic regions in the southern United States and bordering regions of Northern Mexico (Drutz & Catanzaro, 1978a; Dalinka & Greendyke, 1971; Zeppa, Laorr, Greenspan, McGahan, & Steinbach, 1996). The fungus is a non-fastidious organism with spores that are hardy and resistant to drying. The primary site for infection is the lungs and in endemic regions the disease is as common as chicken pox (Drutz & Catanzaro, 1978a). It is asymtomatic in 60% of individuals with pulmonary involvement and in 40% manifests as mild flu-like symptoms (Drutz & Catanzaro, 1978a). Dissemination of the disease is rare, occurring in 0.5% of cases with 20% of those exhibiting skeletal lesion (Dalinka & Greendyke, 1971). Other studies report 10-50% of individuals with disseminated disease exhibiting skeletal lesions (Drutz & Catanzaro, 1978a; Zeppa et al., 1996).

Incidence and Location: There are approximately 100,000 cases of coccidioidomycosis that occur in the United States per year with 70 deaths occurring annually (Drutz &

Catanzaro, 1978b). The fungus is acquired via the respiratory tract through the inhalation of arthrospores, especially during dry and windy conditions, though any contact with contaminated soil will allow passage of the fungus into a person. There appears to be no sex, race or immunological predisposition in the acquisition of primary coccidioidal infection (Drutz & Catanzaro, 1978b), however there is a predilection for certain individuals for the subsequent dissemination of the disease. Males are affected far more than women, with the exception of pregnant women. Individuals of Filipino, African, and Mexican decent are also more susceptible to disseminated disease. Other individuals at high risk for disseminated disease are children under 5 and those who are immunosuppressed (Drutz & Catanzaro, 1978b; Zeppa et al., 1996).

Lesion Description: Lesions can occur in virtually any bone of the body and can be single or multiple. Involvement of the spine is common and generally manifests as vertebral osteomyelitis or, in rare cases, disc space infection. Any part of the vertebrae can be affected and cases of almost complete vertebral destruction have been reported (Zeppa et al., 1996). Vertebral lesions present both as punched out lytic lesions and permeative lesions. Coccidioidomycosis is characterized by a lack of acute anterior angularity (gibbus deformity), even in the event of vertebral collapse, unlike tuberculosis. Lesions tend to have thin sclerotic margins and varying degrees of surrounding reactive sclerosis (Zeppa et al., 1996).

Why this Condition is Possible: Coccidioidomycosis is a possible cause of the lytic lesions seen at SCL-38 for a number of reasons. The region in which the individuals of SCL-38 are buried is considered to be part of the endemic zone for coccidioidomycosis. This creates a situation in which it is more than likely that the individuals from SCL-38

had, at some point in their lifetime, come into contact with *C. immitis*, the organism responsible for coccidioidomycosis. Involvement of the spine in coccidioidomycosis is quite common. All portions of the vertebra can be affected and infection can lead to lytic lesions in the vertebrae as well as complete destruction of the bone. While coccidioidomycosis does tend to affect those who are immunocompromised, immunocompetent individuals can also be affected and once infected, certain groups, such as Native Americans, are more prone to disseminated disease.

4.6.2 Blastomycosis

General Features: Blastomycosis is a rare fungal infection caused by the dimorphic fungus *Blastomyces dermaititdis*. The disease is endemic to the south eastern, south central and midwestern United States (Bradsher, 1992; Gottlieb, McAllister, Guttman & Vine, 1995), with most clinical cases occurring in the states that surround the Mississippi and Ohio rivers and central Canada (Bradsher, 1996; MacDonald, Black & MacKenzie, 1990). In humans the disease is transmitted though the inhalation of spores from the soil into the lungs. Once in the tissues the fungus undergoes a phase transition from conidial stage to yeast cells, increasing in number in the parenchyma of the lungs and spreading to other organs via the bloodstream (Bradsher, 1996). The most common presentation of the disease is pulmonary blastomycosis. Often individuals with pulmonary blastomycosis will experience spontaneous resolution of the disease, though endogenous reactivation may occur at either pulmonary or extrapulmonary sites, with or without therapy (Bradsher, 1996). In disseminated blastomycosis, bone is affected in up to 25% of cases (Bradsher,

1996). Blastomycosis tends to occur in healthy, immunocompetent hosts in which multisystemic disease can develop (Bradsher, 1992; Gottlieb et al., 1995).

Incidence and Location: Bone is the third most common site for manifestation of blastomycosis. It is reported that as many as 60% of individuals with systemic blastomycosis will also have skeletal involvement (Bradsher, 1996). The typical individual affected with blastomycosis will be a young to middle age male who works outdoors or is involved in outdoor recreation. Unless an epidemic arises, women and children are unlikely to become affected. The reported male to female ratio for infection ranges from 4:1 to 15:1 in endemic infections (Bradsher, 1996). Children are rarely affected in endemic situations (Bradsher, 1996). Blastomycosis can affect any bone in the body, with vertebrae, pelvis, sacrum, skull, ribs and long bones most commonly affected (Bradsher, 1996; Bradsher, 1992).

Lesion Location: Lesions produced by blastomycosis tend to have soft tissue swelling and subcutaneous abscesses with draining sinuses similar to that found in tuberculosis (MacDonald et al., 1990). Radiographically, lesions appear as eccentric lytic areas with surrounding sclerosis, little periosteal reaction and no formation of sequestra (MacDonald et al., 1990). The lesions are well circumscribed. The other pattern of lesion presentation is a lytic, moth-eaten appearance of the bone radiographically.

Why this is Unlikely: The main reason why blastomycosis is not a likely candidate as the cause of the lytic lesions seen at SCL-38 is due to the geographic region in which the fungus is endemic. The endemic region for blastomycosis is mainly the southeast and central United States. Blastomycosis is not known to inhabit regions as far west as California. While it may not be impossible for one individual to have traveled to an

endemic region and subsequently become infected with blastomycosis, it is unlikely that all six individuals afflicted at SCL-38 had traveled to an endemic region or came into contact with materials infected with the spores of *B. dermatitis*. Even had that been the case, blastomycosis is considered to be a rare disease, even in endemic areas. For individuals simply to have casual and irregular contact with the spores outside of the endemic zone and develop blastomycosis is highly improbable. Blastomycosis is not transmitted from person to person, nor is it transmitted by animals to people.

4.6.3 Aspergillus

General Features: There are 350 known species of fungus in the genus *Aspergillus*, of which only a few are known to be pathogenic for humans. Despite the ubiquitous distribution of this genus, infection due to this organism is rare. The most common pathogen is *A. fumigatus*, followed by *A. flavus*, *A. teneus*, *A. nidulans* and *A. niger* in decreasing order of frequency (Cortet et al., 1994; Mawk, Erickson, Chou & Seljeskog, 1983). The method by which the pathogen gains entry into the host can be through the respiratory or gastrointestinal system, a break in the skin, or through surgical wounds (Mawk et al., 1983). Unlike blastomycosis, infections due to *Aspergillus* resemble coccidioidomycosis in that hosts are generally immunocompromised in some form. It is commonly believed that there must be an alteration of the systemic or local tissue immune response in order for a fungal infection to become established (Cortet et al., 1994; Mawk et al., 1983). However, it has been suggested recently that this need not be the case.

Incidence and Location: While skeletal infections by *Aspergillus* are exceedingly rare, 74% of cases of *Aspergillus* infections of the skeletal system involved the spine (Cortet et

al., 1994). In children there is contiguous spread from a pulmonary focus whereas in adults there is either a hematogenous or direct spread from either a pulmonary focus or infected wound. The lumbar spine appears to be favored in disseminated *Aspergillus* infections.

Lesions Description: The infection appears to cause a narrowing of disk space and erosion of adjacent end plates. The lesions appear to be strictly lytic in nature with no reactive bony sclerosis. Radiographically the vertebrae are demineralized.

Why this Condition is Unlikely: Despite the abundance of *Aspergillus sp.* present in the environment, infection due to this organism is considered rare. For *Aspergillus* infection to occur, the organism first needs entry into the host and for the host to be immunocompromised as well. In a search of Pubmed/Medline database between the years of 1960-1999, there were four cases of *Aspergillus* infection of vertebrae in individuals who were immunocompetent. There were a total of 12 cases of osteomyelitis caused by *Aspergillus* of immunocompetent individuals. This indicates that in normally immunocompetent individuals, osteomyelitis caused by *Aspergillus* is exceedingly rare. It is unlikely that all the individuals at SCL-38 with lytic lesions were somehow immunosuppressed to the extent that they would all be infected with *Aspergillus*. It appears that the major spread of *Aspergillus* infection is through contamination of wounds after or during surgery. This is an unlikely situation in the case of SCL-38. Also, the lesions produced in the vertebrae due to *Aspergillus* infection tend to narrow the disk space rather than destroy it. There is generally no production of bony sclerosis. In the case of SCL-38, three of the six individuals had destruction of disk space; indeed, SCL-38-62 had no vertebral bodies remaining in affected regions. Also, in SCL-38-6 and SCL-

38-33, there is production of bony sclerosis on the bodies of the vertebrae surrounding the lesion.

4.7 Other Conditions

4.7.1 Actinomycosis

General Features: Actinomycosis is a chronic disease characterized by abscess formation, tissue fibrosis and draining sinuses (Smego & Foglia, 1998). It is generally a localized infection of skin and subcutaneous tissues which is secondary to trauma and usually involves a lower extremity (Reiner, Harrelson, Miller, Hill & Gallis, 1987). It is caused by anaerobic bacteria of the genus *Actinomyces* of which 14 species can cause disease in humans. Among the pathogenic members, *A. israelii* is most often implicated in actinomycotic bone infections followed by *A. naeslundii*, *A. odontolyticus*, *A. viscosus*, *A. meyeri* and *A. gerencseriae* (Smego & Foglia, 1998). Pathogenic members of the genus *Actinomyces* do not exist freely in nature. They are normal and commensal inhabitants of the oropharynx, the gastrointestinal tract and the female genital tract. Humans are the natural reservoir for the pathogens that cause actinomycosis. Actinomycosis generally occurs in individuals who are immunocompetent but can also occur in immunodeficient hosts. The organism gains entry through a break in the mucosa of the gastrointestinal tract, anywhere from mouth to rectum (Smego & Foglia, 1998). Breaks can occur through trauma, dental procedures, overt or covert dental sepsis, bacterial suppuration, diverticulitis, appendicitis or surgery (Smego & Foglia, 1998). Other related bacteria which may cause disease similar to actinomycosis are *Propionibacterium propionicus* and *Norcardia* species. *P. propionicus* can produce an actinomycosis-like disease but rarely

disseminates to bone, and *Nocardia*, which can cause Nocardiosis, generally disseminates to the brain or will cause subcutaneous abscesses. Dissemination to bone is rare.

Incidence and Location: In the preantibiotic era, infection of the vertebrae by dissemination of actinomyces was extremely common. In a review of anaerobic bacterial infection of bone and joints, there were at least 475 cases of actinomycotic bone infection reported and out the 475 cases, 106 cases were reported in the vertebrae. The only bone with a higher infection rate was the jaw, with 190 cases reported (Nakata & Lewis, 1984). Vertebrae infection generally occurred as a direct extension from well established cervicofacial, thoracic or intraabdominal infections (Nakata & Lewis, 1984). Of all the forms of actinomyosis; cervicofacial, thoracic, abdominal and pelvis and central nervous systems infection, it is in the thoracic form of the disease in which hematogenous dissemination of the bacteria results most often. In other forms of the disease hematogenous dissemination is rare. In hematogenous dissemination, any organ or tissue can be affected.

Lesion Description: Lesions produced by actinomycosis are characterized by abscess formation with draining sinuses and involvement of contiguous bones.

Why this Condition is Unlikely: Actinomycosis is unlikely to be the cause of the lytic lesions seen at SCL-38. While at first glance the number of cases of vertebral actinomycosis from the pre-antibiotic era seems quite large, it is not really all that common. Dissemination of the bacterium, once it has overwhelmed the host's immune system is quite common, however given that the entirety of the human population is host to this organism, 475 cases is not a large number. What is implied is that skeletal dissemination is common enough once an individual has contracted actinomyocosis, but

the virulence of the organism is low and the majority of individuals with an intact immune system will not contract actinomycosis from the flora and fauna that they harbor.

4.7.2 Brown Tumor Of Hyperparathyroidism

General Features: Despite the name, brown tumors are a non-neoplastic process. Brown tumors occur in cases of hyperparathyroidism, either primary or secondary, which is a progressive chronic endocrine disease caused by the excessive production of parathormone (PTH). PTH controls calcium balance in the body. Individuals with this disorder have an abnormal exchange of calcium and phosphorous which eventually leads to the demineralization of bone by osteoclasts. Clinically, brown tumors are slow growing lesions that can be locally destructive.

Incidence and Location: Brown tumors most commonly affect the pelvic bones, ribs, mandible and extremities. The vertebral column is rarely affected and to date only eight cases of symptomatic brown tumors of the spine have been reported (Fineman, Johnson, Di-Patre & Sandhu, 1999). Individuals affected can be any age but peak incidence is from 40-50 years with fewer than 5% of affected individuals under 20 years of age (Mirra et al., 1989b).

Lesion Description: Radiographically the lesions appear as well defined lytic lesions with cortical thinning and expansion occurring frequently (Scott, Graham, Sato & Robinson, 1999). The earliest radiological sign is generalized osteopenia of the bones. As the disease progresses the bone and the cortices begin to thin and lose substance. On good quality radiographs, fine linear lucencies can be seen within the cortex. The lucencies are caused by osteoclasts that tunnel though the intramedullary and cortical bone and are a

hallmark of this disease (Mirra et al., 1989b). In other diseases, osteoclasts destroy from the perimeter to the center of the bone trabeculus or in a random pattern such as Paget's disease (Mirra et al., 1989b). In vertebrae, the lesion appears to be able to affect any part of the vertebrae, although in the majority of cases the body is the site affected. The tumor can result in the destruction of the vertebral bodies (Fineman et al., 1999).

Why this Condition is Unlikely: Brown tumor of hyperparathyoidism is unlikely to be the cause of the lytic lesions seen at SCL-38. While hyperparathyoidism itself is not rare, the formation of a brown tumor in the vertebrae is. Only eight cases have been reported in the medical literature to date. Brown tumors also tend to occur in older individuals. Only one individual, SCL-38-107 falls into this age category. Therefore, given the rarity of this tumor, as well as the peak age of incidence, it is highly improbable that the individuals at SCL-38 suffered from parathyoidism.

4.7.3 Brucellosis

General Features: Brucellosis, caused by three species of the genus *Brucella*, is a chronic disease, mainly of the lungs, although it can affect other organs. Presently it is considered a clinically rare disease.

Incidence and Location: Skeletal involvement occurs through the hematogenous spread of disseminating bacteria and varies between 2-70% of cases (Ortner & Putschar, 1981). The most common locations of skeletal lesions are the vertebrae and pelvis.

Why this Condition is Unlikely: Despite the predilection of brucellosis for the vertebra during skeletal dissemination, it is not considered a feasible agent for the cause of the lytic lesions seen at SCL-38. The reason for this exclusion is that brucellosis is a disease

passed from domestic animals to humans. The three genera of *Brucella* pathogenic to humans are *B. abortus*, a disease of cattle, *B. melitensis*, transmitted from goats and *B. suis*, found in domestic pigs. The presence of this disease depends on the presence of domestic vectors such as cattle, horses, goats, sheep, pigs, and dogs (Ortner & Putschar, 1981). It is known that the Native American populations of prehistoric California did not domesticate animals and, while bison are know to harbor *Brucella*, there have been no reports of wild cervidae native to California harboring *Brucella*. Therefore, given the lack of domesticated animals present and the known lack of a wild reservoir, it is reasonable to assume that brucellosis cannot be the pathogen responsible for the lytic lesions seen at SCL-38.

4.7.4 Gorham's Disease

General Features: Gorham's disease is also known as vanishing bone disease, since Jackson first reported the boneless arm of a patient in 1838 (Drewry, Sutterlin, Martinez & Brantley, 1994).

Incidence and Location: This disease has been found to occur in almost every bone of the body with the exception of the distal phalanges. It rarely occurs in the spine. This is an extremely rare disease, in a review done in 1993, there has been fewer than 100 cases of Gorham's disease reported worldwide.

Lesion Description: The disease produces lesions which are typically completely lytic in nature with a lack of any sclerosis or osteoblastic reaction. The lesions produced by the disease are erosive. There have been no reports of the production of draining sinus tracts in the affected elements

Why this Condition is Unlikely: This condition is not included as a possible cause of the lytic lesions seen at SCL-38 for a number of reasons. This condition is extremely rare. Also, the description of the lesions presented in Gorham's disease does not match those seen at SCL-38. The lesions at SCL-38, in the cases of SCL-38-6 and 33, have sclerosis on the body of the vertebrae and, in the case of SCL-38-62, a great deal of osteoblastic activity. There are also draining sinus tracts present in four of the six individuals.

4.7.5 Paget's Disease

General Features: Paget's disease occurs due to abnormal bone remodeling characterized by an increase of osteoclast mediated bone resorption followed by an increase in bone formation. The etiology of the disease is still unknown but since the early 1970's there has been a suggestion that Paget's disease is caused by a circulating viral agent (Papapoulous, 1997; Siris, 1998). Early ultrastructural studies revealed the presence of nuclear and cytoplasmic inclusions characteristic of paramyxovirus nucleocapsid protein in osteoclasts from patients with Paget's disease (Papapoulous, 1997). More recent, studies have detected respiratory syncytial virus, measles virus, canine distemper virus antigens or transcripts in osteoclasts of individuals with Paget's disease. Paramyxovirus sequences have also been detected by some investigators (Papapoulous, 1997). There also appears to be a familial pattern of involvement. It has been known for many years that Paget's disease is often present in more than one member of a family and is inherited in an autosomal dominant pattern. Geographically, Paget's disease is common in England, North America, Australia, New Zealand, France and Germany. It is rare in Africa and throughout Asia. In the United States, approximately

3% of white subjects over the age of 55 are affected. It is less common in individuals of African descent, although the data on this is not definitive (Ankron & Shapiro, 1998).

Incidence and Location: Paget's disease is a disease of older individuals with frequencies increasing with age. The disease can be asymptomatic for 20-30 years before the full clinical picture with characteristic bone deformities appear (Dorfman, 1998). The disease rarely presents before the age of 35 and tends to affect anywhere between 2-5% of the population after the age of 40 (Papapoulos, 1997; Siris, 1998; Davis, Bruffey & Rosen, 1999). Males are slightly more likely to be affected than females. The skeletal deformities and lesions involved with Paget's disease are most often located to the pelvis, sacrum, spine, skull and femur. One third of individuals with Paget's exhibit only one lesion. The disease first onsets with the resorptive phase in which osteolytic activity increases and normal bone is replaced with hypervascular tissue. There is then a secondary increase in bone formation due to the coupling of these two processes which produces the high rate of bone turnover seen in Paget's disease (Papapoulos, 1997). The increased turnover rate destroys normal bone architecture and produces poor quality bone which is dense and disorganized.

Lesion Description: Radiographically, resorptive lesions appear irregular and spotty. The early lesions are locally osteolytic. In the vertebrae, lesions due to early Paget's disease may mimic malignancy. As the disease progresses, lesions usually have a mixed lytic and sclerotic appearance with vertebral bodies becoming enlarged and dense.

Why this is Unlikely: Paget's disease is an unlikely cause of the lytic lesions seen at SCL-38. Only in the early stages of Paget's disease are the lesions produced completely lytic. As the disease progresses, osteoblastic activity begins to increase, producing a great

deal of new bone. The lesions seen at SCL-38 were purely lytic in nature and from appearances, the majority were long standing cases of infection. The lesions, on radiograph, showed no signs of osteoblastic activity within the vertebral bodies, a sign that would be expected as Paget's disease progressed. Also, the individuals from SCL-38 are younger than what would be expected for the onset of Paget's disease.

4.7.6 Rheumatoid Arthritis

General Features: Rheumatoid arthritis is a chronic inflammatory disease of the connective tissues with a predilection for synovial joints (Kilgore, 1989). It is an autoimmune disease whose incidence increases with age, with females three times as likely as males to become afflicted by the disease.

Incidence and Location: Lesions produced in rheumatoid arthritis are small resorptive lesions located mainly in the proximal interphalangeal joints of fingers (Buikstra & Cook, 1981). Other joints of the hands and feet are also commonly affected. Any joint can be affected. In the vertebral column, the cervical spine is most often affected.

Lesion Description: The lesions produced by rheumatoid arthritis are lytic and erosive in nature. Involvement of joints is often symmetrical and the lesions produced destroy joints in an ever expanding radius; however, it does not produce sinus tracts.

Why this Condition is Unlikely: Rheumatoid arthritis also is not included as a possible cause because of the nature of the lesions produced by this disorder. Rheumatoid arthritis is discounted as a possible cause of the lytic lesions seen at SCL-38 due to the nature of the lesions that it produces. The lesions seen in rheumatoid arthritis are, indeed, erosive and lytic, but they do not produce the draining sinus tracts seen in four out of the six

individuals at SCL-38. Also, rheumatoid arthritis is a disease of the joints. In two of the individuals at SCL-38 the lytic lesions do not occur in the body of the vertebrae and therefore are not associated with the disk space. Moreover, the joints that rheumatoid arthritis affects are synovial, not diathroidal. Rheumatoid arthritis does not attack bone in areas where there is not an associated joint.

4.7.7 Sarcoidosis

General Features: Sarcoidosis is a disease of unknown etiology. It is a systemic disease characterized by noncaseating granulomas in many tissues and organs. Given the granulomatous nature of the inflammatory response in the lesions, it has been suggested that sarcoidosis is caused by an infectious agent of some sort. However, sarcoidosis is considered to be a protean clinical disease due to the varying severity and inconsistent distribution of the lesions (Cotra et al., 1999; Lynch, Sharma & Baughman, 1998). In 90% of cases, the lung is the site of involvement. However, multisystemic involvement is a characteristic of the disease and any organ system can be involved. In some individuals, the extra-pulmonary manifestation is the presenting feature of the disease. In a large percentage of individuals, there may never be any manifestation of clinical disease, and up to 30% of individuals experience spontaneous remission of the disease (Rybicki, Maliarik, Major, Popovich & Iannuzzi, 1998). Diagnosis of sarcoidosis is made by exclusion of other diseases which can also produce noncaseating granulomas. There appear to be certain risk factors which make individuals more prone to develop sarcoidosis. The strongest identified risk factors are age, race and family history. African Americans are three to four times as likely as Caucasians to develop sarcoidosis and African American

women in the 30-39 year range had the highest incidence of disease (Rybicki et al., 1998). African American men between 30-39 followed. For Caucasians, the incidence of disease peaked later, 40-49 years of age for both men and women. There does not appear to be a difference in incidence between male and female Caucasians. In terms of mortality, while sarcoidosis is not generally a fatal disease, the mortality rate among African Americans with sarcoidosis is ten times higher than Caucasians. Women of both races had a 30-40% higher mortality rate than men of either race (Rybicki et al., 1998). The mortality rate among African Americans also peaks approximately two decades earlier than Caucasians. Sarcoidosis is virtually unknown among Chinese and Southeast Asians (Cotra et al., 1999).

Incidence and Location: The overall incidence of bone involvement in sarcoidosis is 5%, but the range is large, from 1-14% (Lynch et al., 1998). The granulomas can be found in bone marrow and cortex. Extension of the granulomatous infiltration from the bone marrow into the cortex can cause reactions ranging from bone resorption and destruction to osteosclerotic lesions or excessive bone formation (Lynch et al., 1998). Bone formation is rare, the lesions are usually lytic in nature. Any bone can be involved but the small bones of hands and feet are most commonly affected. Long bones, calvarium, skull, paranasal sinuses, orbital bones, vertebrae, ribs and pelvis are rarely affected. African Americans and women are more likely to present osseous sarcoidosis.

Lesion Description: Sarcoidosis of the spine may result in destruction of the vertebral bodies, with areas of osteolysis and marginal sclerosis. Disk space is generally preserved, a characteristic which distinguishes it from spinal tuberculosis or metastastic disease (Lynch et al., 1998). The appearance of the lesions radiographically is variable.

Generally, they appear as small punched out lytic lesions. Other radiographic features are osteopenia, "stippled" or "mottled rarefaction", a honeycomb pattern of coarse or fine permeative lesions (Lynch et al., 1998). Osteosclerotic lesions are rare.

Why this Condition is Unlikely: Given the wildly varying physical manifestations which can be produced by sarcoidosis, it is difficult to say that the lesions seen at SCL-38 may not be simply an extreme variation of lesions seen in sarcoidosis. There are however, certain aspects to the lesions seen at SCL-38 which cast doubt on the diagnosis of sarcoidosis and thus it is unlikely that sarcoidosis is the agent which produced the lytic lesions seen at SCL-38. While the incidence of bone involvement in sarcoidosis is quite variable and can be quite high, up to 14% of cases, it rarely occurs in vertebrae. When it does occur in the vertebrae, characteristically disk space is preserved. At SCL-38 there is destruction of the disk space in three individuals. Also, sarcoidosis appears to be widely prevalent in Caucasians and African Americans only. Other ethnic groups do not appear to be commonly afflicted with this disorder. A search of Pubmed and Medline databases for 1960-1999 turned up only one case of possible sarcoidosis in a Native American child.

4.7.8 Vertebral Osteomyelitis (Non-Mycobacterial)

General Features: Vertebral osteomyelitis is an uncommon disease. A variety of organisms can be responsible for vertebral osteomyelitis with *Staphylococcus aureus* accounting for the majority of isolates from cases (Sapico & Montgomerie, 1990; Rubery, Smith, Cammisa & Silane, 1995). Other organisms which may be isolated are gram negative aerobic bacteria, with *E. coli* in 30% of cases, *Proteus spp.* and *Pseudomonas aeruginosa* are also seen. In cases of gram negative bacillary infection, the genitourinary

tract is often the source of the organism. The vertebrae are the third most common site involved in hematogenous osteomyelitis. The rich, cellular bone marrow, lack of true epiphyseal growth and the presence of a sluggish, voluminous blood supply in the adult vertebrae are all factors which are responsible for the preponderance of osteomyelitis in adults (Sapico & Montgomerie, 1990). Foreign organisms travel to the vertebrae through the arterial blood supply which branches from the posterior spinal artery. The arterial supply then enters the intervertebral foramen and divides into an ascending and descending branch which supplies the lower portion of an upper vertebrae, the upper position of a lower vertebrae and the intervening disk. This hematogenous route explains the predictable involvement of adjacent segments of vertebrae in vertebral osteomyelitis (Sapico & Montgomerie, 1990).

Vertebral osteomyelitis is usually a monomicrobal disease (Sapico & Montgomerie, 1990; Rubery et al., 1995). Other sources of infection include soft tissue infection, respiratory tract infections, infected vascular sites, dental infections, surgical manipulations of the spine or disk, intravenous drug use and infective endocarditis (Sapico & Montgomerie, 1990). There are also factors which pre-dispose individuals for developing vertebral osteomyelitis. The common factors include diabetes mellitus, individuals who are immunocompromised, drug addiction, old age, oral steroid therapy, dialysis, urinary tract infections, genitourinary instrumentation and anecendent bacteremia due to other causes (Sapico & Montgomerie, 1990; Torda, Gottlieb & Bradbury, 1995).

Incidence and Location: The vertebrae are the most common site of hematogenous osteomyelitis in adults (Sapico & Montgomerie, 1990; Torda et al., 1995; Babinchak, Riley & Rotheram, 1997). The lumbar vertebrae are involved in at least 50% of cases,

with the lower lumber involved more often than the upper (Sapico & Montgomerie, 1990). The thoracic are the next commonly involved, ~35% of the time, and the cervical are the least commonly involved. In vertebral osteomyelitis it is the anterior part of the body which is usually involved. Extension and involvement of the posterior elements (pedicles, transverse processes, posterior spinous processes and laminae) are rare and occur in 3-12% of cases (Babinchak et al., 1997). Infection of posterior elements occur most commonly in the lumbar vertebrae, followed by the cervical vertebrae (Babinchak et al., 1997). The majority of individuals involved are males, with a ratio of 2:1, males to females (Torda et al., 1995; Babinchak et al., 1997). Individuals are generally older, over 50 years of age. The disease is rare in younger individuals.

Lesion Description: Lesions tend to involve adjacent vertebral end plates and intervening disks. Radiographically, lesions appear as erosive irregularities of contiguous end plates.

Why this Condition is Unlikely: Non-mycobacterial osteomyelitis is considered a rare disease. The majority of individuals contracting this type of infection are generally predisposed due to certain risk factors such as an immunocompromised state of health, old age and drug addiction. Infection is also common in individuals undergoing treatment such as dialysis or insertion of genitourinary instrumentation. It is unlikely that all five individuals from SCL-38 were immunocompromised, nor did the individuals fall into the category of elderly, the oldest individual being 35-45 at age of death. There was no risk of infection due to dialysis, intravenous drug abuse or the possibility of the use of genitourinary instrumentation.

5. Mycobacterium

5.1 Mycobacterium bovis

General Features: *Mycobacterium bovis* is one of the four species within the *M. tuberculosis* complex. Although the *M. bovis* and *M. tuberculosis* bear different species names, the two organisms are so closely related that they are merely variants of a single species. *M. bovis* is a slow growing , acid fast bacillus and is the agent of bovine tuberculosis. However, *M. bovis* has one of the broadest host ranges of any known pathogen. It is known to exist endemically in white tailed deer, elk and mule deer, as well as a large number of other animals. In cattle, the route of infection is usually through inhalation of aerosolized bacteria. Infection can also occur through ingestion of food and water contaminated by the organism. Human infection by *M. bovis* is often through ingestion of contaminated meat and milk, but close contact with infectious animals can also introduce the organism by inhalation. Aerosol inhalation of the organism leads to lung and lymph node involvement, while ingestion can lead to the development of a primary focus in the lymph tissues associated with the intestinal tract (Thoen & Bloom, 1995). Despite the identification of *M. bovis* over 100 years ago, the pathogenesis of this organism in cattle and other bovines are not available. Very little is known about the virulence factors of *M. tuberculosis* or *M. bovis* and how they trigger the protective immune response within the infected host (O'Reilly & Daborn, 1995; Thoen & Bloom, 1995). It is known that upon inhalation, the organism passes though the terminal ends of bronchioles and gains access to the alveolar spaces. The organism is able to gain access to the alveolar spaces since the size of the terminal ends of bronchioles is approximately 20μm compared to the 1-4μm size of the bacteria (Thoen & Bloom, 1995). After

exposure, the organism is carried to the small air passages and ingested by phagocytes which then carry the organism to the lymph nodes, parachyma of the lungs or other sites. If transmission of the organism is through ingestion, the primary tuberculous lesion is in the gut, but the immunological reaction remains the same. The bacteria are able to either resist or escape being killed after ingestion by macrophages. Recent evidence suggests that the bacteria escape the phagolysomes into nonfused vacules in the cytoplasm, upon which the organism multiplies and kills the phagocyte (Thoen & Bloom, 1995). It may be that there is a failure of phagosomes to fuse with the lysosomes containing the microcidal agents and hydrolytic enzymes needed to kill the organism. Other macrophages then move into the area, continuing to ingest organisms, while the number of organisms continues to multiply. The cellular responses attempting to control the spread and growth of the organism results in the accumulation of large numbers of phagocytes and the formation of a macroscopic lesion known as a granuloma (Thoen & Bloom, 1995). After 10-14 days, cell mediated response develops and activates macrophages, which now have a greater capacity to kill. T-lymphocytes release cytokines which attract and activate increased number of macrophages to the site of infection. The cellular hypersensitivity which develops results in increased cell death, tissue destruction, and caseous necrosis. Cavity formation and liquefaction of tissue can occur. Rupture of the cavities in the bronchi then allows the aerosol spread of the bacilli. The formation of the granuloma is an attempt by the host to localize the disease. As the lesion heals, the granuloma becomes encapsulated by well organized connective tissue. However, the lesions can continue to contain viable bacilli. Reactivation of the primary focus of infection due to immunosupression resulting from old age, intercurrent infection and disease, poor

nutrition and/or stressful life events can result in the development of clinical and open disease (O'Reilly & Daborn, 1995). The latent period between infection by either *M. bovis* or *M. tuberculosis* and the development of clinical disease can be long, from months to decades. The primary infection, primary tuberculosis, may be without clinical symptoms, and immunity to further infection develops (Manchester, 1988). At the end of this first course of infection, the individual can either begin to recover and there is resolution of the primary complex, or the disease may continue to progress and disseminate, resulting in death of the individual. Individuals that die at this stage show no signs of skeletal changes. It is the reactivation of viable bacilli in the host that leads to secondary infection. Secondary infection can also be the result of re-infection by the pathogenic organism in an individual with some measure of resistance and thus the infection becomes chronic.

Incidence and Location: In humans, cases of pulmonary disease due to *M. bovis* strains of bacillus are clinically, radiologically and pathologically indistinguishable from pulmonary disease due to *M. tuberculosis* (O'Reilly & Daborn, 1995). Human infection is generally higher among population living in a rural environment. It is not really possible to determine the prevalence of *M. bovis* infection in human populations because of the inability to differentiate between *M. bovis* and *M. tuberculosis*. It is, however, thought that *M. bovis* has a greater difficulty in establishing itself in the lung and does not spread readily from person to person. Once established in the lungs however, it is just as virulent as human tuberculosis (O'Reilly & Daborn, 1995). Once again, it is difficult to determine the prevalence of *M. bovis* in cases of disseminated tuberculosis. In an early study of cases of non-pulmonary tuberculosis caused by *M. bovis* in England and Wales, 1901-

1932, it was estimated that for all age groups, the rate of bone and joint infection was 20% (Grange, 1995), making bone and joint infection the fourth most common non-pulmonary site of infection. In Denmark, 1966, a study of 20 Danish counties, using a mathematical model to estimate the approximate proportion of the population infected with each of the two kinds of bacilli, determined that a fairly high proportion of tuberculin reactors owed the positive tuberculin result to exposure from tuberculous cattle at some point in the past, and that individuals exposed from a bovine source had a lower risk of pulmonary tuberculosis than those whose exposure was from tuberculous humans (O'Reilly & Daborn, 1995).

Lesion Description: Bone and joint lesions due to *M. bovis* infection is indistinguishable from that of *M. tuberculosis*. Refer to the following section, lesion description of *M. tuberculosis*, for a detailed description of bone lesions due to *M. bovis* .

Why this Condition is Possible: It is possible that *M. bovis* is the pathological agent which produced the lytic lesions seen at SCL-38. While tuberculosis due to *M. bovis* is not common presently, and when it does occur, it is through contact with infected cattle, it can be transmitted to humans through wild bovines. Although there are no statistics on the incidence of *M. bovis* in wild Cervidae in the San Francisco bay area, it is highly likely that the organism has some reservoir in the wild. It is also likely that the individuals living in the area would come into contact with an animal with *M. bovis* infection. The organism could be transmitted from animal to human either though ingestion of contaminated flesh or close contact with infected pulmonary secretions. The lesions seen at SCL-38 greatly resemble those produced by tuberculosis; however, the lesions produced by *M. bovis* and

M. tuberculosis clinically are identical, and thus it is not possible to discount this organism.

5.2 Mycobacterium tuberculosis

General Features: The tuberculosis bacilli was discovered in 1882 by Robert Koch and is the cause of a chronic, necrotizing, infection with a wide variety of manifestations (Moulding, 1995). The bacillus is slow growing and often remains in a dormant state. In human tuberculosis, the lung is generally the point of entry for *M. tuberculosis*. Bacilli are discharged into the environment in aerosolized form from the pulmonary secretions of infected individuals through sneezing, speaking, coughing and singing (Stead & Dutt, 1995). The smaller aerosol droplets, from 1-10μm, can remain suspended in the air for a considerable period of time. Once the droplet is inhaled it migrates to the bronchioles and alveoli where the pathogenesis of the disease is the same as that described for *M. bovis* in the previous section. Both *M. bovis* and *M. tuberculosis* have no known endotoxins or exotoxins. Therefore, upon infection there is no immediate host response. It is also thought that there are certain risk factors which may influence the development of tuberculosis in certain individuals and groups. Certain ethnic groups appear to have a higher resistance to tuberculous disease than others. African Americans are more susceptible to clinical disease and death from tuberculosis. From 1922-1936 the tuberculosis mortality rate was 24 per 100,000 for Caucasian soldiers compared to 99 per 100,000 for African American soldiers, under identical conditions (O'Reilly & Daborn, 1995). It appears that the chances of an African American individual becoming infected by *M. tuberculosis* is no greater than that of Caucasians, but their chances of developing

tuberculosis and dying of it are three times as great. Individuals of Jewish descent, with the exception of Yemenite Jews, have a higher resistance to the development of disease, although their chances of infection due to *M. tuberculosis* is no greater or less than other groups (O'Reilly & Daborn, 1995). It is suspected that the different rates of disease development is due to selection over generations. Certain groups have been exposed to tuberculosis for centuries and have acquired a greater degree of resistance. Other risk factors influencing the development of tuberculosis are crowding, especially in industrialized or urban conditions, with poor sanitation. An odd observation that has been made is that among navel personnel it has been noted that tall, thin sailors develop tuberculosis more frequently than sailors with a more average build (Stead & Dutt, 1995). In a study in the Far East, individuals with type O blood are relatively resistant to tuberculosis compared to individuals with type AB, who show an increased risk to development of tuberculosis (Stead & Dutt, 1995). Other factors are diabetes mellitus, lymphoma, any chronic debilitating disease, cancer, silicosis, immunosuppression and alcoholism (Stead & Dutt, 1995). Exposure to *M. tuberculosis*, for healthy individuals, does not equate to the development of clinical disease. It is estimated that up to 90% of individuals exposed to infected persons do not develop clinically significant tuberculosis in their lifetime (Enarson & Rieder, 1995). They are infected but do not have the disease. In the remaining 10% clinical disease develops. Approximately half develop active tuberculosis within the first few years of exposure and the other 5% develop late onset tuberculosis (Enarson & Rieder, 1995).

Incidence and Location: Previous to the introduction of the antituberculosis drug isoniazid, skeletal tuberculosis occurred primarily in children. In a 25 year study

performed by New York's Bellevue Hospital, published in 1963, the incidence of bone and joint tuberculosis was approximately 5% per year in a large group of children hospitalized for primary tuberculosis (Davidson & Fernandez, 1995). Skeletal tuberculosis later developed in another 1% of children with primary tuberculosis during follow up (Davidson & Fernandez, 1995). Today, skeletal tuberculosis is a disease primarily of adults, although in developing countries skeletal tuberculosis is still mainly a disease of children.

In skeletal tuberculosis the regions of the skeleton which are most likely affected are areas with a high metabolic and circulatory rate. In skeletal tuberculosis the vertebrae are the most common site of infection. The reasons which make the vertebrae a popular site of infection in non-mycobacterial vertebral osteomyelitis also apply in the case of tuberculous osteomyelitis of the spine.

Lesion Description: The lesions seen in skeletal tuberculosis are a combination of osteomyelitis and arthritis. The invasion of the joint space may be direct, hematogenously, or from lesions in the surrounding bone eroding into the joint space. Once the infection reaches the joint space the synovium develops an inflammatory reaction followed by formation of granulation tissue. The granulation tissue begins to erode and destroy cartilage and cancellous bone. This leads to progressive demineralization and caseation necrosis. As the disease develops paraosseous abscesses may develop and surround the joint to form the "cold abscess". Erosion and sinus tracts may also appear. As the infection heals, fibrous tissue forms which can result in fibrous and osseous ankylosis (Davidson & Fernandez, 1995). In vertebrae, destruction generally occurs in the body. The destruction is generally purely lytic and leads to cavitation. Pathological fractures can occur leading to collapse of the vertebra. Remaining wedge shaped remnants of affected

vertebrae often remain in contact with the end plate and are displaced anteriorly or posteriorly by collapse (Ortner & Putschar, 1981). There is often formation of uni- or bilateral paravertebral abscess that is characterized on dry bone as a flaring, shelf-like bony extension from the affected vertebra (Ortner & Putschar, 1981).

Why this Condition is Possible: *M. tuberculosis* can be considered a likely candidate as the cause of the lytic lesions seen at SCL-38. The lesions seen at SCL-38 are extremely similar to the photos and descriptions of vertebral lesions seen in skeletal tuberculosis. There is invasion and destruction of the joint space in three of the cases, in all cases the lesions are purely lytic and when the lesions occur in the body of the vertebra, there is cavitation of the body. In the case of SCL-38-62, there is complete destruction of the bodies of all affected vertebrae and fusion of the remaining elements. In SCL-38-6 and SCL-38-33 there is the formation of the flaring shelf-like extension from the affected vertebra onto the adjacent vertebra in what Ortner and Putschar characterize as a paravertebral abscess.

5.3 Mycobacteriosis (Nontuberculous Mycobacteria: NTM)

The lesser known cousins of *Mycobacterium tuberculosis*, *Mycobacterium bovis* and *Mycobacterium leprae*, consist of a group of environmental saprophytes of the water and soil. While these organisms are seldom pathogenic for healthy individuals, some have been known to cause active, disseminated disease when accidentally introduced into a human host. In recent years with the advent of HIV/AIDS and HIV related diseases, the incidence of "atypical" tuberculosis has seen a steady rise (Collins, 1989), although incidences of non-tuberculosis TB has been clearly documented among immunocompetent

individuals as well. In some geographic areas of the United States in recent years, 25% or more of all mycobacterial disease seen may be caused by non-tuberculous mycobacterium (Yeager, 1994).

Historically, the first report of pulmonary infections caused by non-tuberculous mycobacteria was recognized in the 1950's (Hoffner, 1994). The description of *Mycobacterium kanasii*, "the yellow bacillus" was first published in 1953 as the agent of a pulmonary infection which resembled TB, but was not caused by *Mycobacterium tuberculosis*. In general, these environmental mycobacterium are all slow growing and vary from each other biochemically, morphologically, physiologically and genetically (Collins, 1989). Their major common feature is that they are acid fast and are opportunistic pathogens which can cause disseminated systemic disease in humans.

The general route of infection by nontuberculous mycobacteria is through the respiratory tract, by direct mucosal penetration, and by direct inoculation through the skin and soft tissue infections. Person to person transmission does not occur. It is generally believed that there must be some defect in local immune effector cell functions for infection to take place (Yeager, 1994), although this is not always the case, especially in children. The most common manifestation of nontuberculous mycobacterial infection is the presence of a chronic pulmonary infection resembling *M. tuberculosis* lung disease. In general, individuals who are affected are not seriously immunocompromised, and are older, white males, who may have pre-existing lung disease or occupational exposure to dust, neoplastic disease, or chronic renal disease (Yeager, 1994). It is rare for children to exhibit pulmonary infections due to nontuberculous mycobacteria. Rather lymphadenitis, which is the superficial inflammation in the submandibular or submaxillary lymph nodes in

the neck, is the most common involvement of nontuberculous mycobacteria in children. Infections of the axial skeletal by nontuberculous mycobacteria are rare.

Presently, the important human pathogens among the nontuberculous mycobacterium are, *M. kansaii, M. genavense, M. marium, M. simiae, M. scrofulaceum, M. szulgai, M. avium, M. hemophilum, M. intracellulare, M. malmoense, M.ulcerans, M. xenopi, M. abscessus, M. chlone, M. fortuitum,* and *M. smegmatis* (Horsburgh, 1996). In the United States, the *Mycobacterium avium* complex (MAC), consisting of *M. avium, M. intracellulare* and sometimes *M. smegmatis*, is the most common cause of NTM disease. *M. kansaii, M. fortuitum* and *M. chelonae* follow in decreasing frequency (Horsburgh, 1996). Of these organisms, *M. genavese* and *M. malmoense* are not known to produce skeletal lesions.

5.3.1 *Mycobacterium abcessus*

General features: *Mycobacterium abcessus* is a rapidly growing mycobacterium which has been implicated as a cause of post-traumatic infections of the skin, soft tissues and long bones. It can cause chronic lung infections, endocarditis, keratitis and disseminated disease in immunocompromised hosts. Bone involvement in *M. abcessus* infection is extremely rare.

Incidence and Location: There have only been 2 known cases of infection of *M. abcessus* of the vertebral column. The first individual was a young female who was on steroid therapy at the time of infection. The site of involvement was T12-L1. The second individual was a immunocompetent, middle aged man, who presented with extensive bone destruction and collapse of L3-L5 (Sarria, Chutkan, Figuroa & Hull, 1998). It was

speculated that because the individual had a history of intravenous drug abuse, this was the route by which the infection spread. Otherwise the individual had no underlying health problems which would dispose him to disseminated infection by *M. abcessus*.

5.3.2 *Mycobacterium avium* Complex (MAC)

General Features: Mycobacteria in the *Mycobacterium avium* complex (MAC) are classified as slow growing bacilli which can produce a yellow pigment in the absence of light. MAC organisms are composed of a group of opportunistic pathogenic organisms which are capable of causing disease in humans and animals and are *M. avium*, *M. intracellulare* and sometimes *M. scrofulaceum*. In reference to the MAC complex, unless mentioned, the pathogens under consideration are *M. avium* and *M. intracellulare*. Of all nontuberculous mycobacteria, MAC is most frequently associated with human disease and in the United States, 40-50% of clinical infections in non-AIDS patients are caused by *M. intracellulare* (Inderlied, Kemper & Bermudez, 1993). MAC organisms are found ubiquitously in nature and prefer warm, acidic soil. They can be isolated from natural sources of water, both fresh and salt, pools, soil, plants, bedding material and house dust (Inderlied et al., 1993; Yeager, 1994). It has been suggested that environmental sources of water constitute the greatest risk of exposure to humans and both *M. avium* and *M. intracellulare* have been found in aerosols in droplet sizes of 0.7-3.3 mm above fresh water, a size sufficiently small to reach the alveolar spaces after inhalation (Inderlied et al., 1993).

Incidence and Location: Of the three organisms in the MAC complex, serious human disease is caused by *M. avium* and *M. intracellulare*. *M. scrofulaceum* mainly causes

lymphadenitis in children but rarely causes serious disease in the adult. Pulmonary disease is the most common presentation due to MAC. Either pathogen can remain in the lungs as a chronic infection for a long period of time rather than producing disease. Disseminating infection is rare in individuals without HIV or AIDS. Previous to the AIDS epidemic, individuals with disseminated disease usually had some underlying malignancy, inherited disorder or therapy-induced immunodeficiency (Inderlied et al., 1993). In cases of dissemination, the skeleton is a common site. In skeletal dissemination, MAC is most commonly involved in joint and periarticular infections, especially of the hands and wrists. Osteomyelitis, usually with bony lesions, skeletal destruction, contiguous abscess formation and draining sinuses, is rare (Inderlied et al., 1993). Children with hematological malignancies are most commonly affected. Immunocompetent individuals are rarely affected.

5.3.3 *Mycobacterium chelonaei*

General Features: *Mycobacterium chelonaei* is a rapidly growing mycobacterium and was first reported as a cause of human disease in 1953 (Pottage et al., 1982). Infections due to this organism are uncommon generally and most cases occur in immunocompromised individuals with an antecedent history of penetrating trauma (Draick, Duffy, Samlaska & Scherbenske, 1990). This organism is an environmental saprophyte and has been isolated from house dust, soil and water.

Incidence and Location: Disseminated disease due to *M. chelonae* is rare and occurs mainly in two groups; individuals having had cardiovascular surgery and the immunosuppressed. In a search of Pubmed and Medline databases, 1960-1999, only

three cases of osteomyelitis due to disseminated *M. chelonae* were found. There was one case of vertebral involvement in a young man on chronic steroid therapy (Pruitt et al., 1993).

5.3.4 *Mycobacterium fortuitum*

General Features: Very little is known about this environmental mycobacterium. It has been isolated in domestic tap water supplies and soil samples, but its natural reservoir has not been determined. It is a rapidly growing mycobacterium and at least three biovarients are recognized (Wolinsky, 1992).

Incidence and Location: Clinically, skeletal infections caused by *Mycobacterium fortuitum* resemble similar infections caused by *M. tuberculosis* (Wolinsky, 1992). Infections leading to disseminated disease occurs most often in adults. In a review by Sarria et al. (1998) on atypical mycobacterial osteomyelitis, only four cases are attributed to *M. fortuitum*.

5.3.5 *Mycobacterium haemophilum*

General Features: *Mycobacterium haemophilum* was first removed from a cutaneous lesion of a woman with Hodgkin's disease in 1978 in Israel (Saubolle, Kiehn, White, Rudinsky & Armstong, 1996). The first documented case of *M. haemophilum* in an immunocompetent individual was reported in 1981 by Dawson, Blacklock, & Kane in an otherwise healthy child. This organism is known to cause cutaneous and subcutaneous infections, septic arthritis, osteomyelitis and pneumonitis in immunocompromised individuals and lymphadenitis in immunocompetent children (Saubolle et al., 1996). There

are two large populations, immunocompetent children and immunocompromised adults, afflicted by this organism. The organism is a slow growing, fastidious bacterium which requires a lower incubation temperature for growth and iron supplemented media to be cultured *in vitro*. It is not clear what the natural habitat of *M. haemophilum* is and the method by which it is spread is also unclear. It appears that the bacterium is ubiquitous environmentally and its large pH tolerance, 5.4-7.4, suggests that it resides in diverse environments.

Incidence and Location: From 1976 to 1995, there have been 64 cases of *M. haemophilum* reported. Of the 64, nine were otherwise healthy children and the remaining 55 had some underlying disease or were transplant recipients.

5.3.6 *Mycobacterium kansasii*

General features: The first report of pulmonary infection in a human by *Mycobacterium kansasii* was published in 1953 (Hoffner, 1994). *M. kanasaii* is a slow growing environmental mycobacterium which has occasionally been isolated from water distribution systems (Hoffner, 1994). Pulmonary infection due to *M. kansasii* has most often been reported in California, Texas, Louisiana, Illinois and Florida. Disease due to *M. kansasii* occurs more often in individuals from towns or metropolitan areas, and aside from city water supplies, the organism can also be cultured from milk (Yeager, 1994).

Incidence and Location: Chronic pulmonary disease which resembles tuberculosis is the most common manifestation of *M. kansasii* infections (Hoffner, 1994). However, this organism can affect many other organ systems. After MAC it is the second most common cause of opportunistic infections in individuals with AIDS (Wolinsky, 1992). It is also

second after MAC as the cause of disseminated disease in immunocompromised individuals.

5.3.7 *Mycobacterium marinum*

General features: *Mycobacterium marnium* was first identified in 1926 from a fish at a Philadelphia aquarium (Vasquez & Sobel, 1992). *M. marinum* is a well documented cutaneous pathogen and can cause rare cases of dermal dissemination. The infection is generally identified with activities associated with water, such as swimming, fishing, boating and aquarium tending (Vazquez & Sobel, 1992). Infection is usually acquired after superficial trauma to skin and the infection tends to remain localized and self limiting. *M. marnium* infections are believed to stay localized to skin because of the organism's optimal temperature requirement, 31 degrees Celsius. In the rare cases of disseminated infection, the individual's dominant hand is usually involved.

Incidence and Location: *M. marium* is generally associated with cutaneous lesions in humans. Unlike the other non-tuberculous mycobacterium, human *M. marium* infection is not rare (Barton, Bernstein, Struthers & O'Neill, 1997). In most cases a chronic granulomatous skin lesion presents either as single or multiple nodules on the hand or feet. With deeper infections tenosynovitis may occur or in rare cases septic arthritis. Osteomyelitis due to *M. marium* is extremely rare and has been reported in 6 cases. In all cases, infection was of the extremities. In five cases, osteomyelitis involved the fingers and in the sixth case, the infection was of the hand and foot (Barton et al., 1997).

5.3.8 *Mycobacterium simiae*

General Features: The first reported case of *Mycobacterium simiae* infection of a person in the United States was reported in 1975, of an elderly woman with chronic cavitary lung disease from whom *M. simiae* was consistently isolated (Rose, Dorff, Lauwasser & Sheth, 1982). This organism was originally isolated from monkeys imported from India in 1965 and recently has been isolated from hospital tap water. It is assumed that this organism is environmental, although its source in nature is unknown.

5.3.9 *Mycobacterium szulgai*

General Features: The first report of this organism as an human pathogen was in 1962 where it was isolated from the bursa of a man in the United Kingdom who developed oleacranon bursitis after repeated injury to the elbow (Benator, Kan & Gordin, 1997). The natural environment and reservoir of *M. szulgai* is uncertain. It has been isolated from a snail and "tuberculous-like lesions" in a trophical fish (Benator et al., 1997). *M. szulgai* can cause a wide range of disease. Tuberculosis-like pulmonary disease is most common.

Incidence and Location: Compared to other NTM's the contribution of *M. szulgai* to human disease is small. In a Japanese survey from 1971-1984, there were only 8 cases of *M. szulgai* reported, 0.6% of all cases of NTM's (Maloney, Gregg, Stephens, Manian & Rimland, 1987). In the United States between 1981-1983, there were only 8 cases reported, a total of 0.4% of all NTM cases (Benator et al., 1997). As of 1998, in a review done by Hurr and Sorg, from a search of Medline from 1966 to 1988, there were only three cases of osteomyelitis due to *M. szulgai*.

5.3.10 *Mycobacterium ulcerans*

General Features: *Mycbacterium ulcerans* infection typically produces progressive skin ulcerations in humans and other animals. The disease was first described in 1948 in six patients with unusual skin ulcers in rural Australia (Hayman, 1993). The lesion produced is known colloquially as a Buruli ulcer. It is believed that the organism resides naturally in the environment but it has not been isolated at any natural site. The first detection was made by PCR in 1997 (Johnson, Stinera & Hayman, 1999).

Incidence and Location: The organism tends to infect people in very specific regions. Individuals living in rural areas are most commonly affected. The organism affects healthy individuals and is either ingested or inhaled. Skin trauma is also a route of infection. In a seach of Pubmed and Medline databases, 1960-1999, one case of osteomyelitis due to *M. ulcercans* was found. Hofer et al. (1993) reported the individual became infected with *M. ulcerans* after a snakebite.

5.3.11 *Mycobacterium xenopi*

General Features: *Mycobacterium xenopi* was first isolated from the skin granuloma of the toad *Xenopus laevis* in 1957 and was later isolated from the sputum of an individual with chronic pulmonary disease in 1963 (Miller, Perkins, Richardson & Sexton, 1994). Since these reports, *M. xenopi* has been recognized as both a colonizing agent and cause of human disease in individuals with underlying conditions such as chronic obstructive pulmonary disease, alcoholism, cardiovascular disease, cancer and diabetes mellitus (Hoffner, 1994; Miller et al., 1994). Environmentally, *M. xenopi* has been isolated from both hot and cold water sources, most commonly the hot water supply of hospitals (Miller

et al., 1994). The natural habitat of this organism is unknown, however, because of the clustering of cases of *M. xenopi* infections in people residing on the coast, it is speculated that the organism is transmitted either from sea birds or from the ocean itself. However, there have also been numerous cases of *M. xenopi* infection inland and the organism has not been successfully isolated from sea water or freshwater and has been isolated only once in birds (Miller et al., 1994).

Incidence and Location: The most frequent manifestation of disease caused by *M. xenopi* is pulmonary disease which is associated with cough, hemoptysis, fever and weight loss. It is often indistinguishable from pulmonary tuberculosis (Miller et al., 1994). Disseminated disease due to *M. xenopi* is rare and is most common is individuals with AIDS. At present there have been only 6 cases of bone or joint infection with *M. xenopi* reported worldwide (Miller et al., 1994). Three of the individuals had infections located to the spine. In one case, the individual presented the findings typical of Pott's disease with complete destruction of the bodies of T3 and T4 as well as the disk between them. The soft tissue mass which had replaced T3 and T4 had extended into the anterior extraspinal space as well (Miller et al., 1994).

6. Discussion

6.1 Results of Molecular Analysis

The results of the molecular analysis for mycobacterium was negative. There was no amplification of mycobacterium DNA, either for *M. tuberculosis* or *M. bovis*. The PCR was performed on three separate occasions and once, 5µl of the first amplification product was removed and re-amplified using fresh reagents. In all cases, the positive control amplified and a band 185bp in length could be visualized on the gel.

Despite the fact that there was no amplification of mycobacterium DNA, the negative results do not necessarily denote that the individuals were not afflicted by tuberculosis. It is likely that the conditions under which the individuals were preserved was not conducive to the preservation of exogenous DNA. If this disease process was skeletal tuberculosis, then the bacterium would have only been present on the surface of the bone. After death, the bacterium would have been exposed to the environmental conditions of the grave as the individual decomposed. Given that there was no special treatment, in terms of preservation of the remains, it is quite likely that if mycobacterium were present during life, the effect of decay on the bacterial DNA, as well as the environment effects, would have led to the destruction of any genomic material. It is possible that mycobacterial DNA is still present, but in extremely minuscule amounts that the PCR reaction and subsequent staining using ethidium bromide is not sensitive enough to detect.

For future work, it may be interesting to perform a PCR reaction using radiolabeled dNTP's. The use of radioisotopes increases the sensitivity of detection and it may be what is necessary to detect any PCR product. Also, the majority of the affected

vertebrae have been preserved and in the future, newer innovations in technology may result in techniques more sensitive which may detect the presence of mycobacterium in prehistoric remains.

6.2 The Case Against Neoplastic Disease

While there are certain neoplasms which present in bone, either as a primary tumor or as a secondary metastasis, it appear unlikely that the lesions found in the vertebral column of the five individuals of SCL-38 can be attributed to neoplastic disease, whether benign or metastatic.

Presently, neoplastic disease is the second largest killer in the United States. It was second only to cardiovascular disease as a leading cause of death in 1998 (Cotra et al., 1999). However, the majority of individuals suffering from the various neoplasms do not manifest osseous lesions. The majority of cancers do not involve the bones at any stage of the disease and for those that do, either because they are primary bone tumors or are prone to osseous dissemination, the sites of involvement tend to vary. The majority of bone tumors tend to favor bones either of the appendicular or axial skeleton or both. In situations in which there is metastatic dissemination from carcinoma, the dissemination is wide spread to all skeletal regions which are along the hematogenous route.

For primary neoplasms of bone, either benign or metastic, there are few that produce lytic lesions in the vertebrae specifically and with regularity. The majority that do produce lytic lesions in the vertebrae do so rarely. The vertebrae are not the favored sites of skeletal distribution of tumors. While there are two primary neoplasm of bone which do have a specificity for the vertebrae, can produce lytic lesions, and can be located to any

portion of the vertebra, the incidences for aneurysmal bone cysts and solitary myelomas are low. Both aneurysmal bone cysts and solitary myelomas are considered to be rare tumors.

In the case of the metastatic carcinomas, with a propensity for skeletal dissemination, it seems highly unlikely that all six individuals at SCL-38 were suffering from the same form of cancer. It is also not probable that they all suffered from a different form of disseminated metastatic cancer. Under the conditions stipulated in this paper, that all the lytic lesions found in this population are considered to have the same etiology, the likelihood of all six individuals suffering from some form of cancer seems unlikely, especially given that the population under study is prehistoric in origin. While presently the various carcinomas listed in the differential diagnosis kill thousands a year, it is extremely uncommon to find any evidence of cancer in prehistoric remains. In a search of Pubmed and Medline databases for paleopathological cases of cancer, only six cases of probable carcinoma were recorded and among primary bone tumors, eight cases of probable osteosarcoma and one case of probable hemaginamona were found. Given that osteosarcoma is the second most common type of primary bone tumor today, the presence of only eight probable cases worldwide paleopathologically suggests that cancers were comparatively rare in prehistory. Micozzi (1991) states that there is little or no hard evidence of cancer in antiquity and recent epidemological evidence suggests that 80-90% of human cancers present may be due to environmental exposures and that 30-40% can be explained by human diet and nutrition.

It has thus been hypothesized that cancer was a very rare condition in prehistoric populations. The majority of cancers, with the exception of familial cases and those with a

predilection for juveniles, is found in the elderly, a condition produced by an increasing load of genetic mutations built up over decades. It could be that individuals did not live long enough in prehistoric times to incur the majority of cancers that we see today. It could also have been a difference in nutrition and exposure to industrial hazards. In ethnographic studies of hunter-gatherers, subsistence farmers and small groups which do not subsist on refined foods, there are far lower rates for many types of cancer such as bowel, breast and lung (Cohen, 1989). Even when the numbers are corrected for the small proportion of elderly observed, cancer rates are still exceedingly low. Also, in the case of primary bone cancers, which tend to occur in the young more often than the old, if bone neoplasms were a common occurrence in prehistory one would expect to see far more cases of diseases such as osteochondroma, fibrous dysplasia, giant cell tumors, Ewing's sarcoma and osteosarcoma (Micozzi, 1991).

Examination of the mummified remains of ancient Egyptians has also failed to yield evidence proving that neoplasms were prevalent in prehistory. Many of the remains were those of wealthier individuals who lived to an advanced age. It has been argued that if cancer was common in antiquity then it should have been detected in ancient and older mummies (Micozzi, 1991).

6.2 The Case Against Non-Tuberculous Mycobacteriosis (NTM)

In the United States currently, disease due to mycobacteria other than *M. tuberculosis* is far more common than tuberculosis itself, especially given the advent of HIV and AIDS (Wallace, 1994). However, this situation was not always the case. It has only been since the 1950's that there was recognition that these organisms could cause

disease in humans and, while a few reports of disseminated disease due to *M. kansaii*, *M. avium* and *M. intracellulare* could be found in the early tuberculosis literature, the incidence of these infections has increased sharply since the emergence of AIDS (Collins, 1989). Previous to 1980, cases of disseminated disease due to NTM's were extremely rare (Horsburgh, 1996; Wallace, 1994). Systemic involvement by NTM's occurs only when the normal T-cell defenses are depleted as a result of old age, radiation, chemotherapy or HIV infection (Collins, 1989).

It is quite unlikely that the lesions seen in the individuals of SCL-38 are due to NTM disease. While disseminated disease in NTM disease does occur in individuals without HIV or AIDS and has been documented to occur in immunocompetent individuals as well, it is a rare event. NTM's are believed to be organisms which exist commonly in the environment and are considered to be opportunistic pathogens rather than virulent pathogens since some local or systemic immune impairment is generally required for them to cause disease.

In a search of Pubmed and Medline databases, 1960-1999, the number of cases of osteomyelitis in individuals not afflicted by HIV and/or AIDS is as follows: for *M. kansasii* there were 12 cases, of which one involved the vertebrae, one involved the ischium, one case involved the hand, wrist and scaphoid of the individual, five cases of arthritis and 4 cases of bone marrow infection. For *M. marium*, all cases of bone involvement were localized to the hands and feet. There were 8 cases in all. For *M. simiae*, there were three cases total. One of the vertebrae and in the other two cases, there was co-infection of *M. simiae* with another NTM. In one case, the individual was an immunocompetent young woman who had a 10 year history of chest pain. It was

finally determined that she suffered from recurring osteomyelitis of the sternum due to infection from *M. simiae* and *M. fortuitum*. For *M. scrofulaceum* there was one case of cervical adenitis, one case of non-specific inflammatory disease in a 16 year old boy who died of it after a 5 year duration and one individual who contracted *M. scrofulaceum* of the calcaneus at age 8 but later developed multi-foci osteomyelitis at age 14 after BCG vaccination and had a reoccurrence of the osteomyelitis due to MAC at 25. There was only one case of bone involvement with *M. szulgai* in an individual not affected by HIV and/or AIDS and none involved the vertebrae. There were 16 cases of osteomyelitis due to MAC. Three of the cases involved the vertebrae. For *M. haemophilum*, there was one case of osteomyelitis in a cardiac transplant patient. The individual had the predisposing condition of being immunosuppressed due to transplant.

6.3 The Case for Coccidioidomycosis

The San Francisco Bay area is part of the region which is known to be endemic for coccidioidomycosis. In endemic regions, coccidioidomycosis is said to be extremely common, much like chickenpox, and for the most part is an asymptomatic condition. While disseminated disease in coccidioidomycosis is rare, 0.5-1% of all infections (Bried & Galgiani, 1986; Dalinka & Greendyke, 1971), certain groups are more susceptible to dissemination than others. In disseminated disease, the skeletal system is the third most common site of involvement and will occur in 10-50% of cases, with the vertebrae being one of the most common sites of osseous manifestation (Zeppa et al., 1996; Bried & Galgiani, 1985; McGahan, Graves & Palmer, 1980). The incidence of disseminated disease increases in individuals with specific risk factors. One of these factors appears to

be population affiliation. It appears that certain Native American tribes are more susceptible to dissemination than others (Bronnimann & Galgiana, 1989; Drutz & Catanzaro, 1978b; Dalinka & Greendyke, 1971). For individuals residing within the endemic zone, it was found that for some groups, such as the San Carlos Apaches, individuals were 13 times as likely to develop disseminated disease, and 5 times as likely to die, than were the individuals at the Colorado River reservation (Drutz & Catanzaro, 1978b). In contrast, the San Carlos Apaches were only 2 to 3 times as likely, to develop disseminated disease and die, as individuals of the Pima and Papago reservations (Drutz & Catanzaro, 1978b). However, while it appears that there is a genetic factor involved in increased risk, other factors such as environment, age and intercurrent disease among different tribal members could also be involved (Drutz & Catanzaro, 1978b). The risk for disseminated disease is also higher for males.

Osteomyelitis due to disseminated coccidioidomycosis most commonly involves the vertebrae, tibia, skull and ribs (Bronnimann & Galgiani, 1989). In the vertebrae, bony lesions can be single or multiple and destruction of vertebrae is random in location. There is indiscriminate involvement of all portion of the vertebrae, not just the body. In a series taken in 1977 of 112 cases of coccidioidomyocodial osteomyelitis, it was found that vertebrae had the highest incidence of involvement, 25%, followed by tibia (15%), skull and metatarsals (13% each) and metacarpals (10%). All other elements followed in decreasing percentages (Drutz & Catanzaro, 1978b).

Coccidioidomycosis must be considered as a possible cause of the disease process which produced the lytic lesions seen in the individuals at SCL-38. This disease cannot be discounted due to the fact that is very common, especially in endemic regions. The

individuals of SCL-38 did reside in the endemic region and its is very likely that they were exposed early on in life and very frequently to the arthrospores of *C. immitis*. It is not certain what factors are involved which lead to the risk of individuals acquiring primary coccidioidomycosis but once acquired, certain groups, such as Native Americans, appear more at risk for the development of disseminated disease. Once the disease disseminates, bone is the third most common site of involvement and vertebrae are a common site of infection. The lesions produced by disseminated coccidioidomycosis also bear a strong resemblance to those found at SCL-38. In vertebral lesions, both punched out lytic lesion and permeative lesions have been observed in the vertebral bodies. There have also been cases reported of almost complete vertebral destruction due to coccidioidomycosis (Zeppa et al., 1996). Both the almost total destruction of vertebrae and both types of lytic lesions are seen at SCL-38. Also, all portions of the vertebrae can and have been affected. At SCL-38 there is destruction of vertebral bodies, transverse processes, as well as spinous processes. With the lesion formation and the destruction of bone, sinus formation can occur (Drutz & Catanzaro, 1978b). Sinus formation is seen in three of the six affected individuals at SCL-38.

6.5 The Case for *M. tuberculosis* and *M. bovis*

Historically, *M. tuberculosis* and *M. bovis* are two important pathogens which have influenced human history in terms of the human and animal disease that they cause, and the public health hazards which they pose. Genetically, *M tuberculosis* and *M. bovis* belong to the *M. tuberculosis* complex, of which *M. microti* and *M. africanum* are members. However, of this complex, only *M. tuberculosis* and *M. bovis* are important in

cases of human pathogencity. It is thought that because of the genetic concordance between *M. tuberculosis* and *M. bovis*, that *M. tuberculosis* evolved specifically for humans from *M. bovis* sometime after the domestication of cattle between 8000 and 4000 B.C.E (Haas & Haas, 1994).

Presently, evidence suggests that tuberculosis, either due to infection *with M. tuberculosis* or *M. bovis*, arose in Neolithic cultures among the stationary rural and urban cultures. While the presence of tuberculosis in Paleolithic societies is not impossible, there has been no evidence to suggest that this was present. Paleolithic societies were generally hunting/gathering bands composed of small nomadic groups which were not condusive for the spread of *M. tuberculosis*, nor did they have domesticated cattle, which lowers the chances of infection by *M. bovis*. During the Neolithic, however, *M. bovis* spread was promoted through the ingestion of contaminated milk from domesticated cattle and *M. tuberculosis* was spread in aerosolized form among urban populations. The first good paleopathological and archaeological evidence of spinal tuberculosis coincides with the carbon-14 dates of artifacts relating to widespread domestication and confinement of cattle extending across Europe, Asia and Africa (Haas & Haas, 1994). One of the oldest skeletons discovered, which is suggestive of Pott's disease, dates to approximately 5000 B.C.E.

Despite the skeletal evidence of tuberculosis, however, it is thought that perhaps the early finding of skeletal tuberculosis was not the work of *M. tuberculosis* but rather of *M. bovis*. There is no evidence, historically, that *M. tuberculosis* existed previous to 1000 B.C.E. (Haas & Haas, 1994; Hare, 1967). Skeletal tuberculosis due to *M. bovis* infections cannot be distinguished from that of *M. tuberculosis* and previous to the pasteurization of

milk and control of bovine tuberculosis, a great number of cases of skeletal tuberculosis were due to infection by *M. bovis*. Historically, evidence against *M. tuberculosis* as the cause of skeletal tuberculosis before 1000 B.C.E comes from Egyptian medical papyrii, circa 1600 B.C.E., which describes all other conditions of the chest and lungs in great detail, but fails to describe any condition resembling pulmonary tuberculosis (Haas & Haas, 1994; Rowlings, 1967). There is also no mention of a condition resembling pulmonary tuberculosis in either the Rig Veda nor the Old Testament, both written before 1000 B.C.E. Paleopathologically, the first clear evidence of pulmonary tuberculosis comes from the mummy of a five year old boy. The boy was an intrusive burial found in the tomb of Nebwenenef, the high priest of Rames II. The lungs of the child were found intact in the thoracic cavity. Pulmonary tuberculosis was diagnosed on the evidence of pleural adhesion, evidence of hemoptysis (fresh blood in the trachea) and presence of acid fast bacilli in the lungs. The intrusive burials in this tomb date from 1000 B.C.E to 400 C.E. More recent however, molecular evidence from Egypt demonstrated the positive existence of *M. tuberculosis* from an Egyptian mummy dated to the New Kingdom, 1550-1080 B.C.E. The male mummy was not eviscerated and had residues of extensive pleural adhesions in the right lung as well as severe destruction of the bodies L4 and L5 along with irregular osteolyses and reactive new bone formation (Nerlich, Haas, Zink, Szeimies & Hagedorn, 1997).

In the New World, there is growing evidence of the existence of tuberculosis previous to contact with Europeans. While archaeologists and anthropologists are reluctant to accept to the presence of this disease among pre-contact societies in the Americas, both skeletal and molecular evidence strongly implies the presence of the

disease among the populations of the New World. One of the best proof of tuberculosis in the New World comes from the mummified remains of a child from the Nazca culture in Peru. The remains date from 200-800 C.E. are of an 8-10 year old boy. From the remains there is evidence of Pott's disease, psoas abscess and tuberculosis of the lung, pleura, liver and right kidney. Unidentified acid fast organisms were also found (Haas & Haas, 1994; Allison et al., 1973). Molecular evidence of the presence of a "tuberculosis complex" organism among pre-contact societies was established in 1994 when Salo and colleagues amplified mycobacterium DNA from a 1000 year old male mummy found in Peru. The DNA amplification, using PCR primers common to DNA sequence from either *M. tuberculosis* or *M. bovis* but not to other soil dwelling mycobacterium, demonstrated the existence of some form of tuberculosis in the New World prior to contact. More important, the date of the mummified remains, pre-dates European contact but post-dates the origin of *M. tuberculosis*, implying that it is possible that *M. tuberculosis* could quite possibly have be introduced into the New World shortly after the initial peopling of the Americas.

In North America, the evidence of skeletal tuberculosis is not quite as compelling as that found in South America. One of the major reasons is that the best evidence of tuberculosis in South America, as well as the Old World, comes from mummified remains, either natural or artificial. With mummified remains, pathological lesions in soft tissue often remain and under certain conditions, the infectious organism is preserved and can be identified. In North America, conditions very rarely allowed for spontaneous mummification and ritualized mummification of remains did not exist. Therefore, the only evidence of possible tuberculosis is through the diagnosis of skeletal remains without the

presence of a proven pathogen. Consequently, a positive diagnosis of skeletal tuberculosis is not possible, as other pathogens such as coccidioidomycosis, blastomycosis and neoplastic disease can be confused with tuberculosis. However, with such caveats in mind, certain skeletal remains in North America have lesions which are characteristic of tuberculosis, rendering such a diagnosis not unlikely. Two such cases are described: from the Yokem mounds in the Mississippi valley. Buikstra and Cook (1981) describe individuals as having an axial concentration of lesions with extensive sacroiliac involvement and vertebral destruction. Circumferential erosion is common and there is little proliferation of tissue. The surface texture of the bone is coarsened and sclerotic.

Another likely case of pre-historic tuberculosis comes from Pueblo Bonito, New Mexico (NMNH 327127). The specimen described by Ortner and Putschar (1981) is of a nine year old child dating to 828-1130 C.E. There is cavitation of the anterior and left portion of the vertebral body. A cloaca occurs in the left sector of the body and the inferior surface of the body is eroded from the central to the left side. The anterior body of T12 is destroyed. The body of L1 is almost completely destroyed. The left pedicle is fused with the body of L2. The superior body of L2 is eroded and fused with the remnant of L1. There is kyphosis of the spine due to collapse of the vertebral column. The claim that this is a case of tuberculosis is substantiated by Morse in 1961, who concludes that the specimen "is quite typical of tuberculosis with destruction of the vertebral bodies, angular deformity , and very little bone regeneration." (as cited by Ortner & Putschar, 1981, 167).

Other cases of possible pre-contact tuberculosis includes: a burial from Illinois (NMNH 381853) from 200-1000 C.E (Widmer & Perzigan, 1981). An Eskimo skeleton

from the Yukon river in Alaska (NMNH 345394) and six individuals from the Turpin site (33Ha19) in Ohio, 950-1750 C.E (Widmer & Perzigan, 1981). The individuals from this site present lytic lesions affecting the vertebrae and one with lytic lesions presented on the acetabulum. From the Arnold site (40Wm1) in Tennessee, 1200C.E., lytic lesions presented on the bodies of T10 and T11 of one individual have destroyed and collapsed the spinal column in the region resulting in kyphosis (Widmer & Perzigan, 1981).

It is possible to consider either *M. tuberculosis* or *M. bovis* as the pathogen having caused the lytic lesions seen at SCL-38 due to the arguments presented above. From the evidence presented, the presence of tuberculosis in South America is most likely a certainty and in North America, the presence of tuberculosis is probable. In the case of SCL-38 it is quite possible that the lytic lesions associated with the individuals could have been caused by either *M. tuberculosis* or *M. bovis*.

6.5.1 The Case for *Mycobacterium bovis*

It has been well documented that *M. bovis* is a pathogen which can cause human tuberculosis in sites outside of the lungs. Before pasturization became common practice, the rate of tuberculosis due to *M. bovis* was quite high in many European countries. In Great Britain in 1937, *M bovis* was responsible for 85% of primary abdominal tuberculosis, 50% of cervical lymphadenitis, 49% of tuberculous lupus, 25% of tuberculous meningitis and 20% of bone and joint tuberculosis (Thoen & Bloom, 1995). In other European countries during this time period, the rate of tuberculosis caused by *M. bovis* varied widely depending on the different geographic areas. In Germany in 1928,

only 2% of the cases of bone and joint tuberculosis were due to *M. bovis* (Thoen & Bloom, 1995).

Presently, in developed countries infection by *M. bovis* is controlled through strict measures including milk pasteurization. However, the presence of a wildlife reservoir for *M. bovis* represents a continued risk to public health though re-infection of domestic herds by *M. bovis*. In the United Kingdom it is principally the badger and in New Zealand, the possum which are the reservoirs for endemic self-sustaining *M. bovis* (O'Reilly & Daborn, 1995)

M. bovis needs to be considered as a possible source of the lytic lesions seen at SCL-38 due to its presence in wildlife in the region. *M. bovis* is known to have a very broad host range (Grange, 1995). Species in which the pathogen has been reported, other than cattle, are goat, pig, sheep, horse, cat, dog, fennec fox, deer, bison, buffalo, badger, possum, hare, ferret, wild and feral pig, antelope, Arabian oryx, camel, llama, alpaca, humans and non-human primates (O'Reilly & Daborn, 1995). While infection to humans from other species is rare, except in the case of cattle to humans, it is not impossible. In Canada, in 1974, 81 of 394 individuals who came into contact with infected captive elk tested positive for tuberculosis, with one individual developing a full blown case of tuberculosis, while in another case 7 of 24 zookeepers, who came into contract with a tuberculous white rhino, tested positive for tuberculosis in a six month period (Grange, 1995). In this case, all infected individuals were introduced to a regime of anti-tuberculine drugs to prevent development of overt disease. Clinically, *M. bovis* shows a high degree of virulence for both humans and cattle and the low proportion of reported infection by *M.*

bovis may be due to the failure of laboratories to distinguish between *M. bovis* and *M. tuberculosis* (Moda, Daborn, Grange & Cosivi 1996; O'Reilly & Daborn, 1995).

Therefore, with the possibility of transmission of *M. bovis* from a non-cattle source, it is not impossible that the individuals from SCL-38 came into contact with infected wildlife harboring *M. bovis*, most likely through ingestion, although aerosol transmission of the organism is also possible. Cow to human transmission has been documented for years; workers in butchering facilities have been found to have *M. bovis* pulmonary infections (O'Reilly & Daborn, 1995). In the western United States both mule deer and white tailed deer have been known to harbor *M. bovis*. In a report on tuberculosis in deer in 1991, it was indicated that the prevalence of disease in wild deer is less than 5% (O'Reilly & Daborn, 1995). Once infected, dissemination to bone and joint was not uncommon. Statistics taken from England and Wales from 1901-1932, previous to pasteurization, showed that the percentage of cases of tuberculosis caused by *M. bovis*, which disseminated to the bone and joints, was 20%. Once the disease disseminated to the bone and joints its appearance becomes indistinguishable from bone and joint infection caused by *M. tuberculosis*.

6.5.2 The Case for *Mycobacterium tuberculosis*

Mycobacterium tuberculosis is an ancient pathogen whose effects on morbidity and mortality have been great in human history. If we are to accept the evidence, that tuberculosis existed in the Americas previous to European contact, then it becomes possible to consider *M. tuberculosis* as the potential agent which produced the lytic lesions seen at SCL-38.

Skeletal tuberculosis makes up approximately 1-2% of all cases of tuberculosis (Chang, Rafii, McGuinness & Jagirdar, 1998; Rezai, Woo, Errico & Cooper, 1999; Davidson & Fernandez, 1995) and approximately 10% of all extrapulmonary tuberculosis in the United States (Chang et al., 1998). A retrospective survey done in 13 states and two cities between 1969 and 1973 indicated that bone and joint tuberculosis accounted for 1.12% of total tuberculosis (676 cases out of 60,606). It also found that bone and joint tuberculosis contributed 8.8% of all cases of extrapulmonary tuberculosis (676 cases out of 7,891) with spinal involvement contributing 40.7% of all cases of bone and joint tuberculosis (Davidson & Fernadez, 1995). However, in cases of strictly skeletal tuberculosis, the spine is the most common site of infection and accounts for 40-60% of all cases of such skeletal tuberculosis (Chang et al., 1998; Nessbaum, Rockswold, Bergman, Erickson & Seljeskog, 1995; Davidson & Fernadez, 1995).

It has also been noted that spinal tuberculosis in non-Caucasian individuals tends to involve the posterior elements of the vertebrae more often (Jain, Sawhney & Berry, 1993; Boxer, Pratt, Hine & McNicol 1992; Frankel, Daffner & Wang, 1991) and can be the only site of involvement (Boxer et al., 1992). The presentation of vertebral lesions in non-Caucasian individuals can also differ. The infection can be limited to one vertebral body with little to no change in adjacent vertebrae or intervening discs. Bone destruction is often accompanied by sclerotic alterations in bone texture and periosteal reaction (Davidson & Fernandez, 1995; Frankel et al., 1991). At SCL-38, two of the affected individuals had lytic changes in posterior vertebral elements, the transverse process and spinous process. Also three of the six individuals had varying degrees of sclerotic and periosteal bone growth in the vicinity of the lytic lesions.

Comparison of the lytic lesions seen at SCL-38 and photos of the lesions of individuals with known tuberculosis from the Hamann-Todd collection display a great deal of similarity. The Hamann-Todd collection is a series of 2041 cadavers gathered between 1911-1930. The individuals are catalogued by age, sex, race and cause of death. From this collection, there are 34 documented cases of skeletal tuberculosis (El-Najjar, 1981) with 25 individuals displaying vertebral involvement. One individual, specimen number 1116, a 31 year old black male, displayed circumferential lesions with open sinuses along T3 to L1. The lesions seen in this individual strongly resemble those seen in SCL-38-6 and 33. Descriptions and photos of known tuberculous lesions in the Terry collection, housed at the Smithsonian Institution, also resemble those of SCL-38.

From the collection of the Armed Forces Institute of Pathology (AFIP), comparisons between the photos of lesions of individuals with known skeletal tuberculosis and the vertebral lesions from SCL-38 show a marked similarity. Individuals MM 2577, MM718, AFIP 1001343 (MM 70) and MM 715 all present lesions which resemble those found at SCL-38. MM 2577 has involvement of T9-L3. T11 and T12 show tuberculous caries with scalloping and sequestra in T12. There is smooth wall resorption of L1 and L3 with L1 showing tubercular involvement of the right pedicle. MM 718 has involvement of T12-L4. T12, L1 and L2 have smooth wall caries with sequestra. There is no collapse of the vertebrae. AFIP 1001343 (MM 70) has involvement of T5-L5. The destruction of T10-L1 resulted in the collapse and angular kyphosis of the spine. There is a large draining abscess on the anterior portion of the body of L2 and a paravertebral abcess to L3. MM 715 has involvement of T7-L3. T12 and L1 have collapsed due to vertebral destruction. T7-L2 show scalloping of the anterior body due to paravertebral abscess .

7. Conclusion

In any paleopathological discussion on the diagnosis of skeletal lesions, it is not possible to determine with absolute certainty the disease processes which produced the skeletal lesions seen. In a room full of patients who are dead, the only absolute diagnosis which can be produced is that they are dead. The methods by which clinicians produce diagnoses and prescribe treatment is for the most part unavailable. Individuals cannot be asked what is troubling and painful. Symptoms cannot be determined, blood cannot be taken. In the end, we are left with a small piece in a medical puzzle. It is this small piece, the physical observations of skeletal defects, which we attempt to fit into the larger picture of a clinically diagnostic determination.

Very often, however, the skeletal lesions themselves are not enough to diagnosis the disease. The clinical data, to which we compare the skeletal lesions, are produced for a different subset of the population. What is important in the diagnosis of disease from a skeletal population compared to a living population can sometimes be quite different. Oftentimes, the details that are seen in a pathological skeleton are features that cannot be correlated to clinical medicine (Ortner, 1988). Clinically, skeletal lesions are viewed using plain film radiographs, computed tomographs and magnetic resonance imaging. While these techniques can provide a detailed picture of the skeletal defect to the clinician, they fail to provide the fine details of bone involvement that paleopathologists see commonly upon close examination of the gross specimen. Therefore, the correlation between the clinical description of skeletal lesions and those provided by paleopathologists can only be taken to a certain extent. This does not imply that clinical descriptions are not necessary or useful for the diagnosis of skeletal lesions in paleopathology. On the contrary, clinical

data is the ground stone upon which it is possible to build a diagnosis. It is simply that clinical data can only provide a useful array of choices, not an absolute diagnosis.

With these caveats said, the reason for providing a differential diagnosis for the lytic lesions found at SCL-38 become evident. It is also evident why it is not possible to determine with absolute certainly the pathogen responsible for the lytic lesions. Given the nature of the lytic lesions in these six individuals and the descriptions of the lesions produced by possible pathogens and disease processes, the most likely candidates responsible for the production of the lytic lesions seen are *C. immitis*, *M. bovis* and *M. tuberculosis*.

It is also notable that four out of the six afflicted individuals from SCL-38 have both lytic lesions and enamel hypoplasia. Out of 228 individuals, 32 individuals had enamel hypoplasia, six individuals had lytic lesions and four individuals had both enamel hypoplasia and lytic lesions. To determine if there is a correlation between the two conditions a chi-square analysis was performed. According to random probability, if the two events are independent, we should only have 0.83 individuals or, at most, one individual in which both conditions occur in this population. The calculation of the X^2 value from the observed and expected values finds the X^2 value to be 12.13, with one degree of freedom. Examination of a table of X^2 values with one degree of freedom finds that the calculated X^2 value yields a p value < 0.005. Therefore, it appears that there is a correlation between the presence of enamel hypoplasia and the lytic lesions.

The significance between the two conditions may be in the underlying etiology of enamel hypoplasia. Individuals with enamel hypoplasia are suspected of having childhood episodes of stress, malnutrition or illness, which temporarily interrupts their development.

Once the stress has passed, the individuals continue to develop; however, development of the dental enamel does not continue seamlessly. The individual is left with a hypoplastic defect in the enamel. For each episode of stress in which development is slowed or stopped, a horizontal defect is noted in the enamel. It is therefore possible, theoretically, to infer what the health status of the individual might have been during childhood.

For the four individuals with both pathological conditions, it may be that the presence of the enamel hypoplasia signified that these individuals, as children, either suffered from poor health or malnutrition or any other form of stress which may have lowered their immunity and consequently made them more susceptible to the disease process which eventually produced the lytic lesions.

7.1 Inferences

From the discussion above and the possible identification of the pathogens responsible for the vertebral lytic lesions seen, what can be inferred about the health of these individuals as well as the health of the rest of the population? What is known is that SCL-38 was not a typical cemetery site. A considerable proportion of the individuals buried in this cemetery were young men in their second and third decade of life. There is a notable decrease in the number of infants and children in this cemetery. It would be expected that a cemetery population would follow the demographics of a living population. The highest mortality rates should be among the very young and the very old, with the definition of "old" dependent on the particular population.

Instead, what is observed is a population heavily skewed towards young males, as well as individuals with some visible, serious skeletal pathology or defect. Among the 228

individuals at SCL-38, there were 10 cases of trauma, trauma in these cases defined as injuries to due projectile points, penetrating wounds or crushing injuries which are unlikely to have occurred without human intervention. Other pathologies include; six cases of periostitis, 21 cases of fractures, three cases of osteomyelitis not involving the vertebrae, three cases of serious congenital defect, one case of severe arthritis and six cases of vertebral lytic lesions. Cases considered serious congenital defects are those, which would infringe on the individuals ability to live a "normal life", such as cleft palate.

What does this mean? There are two major possibilities to consider concerning this population. The first is that this cemetery is a representative sample of the individuals living in the area and is therefore representative of the health of the individuals living in the area. The implications then, in accepting this assumption, is that among the Native Americans in the area, there was a high rate of mortality of young men in the prime of life for one reason or another. It also appears that children and infants did not suffer a high mortality rate and the majority survived to adulthood. Women appeared to live longer, not dying as young as the men appeared to.

The other possibility is that this cemetery was not representative of the populations living in the area as a whole. It could be that this particular cemetery was a burial ground for individuals who had died in an unusual manner. This may explain the high incidence of individuals with projectile point injuries, fractures and the fairly unusual inflammatory lesions found in the vertebrae. However, in a similar cemetery population CA-ALA-329, which is demographically typical of pre-industrial populations, there is an equal amount, if not greater number, of projectile injuries than at SCL-38 (R. Jurmain, personnel communication). Therefore, it may be that the amount of trauma seen at SCL-38 is no

more prevalent than other similar populations and consistent with a "normal" amount of interpersonal violence.

Either way, the vertebral lytic lesions seen in the individuals at SCL-38 are unusual in that this form of lytic inflammatory condition has not been previously reported California. At the very least, this implies that the population(s) living in the vicinity of the cemetery and who may have used the cemetery, might have had some form of health condition resulting possibly in a depressed immune system which would have left individuals susceptible to certain types of opportunistic disease, i.e. coccidioidomycosis. It may also have been that among this group, there was the presence of a more aggressive, more exotic infectious agent, possibly *mycobacterium tuberculosis*, which resulted in the production of vertebral lytic lesions.

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Appendix A

Inventory of Skeletal Remains

SCL38-6

Element: cranial	
temporal bone	left side, 1 fragment; right side incomplete but includes mastoid
maxilla	1 fragment
zygomatic bone	left side only; incomplete in 2 pieces
left orbit	1 fragment
parietal	9 fragments
occipital	incomplete; 9 fragments
sphenoid	fragmentary; 11 pieces
mandible	incomplete; 5 pieces
hyoid	incomplete; 1 piece of body
indeterminate fragments	33 fragments
Element: axial skeleton	
clavicle	left incomplete, 2 pieces; right incomplete, 1 piece
humerus	left incomplete, 2 pieces; right incomplete, 2 pieces
radius	left fragmentary, 4 pieces; right complete, 3 pieces
scapula	left incomplete, 4 pieces; right incomplete, 3 pieces
sterum	incomplete; 5 pieces
ulna	left complete, 4 pieces; right incomplete, 3 pieces
Element: appendicular skeleton	
femur	left incomplete, 3 pieces; right incomplete, 2 pieces
fibula	left incomplete, 3 pieces; right incomplete, 5 pieces
os coxa	left incomplete, 2 pieces; right incomplete, 2 pieces; 18 fragments
patella	left complete
Element: hand	
navicular	left complete
metacarpal 2	right incomplete, 2 pieces
metacarpal 3	right incomplete, 1 piece
metacarpal 5	fragmentary, 1 piece
phalanges	3 complete elements
Element: foot	
calcaneus	left incomplete, 3 pieces; right incomplete, 1 piece
cuboid	left complete; right complete
1st cuneiform	left incomplete, 1 piece
3rd cuneiform	left complete; right complete
navicular	left complete; right complete
talus	left complete; right complete
metatarsal 1	right complete

metatarsal 5	right complete
phalanges	1 complete element
Element: vertebrae	
C1	incomplete, 2 pieces
C2	incomplete, 2 pieces
C3-7	1 complete vertebra; 1 incomplete vertebra
T1	incomplete, 1 piece
T2	incomplete, 1 piece
T3-10	3 incomplete vertebrae; 24 vertebral fragments
T11-12	1 incomplete vertebra
Element: dentition	
upper dentition	left: I1, I2, C, P1, P2, M1, M2, M3
	right: I1, I2, C, M1, M2, M3
lower dentition	left: I1, I2, C, P1, P2, M1, M2, M3
	right: I1, I2, C, P1, P2, M1, M2

SCL-33

Element: cranial	
cranium	complete
hyoid	incomplete, 1 piece of wing
mandible	complete, 2 pieces
Element: axial skeleton	
clavicle	left complete; right incomplete, 1 piece
humerus	left complete; right complete
radius	left complete; right incomplete, 1 piece
scapula	left complete; right incomplete, 4 pieces
sternum	complete, 2 pieces
Element: appendicular skeleton	
femur	left complete; right complete
fibula	left complete, 1 piece; right incomplete, 1 piece
os coxa	left incomplete, 1 piece; right incomplete, 1 piece
patella	left complete
tibia	left complete; right complete
Element: hand	
hamate	right complete
lunate	left complete
navicular	right complete
metacarpal 1	left complete
metacarpal 2	left incomplete, 1 piece

metacarpal 3	left complete
metacarpal 4	left complete
metacarpal 5	left incomplete, 1 piece
phalanges	3 complete elements
Element: foot	
calcaneus	left complete
talus	left complete
metatarsal 1	left complete
metatarsal 5	1 fragment present
phalanges	2 complete
Elements: vertebrae	
C1	complete
C2	complete
C3-6	1 complete vertebra
C7	complete
T1-12	12 complete vertebrae
L1-5	5 complete vertebrae
sacrum	complete
Element: dentition	
upper dentition	left: I1, I2, C, P1, P2, M1, M2, M3
	right: I1, I2, C, P1, P2, M1, M2, M3
lower dentition	left: I1, I2, C, P1, P2, M1, M2, M3
	right: I1, I2, C, P1, P2, M1, M2

SCL38-62

Element: cranial	
frontal orbits	complete
nasal bone	complete
maxilla	complete
zygomatics	complete
sphenoid	incomplete, 11 fragments
parietal	left complete; right complete
occipital	incomplete, 3 pieces
temporal w/mastoids	left incomplete with mastoid process; right complete with process
cranial fragments	8 indeterminate fragments
mandible	complete, 3 pieces
hyoid	incomplete, 2 pieces
Element: axial skeleton	
clavicle	left incomplete, 2 pieces; right incomplete, 2 pieces
humerus	left incomplete, 2 pieces; right complete

radius	left incomplete, 2 pieces; right incomplete, 1 piece
scapula	left fragmentary, 3 pieces; right incomplete, 1 piece
ulna	incomplete, 1 piece; right incomplete, 1 piece
Element: appendicular skeleton	
femur	left incomplete, 1 piece; right incomplete, 2 pieces
fibula	left fragmentary, 2 pieces; right complete
os coxa	left fragmentary, 4 pieces; right incomplete, 2 pieces
Element: hand	
metacarpal 2	incomplete, 1 piece
phalanges	6 complete, 5 incomplete pieces
Element: feet	
calcaneus	left complete; right complete
cuboid	left complete; right complete
1st cuneiform	left complete; right complete
2nd cuneiform	left complete; right complete
3rd cuneiform	left complete; right complete
navicular	left complete; right complete
metatarsal 1	left complete; right complete
metatarsal 2	left complete; right complete
metatarsal 3	left complete; right complete
metatarsal 4	left complete; right complete
metatarsal 5	left in complete, 1 piece; right complete
phalanxes	10 complete elements
Element: vertebrae	
C1-7	all complete
T1	incomplete, 1 piece
T2-6	all complete
T7-11	incomplete, 5 pieces
T12	incomplete, 1 piece
L1-3	1 fragment
L4	incomplete, 1 piece
L5	incomplete, 1 piece
Indeterminate	1 thoracic fragment
Element: dentition	
upper	left: I1, I2, C, P1, P2, M1, M2, M3
	right: C, P1, P2, M1, M2, M3
lower	left: P1, P2, M1, M2, M3
	right: I2, C, P1, P2, M1, M2, M3

SCL38-107

Element: cranial	
cranium	complete in 20 pieces, except broken sphenoid
hyoid	incomplete, 1 piece (wing)
mandible	complete
Element: axial skeleton	
clavicle	left complete; right complete
humerus	left complete; right complete
radius	left complete; right complete
sternum	complete, 3 pieces
ulna	left complete; right complete
Element: appendicular skeleton	
femur	left incomplete, 1 piece; right complete
fibula	left complete; right complete
patella	right complete
os coxa	left complete; right complete
tibia	left complete; right complete
Element: hand	
capitate	left complete; right complete
greater multangular	left complete
hamate	left complete
lesser mutangular	left complete
lunate	left complete; right complete
navicular	left complete
metacarpal 1	left complete; right complete
metacarpal 2	left complete; right complete
metacarpal 3	left complete; right complete
metacarpal 4	left complete; right complete
metacarpal 5	left complete; right complete
phalanges	19 complete elements
Element: foot	
calcaneus	left complete; right complete
cuboid	left complete
1st cuneiform	left complete; right complete
2nd cuneiform	left complete; right complete
3rd cuneiform	right complete
navicular	left complete; right complete
talus	left complete
metatarsal 1	left complete; right complete
metatarsal 2	left complete; right complete
metatarsal 3	left complete; right complete

metatarsal 4	right complete
metararsal 5	left complete; right complete
phalanges	13 complete elements
Element: vertebrae	
C1-7	all complete
T1-11	all complete
T12	incomplete, 3 pieces
L1-5	all complete
Elements: dentition	
upper	left: I1, I2, C, P1, P2, M1, M2, M3
	right: I1, I2, C, P1, P2, M1, M2, M3
lower	left: I1, I2, C, P1, P2, M1, M2, M3
	right: I1, I2, C, P1, P2, M1, M2

SCL38-109

Element: cranial	
cranium	complete
hyoid	incomplete, 1 piece (wing)
mandible	complete, 2 pieces
Element: axial skeleton	
clavicle	left complete; right complete
humerus	left complete; right complete
radius	left complete; right complete, 1 piece
scapula	left complete; right incomplete, 1 piece
ulna	left incomplete, 1 piece; right complete
Element: appendicular skeleton	
femur	left complete; right complete
fibula	left incomplete, 2 pieces; right incomplete, 3 pieces
os coxa	left incomplete, 4 pieces; right incomplete, 2 pieces; 2 indeterminate fragments
tibia	left complete; right complete
Element: hand	
navicular	right complete
metacarpal 2	left complete; right complete
metacarpal 3	right complete
metacarpal 4	right complete
phalanges	4 complete elements
Element: foot	
calcaneus	left complete; right complete
1st cuneiform	left complete

talus	left complete; right complete
metatarsal 1	left complete
metatarsal 3	left complete; right complete
metatarsal 4	right complete
metatarsal 5	right complete
Element: vertebrae	
C1	complete
C3-4	all complete
C6-7	all complete
T2-12	11 complete vertebrae
L1-5	all complete
sacrum	complete
Element: dentition	
upper	left: I1, I2, P1, P2, M1, M2, M3
	right: I1, I2, P1, P2, M1, M2, M3
lower	left: I1, I2, P1, P2, M1, M2, M3
	right: I1, I2, P1, P2, M1, M2, M3

SCL38-229

Element: cranial	
mandible	incomplete, 1 piece
Element: axial skeleton	
humerus	left incomplete, 1 piece; right incomplete, 1 piece
radius	left incomplete, 1 piece
ulna	left incomplete, 2 pieces; right incomplete, 1 piece
Element: appendicular skeletal	
femur	left incomplete, 1 piece
os coxa	left incomplete, 3 pieces; right incomplete, 3 pieces
patella	right complete
Element: hand	
metacarpal 2	right complete
phalanges	1 complete element
Element: foot	
calcaneus	right complete
talus	right complete
phalanxes	1 complete element
Element: vertebrae	
C3-7	3 complete vertebrae, 1 incomplete vertebra
T1	complete

T2	complete
T3-10	1 complete vertebra, 1 vertebral fragment
T11-12	1 complete vertebra
L1-4	2 complete vertebrae
Element: dentition	
upper	left: C
lower	left: C, P1, M1

Appendix B

Primer Sequence for Mycobacterium Amplification

Primers for *Mycobacterium tuberculosis*

1. oxyRTB-1 (forward primer)

   5'- TGG CCG GGC TTC GCG CGT -3'

2. oxyRMT-1 (reverse primer)

   5'- GCA CGA CGG TGG CCA GGC A -3'

Primers for *Mycobacterium bovis*

1. oxyRTB-1 (forward primer)

   5'- TGG CCG GGC TTC GCG CGT -3'

2. oxyRMB-1 (reverse primer)

   5'- TGC ACG ACG GTG GCC AGG TA-3'

Appendix C

Inventory of Pathologies Other than Vertebral Lytic Lesions at SCL-38

Burial #	Age	Sex	Pathology
1	25-35	M	Severe periostitis on right tibia and fibula
13	30-45	M	Projectile point trauma in right femur
16	30-45	M	Fracture of right femur
17	25+	I	Slight periostitis on tibia
19	25+	F	Reactive bone present on carpals and lunate; possible fracture
24	30+	M	Osteomyelitis in right fibula due to external trauma
27	30+	M	scapula degenerative on both sides; possible congenital defect slipped epiphysis on right radius; possible congenital defect right medial epicondyle underdeveloped cystic changes seen on humeral head
38	45-60	M	Moderate angular defect on left radius from healed fracture Angular deformity of left ulna from healed fracture Fracture of proximal end of middle hand phalanx
42	20-24	M	Left elbow crushed; distal humerus, proximal ulna
44	4.5-6	I	Slight periostitis on right tibia, tibia also slightly bowed Right ulna surface slightly expanded
52	18-23	M	Slight periostitis of right tibia
53	21-18	M	Probable mastoiditis
54	34-50	F	Trauma, humeral head mostly gone; probably compression fracture
55	27-32	F	Ununited fracture of the ulna
57	35-45	F	Extreme hypertrophy of ilium; ilium remodeled with beginning of excavation
61	25-35	M	Fracture of the ulna
69	27-36	M	Circumscribed hole in ilium w/moderate perostitis on internal surface
74	35+	F	Anterior displacement of right radius due to fracture; well healed Medial displacement of right ulna due to fracture; well healed Slight lateral displacement of right radius along epiphyseal plate due to fracture; well healed
76	25+	M	Left hip displaced; femoral head mushroomed; probable trauma Hypertrophy of sacrum L4 is partially collapsed; probable trauma Nasal bone fracture, facial trauma

79	29-35	M	Un-united fracture of right humerus Moderate periostitis on left scapula blade Severe periostitis, remodeled, on left greater trochanter and superior lateral shaft of femur Slight periostitis on clavicles

87	24-40	M	Perforation of body of T6; congenital Wedge shaped hole present in the middle of the centrum of three thoracic vertebrae; remnant of notocord development
90	21-25	F	T11 unfused spinous process
91	15-20	I	Projectile point trauma in phalanx, projectile present
93	45-55	F	Healed fracture of ribs, lipping present
97	18-23	M	Unfused neural arch on one side of C1 and C2; congenital defect
118	30-45	M	Cervical DJD; collapse of C4-7, severe arthritis with wedging of vertebral bodies. Compression fracture of bodies Collapse of L1
120	18-20	F	Large circumscribed hole in cranium on the posterior parietal some of the inner table remaining; possible tumor or trauma at least 2 years prior to death
121	40-50	M	Fracture of right femur; well healed
131	35-45	M	Healed fracture of right pubis; ischio-pubic ramus
138	40-44	M	Depression fracture on right side of cranium, penetrating wound Blunt object trauma of right orbit; some healing present Lower third shaft of radius slightly enlarged and angulated; congenital defect
140	31-40	M	C6, C7, T; large projectile point found in vertebrae; trauma
142	15-18	M	Projectile point present in rib Hole present in T8; possibly perimortem
144	18-22	M	Breaks in cranium, cut marks, slashing wound, on medial aspect; possible perimortem Right mastoid enlarged; possibly due to crushing blow to brow ridge
148	25-35	M	Healed fracture of right tibia
152	20	M	Projectile point trauma; projectile found in chest cavity Healing lesion in left scapula with accompanying lesions on left ribs 6 and 7, anterior to scapula
157	25-35	M	Right external meatus closed; deafness
161	30-45	M	Projectile point in L5, with accompanying inflammation. No reactive bone around projectile, disc space affected.
162	21-30	M	Healed fracture of right humerus; inflammation of the entire posterior distal shaft Inflammatory reaction of left tibia
164	35-3	M	Penetrating wound on left tibia, reactive bone outside of lesion; long standing, wound well remodeled

171	35-39	M	Healed fracture of left ulna, distal shaft swollen and slightly angulated Healed ovoid depression in cranium; possible depression fracture
183*	45-55	F	T12, L1, L2 fused together with extensive rib involvement. Reactive lipping with possible breaks on the sternal ends of ribs, bodies of vertebrae and joints all fused together. Three draining sinuses present on fused vertebrae. L1 is collapsed, severe kyphosis and secondary osteomyelitis. Slight periostitis from upper lateral shaft to head of left femur Healed fracture of right ulna with medial angulation Healed fracture of left ulna and radius at distal ends, angular deformity.
196	16-23	F	Healed fracture of right parietal; bone still slightly depressed Two holes present on occipital; either trauma or congenital
209	16-23	I	Sacralized L5 Inferior facets of L4 missing (spondolysis) T13 present
210	25+	F	Sequestrae present in right femoral shaft
219	25-30	M	T4, T5 fused due to compression fracture on lateral side of vertebrae, compression fracture of pedicle. Dens separated congenitally. T1-5 unusual pattern of DJD Unusual # of Harris lines present
221	25-35	F	Depression fracture of frontal bone
227	15-19	F	Cleft palate
231	30-40	M	Healed fracture of right radius; angular deformity Un-united fracture of right ulna
232	35-50	F	Healed mid-shaft fracture of left ulna; slight angular deformity
234	35+	F	Greenstick fracture of distal shaft of left ulna; slight angular deformity
237	18-25	M	Depression fracture of right parietal
238	25-35	M	Possible Collies fracture of right radius; slight angular deformity Right carpals are crushed Right capitate is deformed due to trauma Right lunate is crushed Only metacapals 1, 2, 3 appear undamaged

Individual #183 appears to be affected by the same pathological process as the other individuals with vertebral lytic lesions. The individual was reburied however before complete analysis could be performed.

Appendix D

Photos of Lytic Lesions found at SCL-38

Order of photos appear as listed:

1) SCL-38-6, anterior view of body of L5.

2) SCL-38-33, superior view of inferior body surface of T12.

3) SCL-38-33, anterior view of surface of body of L1.

4) SCL-38-62, superior view of dorsal surface of T12-L2.

5) SCL-38-62, superior view of ventral surface of T12-L2.

6) SCL-38-107, superior view of inferior surface of the body of L4.

7) SCL-38-109, superior view of superior dorsal aspect of T7.

8) SCL-38-229, superior view of right transverse process of T12.

SCL-38-6, anterior view of body of L5

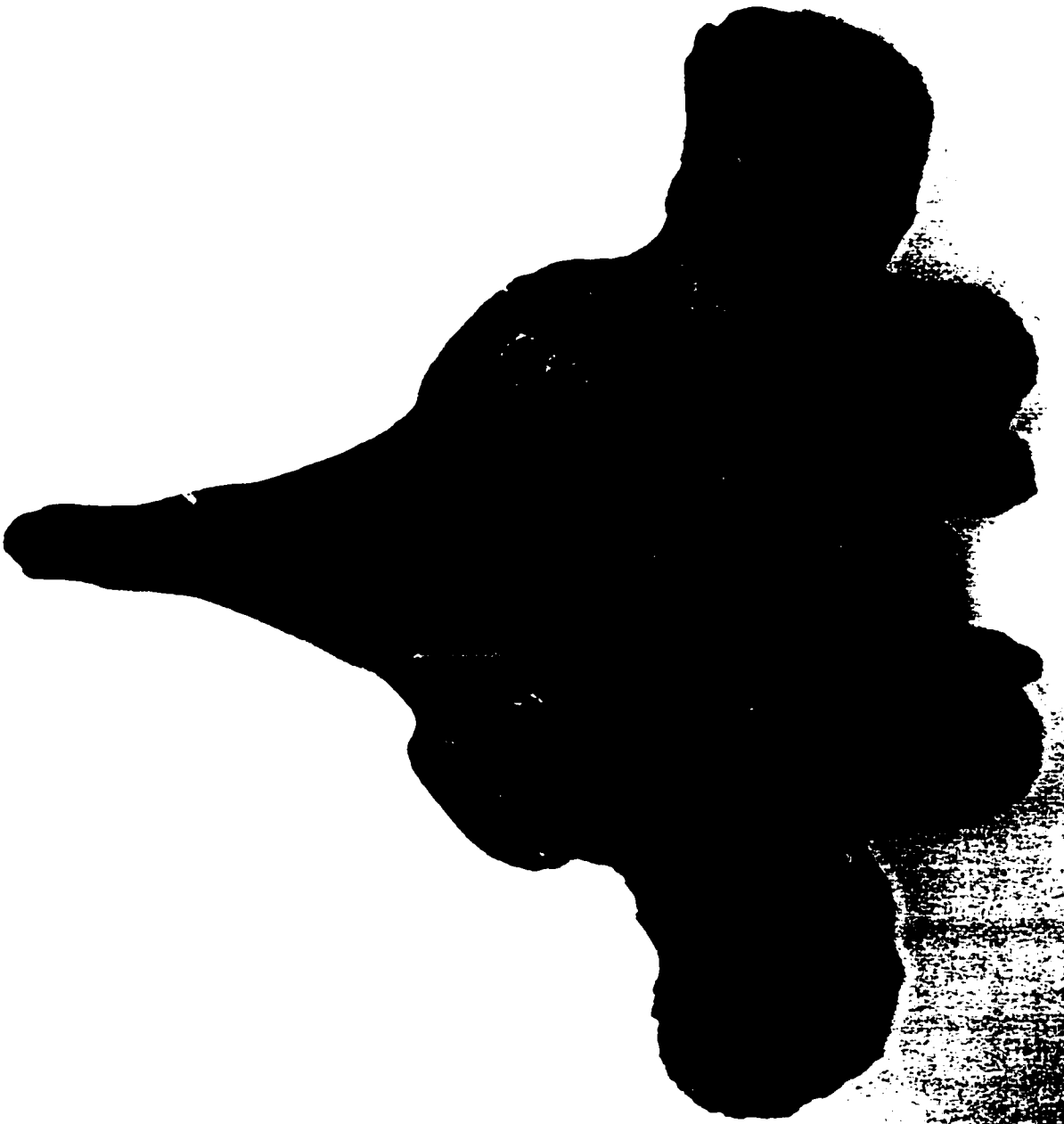
SCL-38-33, superior view of inferior body surface of T12


of surface of body of L1

SCL-38-62, superior view of dorsal surface of T12-L2

SCL-38-62, superior view of ve

SCL-38-109, superior view of dorsal aspect of T7



SCL-38-229, superior vi T12