DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS IN A LATE NINETEENTH EARLY TWENTIETH CENTURY ALMSHOUSE CEMETERY

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ABSTRACT

THESIS: Diffuse Idiopathic Skeletal Hyperostosis in a Late Nineteenth Early Twentieth Century Almshouse Cemetery

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Diffuse idiopathic skeletal hyperostosis (DISH) is a rheumatology term for a particular type of vertebral arthritis involving the calcification of the right aspect of the anterolateral ligament (ALL) and the presence of ligament ossification at particular peripheral joints. DISH is most common among middle to late age males and is thought to be present in 10 percent of males over the age of 65. Although the etiology of the disease is unknown, many have associated it with diabetes and a high status lifestyle. In this thesis, DISH is examined in a late nineteenth, early twentieth century almshouse cemetery known as the Milwaukee County Institution Grounds (MCIG) cemetery. Due to the health and diet of the immigrant peoples living in Milwaukee during the MCIG cemetery’s usage, 1850 to 1974, it is suspected that diabetes would not have been a common disorder, thus leading to little to no DISH presence in the cemetery population. However, DISH is seen in the MCIG population which suggests that the etiology of DISH is not a result of diet or diabetes but other factors altogether.
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# Table of Contents

Abstract............................................................................................................................ i  
Acknowledgements........................................................................................................ ii  
Table of Contents.............................................................................................................. iii  
List of Figures.................................................................................................................. v  
List of Tables................................................................................................................... vi  
Abbreviations Used......................................................................................................... vii  

Chapter I: Introduction.................................................................................................... 1  

Chapter II: Milwaukee Institution Grounds Cemetery: History and Investigations .......... 4  
  Milwaukee County Institution Grounds Cemetery......................................................... 4  
  Excavation.................................................................................................................... 5  
  Poor Farm and Almshouse Cemetery............................................................................ 13  

Chapter III: A Brief History of Milwaukee and City’s Immigrant Occupants................ 19  
  Milwaukee Immigrant Background.............................................................................. 19  
  The Unhealthy City....................................................................................................... 26  

Chapter IV: Diffuse Idiopathic Skeletal Hyperostosis Literature Review.......................... 34  
  Definition of Terms and Anatomical Information....................................................... 34  
  Establishment of Terms and Criteria......................................................................... 46  
  Diffuse Idiopathic Skeletal Hyperostosis and Ankylosing Spondylitis......................... 59  
  DISH Case Studies and DISH in Modern Populations................................................. 61  

Chapter V: Diffuse Idiopathic Skeletal Hyperostosis throughout History......................... 65  
  Middle Paleolithic: Neanderthal................................................................................... 65  
  Egyptians...................................................................................................................... 66  
  Sixth Century Enotrians in Magna Graecia Italy......................................................... 67  
  DISH and Monks......................................................................................................... 67  
  Pima Indians................................................................................................................. 72  
  DISH in Non-Human Subjects..................................................................................... 73  

Chapter VI: Etiology......................................................................................................... 75  
  Diabetes Mellitus and Obesity...................................................................................... 76  
  HLA-B Gene Locus....................................................................................................... 80  
  Other Genetic Involvement......................................................................................... 82  
  Ossification of Posterior Longitudinal Ligament (OPLL)............................................. 83  
  Myelopathy................................................................................................................... 83  
  Dysphagia....................................................................................................................... 84  
  DISH Detection............................................................................................................ 86
List of Figures

Figure 1: 1916 MCIG Map................................................................. 6
Figure 2: Wisconsin County Map......................................................... 7
Figure 3: MCIG Excavation................................................................. 8
Figure 4: MCIG Excavation Divisions................................................... 10
Figure 5: MCIG Cemetery Location..................................................... 15
Figure 6: New Almshouse................................................................. 16
Figure 7: 1930 Milwaukee County General Hospital............................ 17
Figure 8: 1880 Milwaukee Insane Asylum........................................... 18
Figure 9: 1850 Milwaukee Immigrant Population................................. 21
Figure 10: 1850-1910 Milwaukee Population Growth Chart....................... 21
Figure 11: Milwaukee Ward Map........................................................ 22
Figure 12: Catholic Churches in Wisconsin........................................ 24
Figure 13: Infant Mortality Chart......................................................... 27
Figure 14: Milwaukee Death Rates by Ward.......................................... 28
Figure 15: Milwaukee Health Award..................................................... 31
Figure 16: 1870-1915 Mortality Rates per 1,000................................... 32
Figure 17: Human Spinal Column......................................................... 35
Figure 18: Lumbar Vertebra Cranial View............................................. 37
Figure 19: Lumbar Vertebra Lateral View.............................................. 37
Figure 20: Intervertebral Space........................................................... 38
Figure 21: Vertebral Ligaments............................................................ 39
Figure 22: ALL Fusion Location.......................................................... 40
Figure 23: Extraspinal DISH Manifestation Areas................................. 42
Figure 24: Calcaneus Superior View..................................................... 43
Figure 25: Patella Anterior View.......................................................... 43
Figure 26: Ulna Posterior View............................................................. 44
Figure 27: Tibia Anterior View.............................................................. 44
Figure 28: Pelvis Lateral View.............................................................. 45
Figure 29: 3-5mm Ulna Bone Spur....................................................... 91
Figure 30: >5mm Ulna Bone Spur......................................................... 91
Figure 31: 3-5mm Tibia Bone Spur...................................................... 92
Figure 32: >5mm Tibia Bone Spur....................................................... 92
Figure 33: >5mm Patella Bone Spur..................................................... 93
Figure 34: >5 Iliac Crest Bone Spur...................................................... 93
Figure 35: 3-5mm Calcaneus Bone Spur............................................... 94
Figure 36: Non-DISH Vertebral Column.............................................. 100
Figure 37: Ankylosing Spondylitis....................................................... 102
Figure 38: Puzzle Piece Kissing Osteophytes........................................ 103
Figure 39: Puzzle Piece Kissing Osteophytes........................................ 106
Figure 40: Cervical Fusion................................................................. 115
List of Tables

Table 1: Results of Study................................................................................................................. 98
Table 2: DISH Results.................................................................................................................... 105
Table 3: DISH Age.......................................................................................................................... 107
Table 4: DISH Individuals with Extraspinal Involvement............................................................... 107
Table 5: DISH Patient Manifestations........................................................................................... 107
Table 6: DISH Extraspinal Presence by Grade.............................................................................. 109
Table 7: DISH-like Results............................................................................................................ 110
Table 8: DISH-like Age.................................................................................................................. 111
Table 9: DISH-like Individuals with Extraspinal Involvement........................................................ 111
Table 10: DISH-like Patient Manifestations.................................................................................. 111
Table 11: DISH-like Extraspinal Presence by Grade..................................................................... 114
Table 12: Notable DISH studies..................................................................................................... 117
Abbreviations Used

AH – Ankylosing Hyperostosis

ALL – Anterior Longitudinal Ligament

AS – Ankylosing Spondylitis

BMP-2 - Bone Morphogenic Protein-2

CT - Computed Tomography

DISH – Diffuse Idiopathic Skeletal Hyperostosis

EVOS - European Vertebral Osteoporosis Study

GLARC - Great Lakes Archaeological Research Center Inc.

IGF-1 - Insulin-like Growth Factor-1

MCIG – Milwaukee County Institution Grounds

MGP - Matrix Gla Protein

MRI – Magnetic Resonance Imaging

NASS – North American Spine Society

OALL – Ossification of the Posterior Longitudinal Ligament

OPLL – Ossification of the Posterior Longitudinal Ligament

PA – Posterior Anterior

PLL – Posterior Longitudinal Ligament

SDCHSR – Standards for Data Collection of Human Skeletal Remains

WHO - World Health Organization
Chapter I
Introduction

Diffuse idiopathic skeletal hyperostosis (DISH) is a rheumatology term for a particular type of vertebral arthritis involving the calcification of the right aspect of the anterolateral ligament (ALL) and the presence of ligament ossification at particular peripheral joints. The World Health Organization defines diffuse idiopathic skeletal hyperostosis as “Ankylosing Hyperostosis [Forestier’s]” (M48.1) and files the disease under “Diseases of the musculoskeletal system and connective tissue (M00-M99)” (WHO, 2007). This particular disorder has an unknown etiology although several varying genetic, environmental and dietary influences have been suggested (Resnick et al., 1975). One of the most commonly suggested causes of DISH is diet, since it is common in individuals suffering from adult onset diabetes (Julkunen et al., 1971).

The main purpose of the following thesis is to support the interpretation that DISH occurs independently of diet and is most likely a genetic manifestation. The research goal of this thesis shall be achieved through presentation of human skeletal data from the Milwaukee County Institution Grounds cemetery. In this skeletal data set DISH was found to be 1.23 percent prevalent. The MCIG cemetery is an important sample because it shows that those buried within it received less than adequate nutrition, further implying that adult onset diabetes, one of the current suggested causes of DISH, was quite uncommon. This thesis will go on to suggest a new grading scale for fused vertebrae, one of the crucial aspects of DISH identification. A new term will be introduced: “puzzle piece kissing,” which implies an inevitable ossification between vertebrae without the ossified attachment of adjacent discs. This thesis will then address the need for a uniform categorical system for extraspinal DISH manifestations, which, when placed on a
three stage scale, help the examiner to better identify the disease in skeletal collections. This thesis will also present one case in which DISH is present with ankylosing spondylitis (AS), another vertebral ligament ossification disorder. Both these diseases exist together in a transitional or early form. The conclusions reached within this thesis will add to the current literature by suggesting a revision of the current criteria for qualifying an individual as having DISH, and more importantly, encouraging that more emphasis be placed on genetic influences and less on diabetes and dietary suggestions.

This thesis will begin with a general background of the Milwaukee County Institution Grounds and the excavation of the cemetery grounds. A general overview of the Milwaukee immigrant background and the general health of the city over time will also be addressed. The point of this section is to establish information about the area around MCIG and discuss the hardships that those buried within the cemeteries faced. It was not easy being a first generation immigrant in America at the turn of the century (19th to 20th) and it was a daily struggle for many to keep themselves and their families housed, clothed and fed.

The origins of DISH including possible etiologies, population studies, and case studies involving the disease, are discussed in Chapter IV. DISH was not always known as DISH and the criteria for the disease did not spring up overnight. It is important to establish how knowledge of the disease progressed over time before attempting to amend the current criteria for the disease. Chapter V will include information about DISH throughout prehistory and history, including DISH in non-human subjects. DISH is by no means a new disease, and this chapter will show the geographic and temporal variation of the disease.

The suggested etiologies proposed for DISH over the years are presented in Chapter VI, along with arguments for and against each suggestion. The cases for and against the suggestion
of diabetes as a cause of DISH and possible genetic involvement, most particularly that of the HLA-B gene locus, are also explored in this chapter. Other medical issues concerned with DISH including dysphagia are summarized in Chapter VI.

In Chapter VII the methods and materials used in this thesis are presented. The criteria used in examining the skeletal sample and identifying DISH and DISH-like characteristics in the sample are discussed. The skeletal analysis methods used in this study are also summarized in Chapter VII. In Chapter VIII, the qualitative and quantitative results of the thesis are presented. A thorough account of the individual skeletons examined can be found in Appendix C. In Chapter IX, the results of the thesis are examined in detail. In this chapter the background information about Milwaukee and the DISH literature are used to interpret and explain the results generated from this thesis. Specifically, changes needed in the criteria for DISH at the spinal and extraspinal levels are proposed in this chapter. A case is also presented which suggests that it is possible for both DISH and AS to exist in early or transitional form in a single individual. Lastly and most importantly, the data gathered from this study suggests that the cause of DISH is most likely not directly related to diabetes.

The conclusions of this study are summarized in Chapter IX. As discussed in detail in Chapter IX, the most important finding of this study is the refutation of the connection between diabetes and DISH. The MCIG cemetery collection reinforces the conclusion that DISH is most likely a hereditary disorder, but keeping in mind that the etiology is still unknown at this time.
Chapter II

Milwaukee Institution Grounds Cemetery: History and Investigations

Background information about the MCIG cemetery excavation, the history of the cemetery and the associated internments are discussed in Chapter II. The location of the MCIG cemetery in relation to the city of Milwaukee and a brief history of the area are also presented. An understanding of these elements of Wisconsin history is integral to creating a timeframe for the MCIG cemetery collection being examined in this thesis.

Milwaukee County Institution Grounds Cemetery

In August of 1991, construction of the Milwaukee County Medical Complex began in Wauwatosa, Wisconsin (Richards, 1997). Construction was halted in the early stages, however, when disturbed human skeletal remains were uncovered at the site (Richards, 1997). Representatives from the State Historical Society of Wisconsin were called in to conduct an evaluation and determined that as many as a few hundred burials may exist at the site (Richards, 1997). It was soon realized however, that historical records show the cemetery was acknowledged prior to the date of construction (Bruhy, 1980; Richards, 1997). The particular 1980 report revealed that as many as 5,000 burials had been made in MCIG (Milwaukee County Institution Grounds, as it is known) between 1850 and 1974 (a statistic Richards’ later confirms through report investigation) (Bruhy, 1980). Excavation began in September 1991 and continued until December then began again in March of 1992, and continued until November of that year (Richards and Kastell, 1993). The fieldwork revealed a total of 1649 excavated burials with
varying levels of fragmentation and preservation (Richards, 1997). Although a manifest of burials existed, the disintegration of wooden burial tags in the cemetery made the task of connecting names with burials almost impossible (Richards, 1997). The cemetery itself goes by a number of various names: The Poorhouse Cemetery, the Almshouse Cemetery, the Potter’s Field, the Milwaukee County Poor Farm Cemetery and the Milwaukee County Pauper Cemetery (Richards, 1997). Throughout this thesis the cemetery will be referred to as MCIG cemetery, the Milwaukee County Institution Grounds cemetery. The title MCIG referred to the area of land that housed several important medical buildings (Figure 1).

**Excavation**

Great Lakes Archaeological Research Center Inc. (GLARC) began excavating the MCIG on September 4, 1991 under the direction of principal investigator Patricia Richards and Matthias Kastell (Richards and Kastell, 1993). The cemetery is located in the: “NE1/4, SE1/4, SW1/4, NW1/4 of section 28, T7N, R21E, in the city of Wauwatosa” (Richards, 1997:38). Figure 2 illustrates the location of the cemetery on a state map of the counties of Wisconsin. The state began burying paupers in the cemetery in 1853 and continued until 1974 when the county began using private funeral homes to bury the poor in private cemeteries (Richards, 1997). Burials were excavated from three distinct sections of the cemetery (Richards, 1997). One of these sections was located near a nursing school residence hall, construction of which apparently had disturbed an unknown number of MCIG burials in 1932 (Richards, 1997). Research and testing soon confirmed that instead of the 100 to 150 burials originally thought to be held in the cemetery, the number was actually several thousand (Figure 3) (Richards, 1997).
Figure 1: A 1916 map of the Milwaukee County Institution Grounds. This area is located six miles west of Milwaukee and encompasses 1,200 acres. (Figure Credit: Avella, 1987: 214)
Figure 2: Wisconsin county map. The dot in the lower right is the location of the MCIG, on the western edge of the city of Milwaukee, also known as Wauwatosa.
Figure 3: A map of the MCIG cemetery excavation. (Figure Credit: Richards, 1997:45)
The complete construction site was divided into 20 areas, lettered from A-N (no burials were recovered from I or M (Figure 4) (Richards, 1997). The datum point, the point from which all the burials in the excavation were measured, can be seen in Figure 3. The areas were then assigned particular lot numbers, the numbers differing depending on whether the burial was a primary (one or more individuals per coffin or pit), secondary (skeletal remains from one or more individuals) or surface collection (from disturbed sections) (Richards, 1997). The excavation was then carried out with a back hoe, and based on the reports, many of the grave outlines were determined based on soil matrix (Richards, 1997). A data form was created for each burial containing the lot number, elevation and coordinates, any photos taken, and the name of the recorder; as well as the coffin shape, head position, burial type (extended, disturbed, other), age (when applicable from burials reports) and a sketch of the burial (Richards, 1997). The skeletal materials were then separately bagged and labeled, boxed up and sent off to Marquette University for analysis (Richards, 1997).

Several laws were in put in place to protect the preservation of cemeteries like the MCIG:

The 1894 Milwaukee County Rules and Regulations for the County Farm and Almshouse include Rule 17. This Rule relates to pauper burials and stipulated, among other things, required depth of grave, the placement of a painted and numbered head board for each grave, decent order as related to the condition of the cemetery and a record for each burial that included name, date and cause of death, number of burial permit and number of grave. As it will be seen, the extent to which these rules were followed varies, but they served as the template for the burials of individuals in the poor farm cemetery (Richards, 1997: 9).
Figure 4: Map of cemetery divisions. (Figure Credit: Richards, 1997: 108)
As Richards describes, these laws were sometimes not completely followed when the paupers were originally buried (1997). The situation was further complicated by the negligence of the construction workers and lack of law enforcement throughout the excavation process (Richards, 1997). As a result of both these, the collection itself and burial records are flawed (Richards, 1997).

It is important to mention that there is a Registry of Burials for the Milwaukee County Poor Farm, the authors of which are unknown. Within this book are the burial records for many of those individuals buried in the MCIG cemetery during the time of its use, 1882-1974 (Richards, 1997).

This register [Register of Burial at Milwaukee County Poor Farm (1882-1974)] was consulted in a general sense to characterize the population buried in the Milwaukee County Poor Farm Cemetery, and in a specific sense for those very few individual cases where burial ID information was recovered archaeologically. In most, but not all, cases it was impossible to link the individuals listed in the ledger to specific burials. Furthermore, the nature of the information recorded in the register differs from year to year. As a result, the set of information for each recorded burial is inconsistent. (Richards, 1997: 5).

Richards’ examination of the records revealed more than 3,500 burials in the MCIG cemetery including over 1,000 subadults (Richards, 1997). Based on the number of bodies recovered, this is highly suggestive of a potential mass disturbing of the cemetery when the nurses’ residence was built in the 1930’s (Richards, 1997). The burial list also contained a compiled cause of death for many individuals between the years 1881 and 1925 and it is important to mention that of the total number of entries only 5 individuals were listed as having died from “diabetes” or “diabetes millitas” (original spelling from document) (Richards, 1997: 82). Although this does not imply the total presence of diabetes, only that which led to death, the astonishingly small number is an
important piece of information in the current discussion of DISH. In the late nineteenth, early twentieth century, before the discovery of insulin in 1922, an individual was lucky to live two years with diabetes (Banting et al., 1922; King and Rubin, 2003). In spite of this fact, the burial records do not show a high number of diabetes death, thus suggesting that diabetes was not highly prevalent in the MCIG cemetery collection.

Richards admits that financial constraints on cemeteries during the turn of the 20th century were common. Such is the case with MCIG: "The Milwaukee County poor farm cemetery existed on one end of the financial continuum" (Richards, 1997:10). Richards used archaeological evidence and grave goods within the Milwaukee context to determine the types of individuals buried within the cemetery. She states that although the individuals do not vary in terms of status, they are distinct populations:

(1) community poor; (2) residents of various county institutions; and (3) suicides, victims of murder or accidents, other unidentified individuals, and those with no kin. (Richards, 1997:11)

However, particular scholars were apt to disagree with her assumptions of status based on grave goods alone:

Shawn Phillips’ comment that ‘economic poverty was not the only road to pauperism in New York state during the nineteenth century’ and her warning ‘it is risky to assume that a skeletal sample associated with an almshouse represents the poorest individuals from a society’ (1997:81), struck a chord…The results of this analysis indicate, instead, that community paupers make up the largest category of the cemetery. Supported by demographic data, the archaeological analysis of grave goods recovered from the Milwaukee County Poor Farm Cemetery has shown us at least three separate roads to pauperism during the late nineteenth and early twentieth century in Milwaukee. These include (1) mental illness, (2) very poor relatives or lack of relatives and (3) accident, suicide or murder” (Richards, 1997:273)
An analysis by Norman Sullivan of Marquette University in the years following the collection’s arrival at Marquette University, yielded specific data concerning the number of burials within the collection. A grand total of 1,649 burials from an area of 2.82 acres were examined (Richards, 1997). A total of 985 adults, 588 subadults and 76 remains too fragmented to classify had been excavated from the MCIG Cemetery (Sullivan, 2007). Sex determination using Buikstra and Ubelaker’s Standards for Data Collection from Human Skeletal Remains (SDCHSR) (1994) suggested that the ratio of males to females was 7:1, placing the number of males in the collection at approximately 862 (Sullivan, 2007). This statistic has some importance in DISH studies since DISH is considered to be a predominantly male disorder. It is also important to notice that this skewed ratio is not reminiscent of the male to female ratio of Milwaukee at the turn of the century according to demographic records (White et al., 2006)

**Poor Farm and Almshouse History**

The first Milwaukee almshouse was built on the site now known as the MCIG site in 1852 and housed 24 people (Richards, 1997). The almshouse was a remodeled farm house originally owned by Hendrik Gregg in Wauwatosa, Wisconsin (Avella, 1987; WHS, 2004). In the 1900’s, Gregg donated the rest of his 160-acre farm to Wauwatosa to be used as a poor farm and it was soon expanded to nearly 1,200 acres (WHS, 2004). The complex was located between 85th and 108th streets, between Wisconsin Avenue and the Menomonee River (Figure 5) (Richards, 1997: 74,76,77; WHS, 2004: 49). The Almshouse itself and the institution grounds were originally created to house the elderly, the children, the sick and the insane of Milwaukee (Figure 6) (WHS, 2004). And although it was designed with good intentions and to save the county money, it was consistently in the red, which forced its early closure (Avella, 1987). It was
also under intense scrutiny during those years due to its poor sanitary conditions and questionable treatment of the inmates (Avella, 1987). It closed in 1859 but reopened the following year as a large 31-bed county hospital (WHS, 2004). The area was renamed the Milwaukee County Infirmary in 1917 (WHS, 2004). In the 1930’s the 650-bed Milwaukee County General Hospital opened, and was in use for almost 60 years until it was torn down in 1990 (Figure 7) (WHS, 2004). The MCIG cemetery is situated on the Milwaukee County General Complex Grounds (Figure 1) which contained the Poor Farm, the Insane Asylum (Figure 8) and the General Hospital (WHS, 2004).
Figure 5: Location of the MCIG cemetery (cemetery 2). (Figure Credit: Richards, 1997: 77)
Figure 6: A postcard showing the new almshouse, built in 1890. (Figure Credit: WHS, 2004: 50)
Figure 7: The Milwaukee County General Hospital (Circa 1930). (Figure Credit: WHS, 2004: 51 (WHS Photo LGP 904 and Courtesy of James Cerletty))
Figure 8: An artist’s rendering of the Insane Asylum (circa 1880). (Figure Credit: Avella, 1987:212)
Chapter III

A Brief History of Milwaukee and the City’s Immigrant Occupants

In this chapter a brief history of the city of Milwaukee around the time the MCIG cemetery was in use is presented. Internments in the MCIG cemetery mainly date to the early 20th century. Regarding historic context, Richards stresses that: “The questions asked of historic burials must be questions concerning the presence and place of the individual within social structure” (1997:35). The primary question of this thesis is: Can we assume that those individuals buried in the MCIG cemetery who display DISH were most likely not affected by dietary issues such as obesity and diabetes? This question is obviously one of inference but examining historical data may lead us to postulate that due to their living conditions and diet, the paupers of Milwaukee were not part of the high status lifestyle that would lead to obesity, currently suggested as a cause of DISH itself. The historic information in this chapter is intended to establish that the immigrants of early Milwaukee were relatively unhealthy individuals that would most likely not be afflicted with diabetes.

Milwaukee Immigrant Background

In 1890, Milwaukee had the largest percentage of immigrants of any American city (Leavitt, 1982: 13)

What would eventually be known as Milwaukee was first discussed in the literature when Father Marquette, a French Missionary, first moved up the shore from Chicago in 1674 to a land
inhabited by 1,000 to 1,500 native Indians (Anonymous, 1932). The area was founded as a trading post in 1751 by the American Fur Company and soon grew into a small village (Anonymous, 1932). On January 31st, 1836 the settlement became the city of Milwaukee when it elected Solomon Juneau, a fur trader, as its first mayor (Anonymous, 1932). In 1850, of the 20,000 individuals living in Milwaukee, 2/3 of them had immigrated within the past two years (Figure 9) (Rippl, 1985). In that same year, there were 200,000 U.S. born citizens in the state compared to a staggering 107,000 foreign born individuals (Rippl, 1985). Despite the influx of Irish immigrants due to the potato famine, Germans were by the far the most common European presence in Wisconsin, at 12 percent in 1850 (Rippl, 1985). By 1910, Milwaukee was the 12th largest city in the United States (Figure 10) (Leavitt, 1982). Immigration became the life blood of Milwaukee businesses; manufacturers built ports and canals in order to combat the onset of the great depression of 1929 (Rippl, 1985). Needless to say, the occupation of Milwaukee happened fast and with large numbers (Rippl, 1985).

Things seemed to be going well for this young city. People were finding their place and although the immigrants still arrived by the boatload (literally) the city itself could handle the influx (Rippl, 1985). In the 1860’s, each nationality settled into a different area of Milwaukee and found a place among various professions (Rippl, 1985). Milwaukee was sectioned off into various wards, (Figure 11) each nationality tending to group near each other and taking on the same sorts of occupations. The Germans (there being more of them) took to liquors, banks, real estate and lumber (Rippl, 1985). The Germans were situated, for the most part, on Milwaukee’s west side (Rippl, 1985). Many took to English very well, and were soon able to place themselves within upper level professions, usually law or medicine (Rippl, 1985). It is difficult to find a text on the history of Milwaukee that doesn’t declare it to be a German city.
Figure 9: Milwaukee immigrant population in 1850. Chart data gathered from Rippley, 1985.

Figure 10: Milwaukee population growth chart. Photocopied. (Figure Credit: Leavitt, 1982: 11)
Figure 11: Milwaukee ward map. Still in use to this date.
In 1880, 35 percent of Milwaukee residents were German born, the next closest being the Poles (Rippley, 1985). In 1900, a staggering 70 percent of Milwaukee residents were first or second generation Germans (Rippley, 1985).

The Poles were the second largest immigrant group in Milwaukee making up roughly 22 percent of the city’s population by 1900 (Leavitt, 1982). The Poles tended to gravitate towards church affairs (mainly Catholic) and settled into the south side of the city (Figure 12) (Leavitt, 1982; Rippley 1985). Since they were largely unskilled, the Poles never achieved the success that the German immigrants did (Leavitt, 1982). There were other immigrant groups present at the turn of the century in Milwaukee as well including “Irish, Italians, Russian Jews, Greeks, Bohemians, Hungarians…Scandinavians [and] a small black community” (Leavitt, 1982: 13).

Many of these immigrants took up arms in defense of the north during the Civil War of the 1860’s (Rippley, 1985). The German, Norwegian and Irish natives had the highest percentage of European presence in Wisconsin during the Civil War (Rippley, 1985). However, the people from these nationalities did not go willingly. When the drafts were implemented, an overwhelming majority failed to report for service (Rippley, 1985). Even when they did, many would remain behind the English speaking soldiers in battle and some sources say quite a few immigrants, particularly Germans, were not so against the idea of slavery (Rippley, 1985).

Milwaukee continued to be a Midwest melting pot, with 39 different nationalities present in 1870 and 46 in 1900 (Rippley, 1985). As one would assume, the cost of immigration began to take a toll on the small city and overcrowding began to have negative effects on Milwaukee culture:

Industrialization and the population explosion accentuated these negative aspects of the urban environment and allowed disease and death to flourish (Leavitt, 1982: 22).
Figure 12: Church breakdown in Wisconsin (by founding ethnic group). Chart data gathered from Rippley, 1985.
During that time the city’s death statistics ranked among the worst in the nation (Leavitt, 1982: 24).

Although immigrants were great for the thriving business district of Milwaukee (especially along the Menomonee river, where hydroelectric power was utilized) the facts do not lie: “The larger the percentage of foreign-born in a given ward, the greater the chance of high mortality rates” (Leavitt, 1982: 31). The only exception to this however, was the German-born infant mortality rates as compared to those of other immigrants (Leavitt, 1982). Is it possible that German nutrition and hygiene habits accounted for the differences in infantile diarrheal deaths? (Leavitt, 1982). Unfortunately in the MCIG cemetery collection there is no easy way to be sure of the percentage of Germans, but Richards (1997) consulted 190 death certificates of individuals assumed to be present in the cemetery based on grave good information. Roughly 12 percent of those individuals were of German descent (Richards, 1997). This number is far lower than the total percentage of persons of German ancestry in Milwaukee at the time. It is nevertheless helpful in learning more about the MCIG cemetery. Determining the immigrant population within each ward and the percentage of each nationality housed within the cemetery is almost impossible given the fragmented historical data. But the health of various groups in Milwaukee leading up to and following 1900 may give us details concerning diabetes and obesity; thus leading to conclusions regarding DISH in the MCIG cemetery. As Leavitt states however: “Other components that one would want to consider for various urban groups—such as immunity levels, availability of medical services, sanitation, and water, occupation, religion, breast-feeding data, and income levels—are not available or quantifiable on the ward level” (Leavitt, 1982: 34-35). She continues on: “Changes in life style and diet, impossible to measure, undoubtedly contributed to improving statistics…” (Leavitt, 1982: 38). Understanding exactly what types of health
hardships the people of Milwaukee had to go through is the next step in getting a better overall idea of life during the timeframe in which individuals were buried in the MCIG cemetery.

The Unhealthy City

Throughout the years leading up to the 20th century, Milwaukee was plagued by a number of various health related lifestyle issues. The influx of immigrants into the city of Milwaukee and the surrounding suburbs caused a number of problems. Overcrowded suburbs emphasized the need for public sanitation and encouraged the spread of many illnesses. Food contamination was also an issue, especially with diary: “Both urban and rural milk thus had many opportunities to become contaminated from warm temperatures, unsanitary handling, and human contact” (Leavitt, 1982: 157-158). During the years of the milk crisis, infantile diarrhea and cholera rose steadily to almost 750 deaths combined in 1893 (Leavitt, 1982). Milwaukee saw 85 percent of its milk pasteurized by 1914 as a result of the “milk wars,” which reduced infant mortality significantly (Figure 13) (Leavitt, 1982). Figure 14 illustrates the Milwaukee mortality rate through the decades, based on ward.

As Leavitt describes, sanitation was a major health concern:

Garbage repeatedly polluted Milwaukee’s water supply; it also littered the city streets, mixing with horse manure and other street droppings to create an irritation and offense to all who tried to maneuver in the crowded thoroughfares (Leavitt, 1982: 123).

The city garbage dilemma was not handled until 1887 when Milwaukee began to pay for both the collection and disposal of waste instead of relying on individual garbage collectors (Leavitt,
Figure 13: Infant mortality through the years, showing the influence of milk agendas. (Figure Credit: Leavitt, 1982: 189 (Milwaukee Health Department Annual Reports))
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\(^a\) 1 April 1870 to 1 April 1871.

\(^b\) Mortality statistics by ward not available for 1880; rate based on 1880 population.

\(^c\) City rate 1880 figures.

Figure 14: Death rates in Milwaukee Wards. Photocopied. (Figure Credit: Leavitt, 1982: 39)
1982). But the disposal techniques did not yet match the demands of the city’s forty tons of garbage produced each day (Leavitt, 1982). In addition to that, the city council could not agree on one Disposal Company and the location of plants, setting off a bidding war between the two possible companies: the Wisconsin Rendering Company and Forrestal Mertz (Leavitt, 1982). The companies decided among themselves to choose the Wisconsin Rendering Company until their contract expired in 1898, but during the years leading up to the 20th century, garbage disposal was one of the most common topics of discussion in council meetings (Leavitt, 1982).

Leavitt states that: “With the exception of the 1892 crisis over garbage contaminated water, it is not possible to blame garbage for creating any specific health problems” (Leavitt, 1982: 154) but goes on to say that “Garbage exacerbated health-related problems, but probably did not itself cause the major hazards” (Leavitt, 1982: 155).

Epidemics were a common occurrence and almost accepted as inevitable:

Milwaukeeans accepted as unavoidable the ravages of the familiar diphtheria, as they did tuberculosis, scarlet fever, and typhoid fever, and developed ways of coping with these killers. They found it more difficult to adjust to a disease that struck the city only occasionally (Leavitt, 1982: 76).

In 1878, Mayor Juneau appointed a board of health to oversee the growing crisis in the city of Milwaukee (Anonymous, 1921). Only then did officials first realize that preventative measures could and should be taken to prevent any epidemics, prior to which: “The city willingly accepted this limited responsibility for emergencies caused by periodic epidemics” (Leavitt, 1982: 78). Despite the creation of this permanent board, Milwaukee still struggled with epidemics and outbreaks (Leavitt, 1982). In the years following, 1868 to 1869, 1871 to 1873, and 1876 to 1877 Milwaukee saw three separate smallpox outbreaks, mostly among German and later on Polish immigrants (Leavitt, 1982). The disease was successfully prevented in 1881 and 1882 thanks to
community support but came back to strike even harder in 1894 and 1895 prompting the stark impeachment of health commissioner Walter Kempster (Leavitt, 1982).

Tuberculosis, despite being one of the city’s major killers at the turn of the century received very little attention since it took an extended period of time to kill its victims (Leavitt, 1982). But an epidemic like influenza garnered much public attention. It broke out in the late 1910’s; the health commissioner citing 30,000 cases at the end of 1918 the cause of which can be traced back to two naval officers who brought Spanish influenza into Milwaukee just months prior to the outbreak (Leavitt, 1982). Only 500 individuals lost their lives to influenza, proving that Milwaukee was becoming more capable of staving off epidemics as opposed to previous years (Leavitt, 1982). Milwaukee had the lowest death rate in the U.S. during the influenza outbreak, with 0.6 deaths per 1,000 (Leavitt, 1982). The next closest was Minneapolis with 1.9 deaths per 1,000 (Leavitt, 1982). Although Milwaukee did have its fair share of health problems well into the 20th century, its health program appeared to be working. So much so, that it became nationally recognized for its efforts.

As the title of Leavitt’s book implies, Milwaukee was eventually awarded first place in the first annual U.S. Chamber of Commerce and American Public Health Association Health Conservation Contest in 1930 (Figure 15) (Leavitt, 1982). Thanks not only to laws regarding sanitation and dairy production but also from the aid of organizations like the Daughters of Charity, the Child Welfare Commission, and the Milwaukee Medical Society (Leavitt, 1982). Figure 16 shows the declining mortality rates in Milwaukee per 1,000 individuals (Leavitt, 1982). Some urban planning reconstruction issues arose (an aging water system infected 400,000 Milwaukeeans with parasites in 1993) but even years later, the city and its citizens were able to cope with whatever problem came their way (Leavitt, 1982). Leavitt’s book shows that “the road
Figure 15: A certificate awarding to Milwaukee in 1929 (Figure Credit: Leavitt, 1982:215 (Milwaukee Health Department))
Figure 16: Mortality rate per 1,000 individuals in Milwaukee (Figure Credit: Leavitt, 1982: 25 (Milwaukee Health Department Annual Reports))
to health reform was neither direct nor easy” (Leavitt, 1982: xiv) and although Milwaukee was able to overcome their health concerns, life was not easy for those individuals (many of whom were immigrants) who lived around the turn of the century. The individuals with the least access to resources and healthy living arrangements were from the lower class, some of which, according to Richards, happened to be buried in the MCIG cemetery (Richards, 1997).
Chapter IV

Diffuse Idiopathic Skeletal Hyperostosis (DISH) Literature Review

The criteria used to identify DISH by researchers over the years and the population studies involving the disease are summarized in this chapter. Brief descriptions of human anatomical and skeletal terms are presented followed by the early history of the study of spinal fusion. The history and development of the diagnostic criteria are also discussed in Chapter IV. Lastly, a description of the population studies and case studies involving DISH are presented in this chapter. A general understanding of what DISH is and how it came to be is an important aspect of this thesis.

Definition of Terms and Anatomical Information

The normal human vertebral column consists of 33 segments: 7 cervical vertebrae, 12 thoracic vertebrae, 5 lumbar vertebrae, 5 sacral (making up the sacrum) and 4 coccygeal (making up the coccyx) (Standring, 2005). In DISH involvement, the thoracic vertebrae are the most commonly affected, followed by the lumbar and the cervical. The thoracic spine is thought to be involved 97 percent of the time, the lumbar 93 percent and the cervical 78 percent (Resnick and Niwayama, 1976). The sacrum is only sometimes involved (and more commonly in ankylosing spondylitis), usually in the form of a fusion with the pelvis. The spinal column acts to support the trunk, provide connections for muscle attachments and, of course, protect the spinal
Figure 17: The human spinal column with indication of the cervical, thoracic and lumbar vertebrae (Figure Credit: Standring, 2005:737).
cord and the surrounding nerves. Each vertebra is linked through cartilaginous intervertebral joints and connected to others by a series of ligaments and muscles. The skeletal structure of each vertebra consists of a ‘body’ and an ‘arch’ (except the special cases of C1 and C2. These will be ignored, due to their noninvolvement in DISH). The ventral body, or the centrum, is attached to the dorsal neural arch, which connects to an anteriorly oriented spinous process (Figure 18). The transverse processes of the neural arches are laterally oriented in cervical and some thoracic vertebrae, becoming increasingly posteriorly oriented in the lower thoracic and lumbar vertebrae (Figure 19). In cervical vertebrae the laterally oriented foramen are known as the transverse foramen while the large foramen present in all the vertebrae is termed the vertebral foramen. The intervertebral space, between vertebral bodies, contains hyaline cartilage, the nucleus pulposus, and the annulus fibrosus (Figure 20). There are also several ligaments associated with the vertebral column. The ligamentum nuchae runs parallel to the cervical vertebrae on the posterior side, and acts as additional support to the head and neck. The ligamenta flava connect the lamina of each vertebra on the anterior side of the spinal column. The interspinous ligaments are small, thin membranous structures that connect the spines of the neural arches, while with the supraspinous ligaments connect the tips of the spinous processes (Figure 21). The two most important ligaments in a discussion of DISH are the posterior longitudinal ligament (PLL) and the anterior longitudinal ligament (ALL). The PLL attaches to the posterior side of the vertebral bodies (including the intervertebral ligaments) and is situated within the vertebral canal. The ALL runs along the anterior aspect of the spinal column attaching to the vertebral bodies. The ligament itself becomes broader as it moves from the cervical down to the lumbar regions. The particular section of the ALL of interest in this thesis is the right
Figure 18: A lumbar vertebra, cranial view, anterior is down, posterior is up (Figure Credit: Bass, 1995:109)

Figure 19: A lumbar vertebra, lateral view, anterior is left, posterior is right (Figure Credit: Bass, 1995:109)
Figure 20: The intervertebral space: the area between vertebrae. The colors represent different types of tissue. The intervertebral area is enclosed by the intervertebral plates (blue), on the superior and inferior sides. The hyaline cartilage (light yellow) lines this area and encloses the annulus fibrosus (light pink) and the nucleus pulposus (dark pink).
Figure 21: Three adjacent (thoracic) vertebrae. The colors represent various ligaments. Anterior Longitudinal Ligament (blue), Posterior Longitudinal Ligament (orange), Supraspinous ligament (red), Interspinous Ligament (yellow), Ligamentum Flavum (green).
Figure 22: A rough indication of where a DISH-type ossification would occur. The right aspect of the anterolongitudinal ligament of the spine. AS is a more symmetrical fusion of both the right and left aspects of the ALL, along with a fusion of the sacroiliac area. (Figure Credit: Standring, 2005: 737)
anterior aspect, the type of where ossification most commonly appears with DISH (Figure 22). There are several layers to the ALL, the fibers of the first layer attach to three or four vertebrae; the next layer of fibers attach only two or three, and the last connects only two vertebrae to each other. In addition to the ligaments mentioned here, there are a cavalcade of arteries, veins and muscles that ensnare each vertebrae of the column. These will not be mentioned here because for the most part, they are not directly pertinent to studies of DISH.

There are several relevant peripheral ligaments and bones that are involved in the diagnosis of DISH, which should be mentioned here. The pathologies which occur at particular areas of the body are known as enthesopathies (usually referring to arthritic buildup around vertebrae) or osteophytes (usually referring to extraspinal arthritic buildup; these are known as skeletal spurs) (Figure 23). It should be mentioned that authors cited in the literature review at times use osteophytes and enthesophytes interchangeably. One of these locations is the M. triceps surae insertion point on the posterior side of the calcaneus. The attachment of the plantar fascia to the calcaneus can also become ossified to varying degrees (Currey, 1983). The anterior patella also sees bone spurs associated with DISH (on the M. quadriceps femoris) along with the ulnar olecranon (M. triceps brachii), two different areas of the femur on the greater trochanter (M. gluteus medius and M. obturator externus) (Figure 24 to Figure 28) (Crubézy and Trinkhaus, 1992). Osteophytes can also occur on the iliac crest of the pelvis, and at times, the ischial area as well (Figure 28). Osteophytes have also been known to occur on the metacarpals and hand phalanges and the glenoid fossa of the scapula. It should be mentioned that the trochanters of the femur, the metacarpals and phalanges and the glenoid fossa of the scapula were not examined in this thesis.
Figure 23: A skeleton exhibiting the possible extraspinal manifestations of DISH. The glenoid fossa of the scapula, the olecranon of the ulna, the metacarpals and phalanges, the iliac crest and ischium of the pelvis, the greater and lesser trochanters of the femur, the anterior patella, the tuberosity on the tibia and the calcaneus. (Figure Credit: Bass, 1995: 3)
Figure 24: (left) Superior view of calcaneus, anterior aspect (involved with DISH) emphasized. (Figure Credit: Bass, 1995:261).

Figure 25 (right) Anterior view of patella (Figure Credit: Bass, 1995:238).
Figure 26: (left) Ulna, posterior aspect, olecranon area emphasized. (Figure Credit: Bass, 1995:171).

Figure 27: (right) Tibia, anterior aspect, tibial tuberosity emphasized. (Figure Credit: Bass, 1995:240).
Figure 28: Pelvis, lateral aspect, iliac crest (red) and ischium (pink) emphasized. (Figure Credit: Bass, 1995:197).
Establishment of Terms and Criteria

The nosology of diffuse idiopathic skeletal hyperostosis and the criteria associated with it did not appear instantaneously, but rather through a long line of research and study over a number of decades across many countries. As the definitions of the disease kept changing, so did the nomenclature, with quite a few synonymous terms applying to essentially the same disease. DISH was first described (but not titled or studied) in the 19th century by Wenzel and Bechterew (in 1827 and 1893 respectively) and the associated rheumatic terminology first began to evolve around this time (Ho, 1958; Rothschild, 1988). It was thought to have been mentioned in some medical journals in the first part of the 20th century, but the disorder first became a topic of debate in the 1940’s (Forestier and Rotes-Querol, 1950). In the 1940’s, little was known about vertebral ossification and calcification which sparked an influential article by Albert Oppenheimer, a roentgenologist at the American University of Beirut (1942). At the time, the ossification of longitudinal ligaments of the spine was thought to cause a rigid vertebral column, but rheumatologists were unsure how this affected the individual (Oppenheimer, 1942).

Oppenheimer’s results from a controlled series of clinical observations and x-rays resulted in several important breakthroughs (1942). Oppenheimer was the first to declare that the ossification of any vertebral ligaments were uncharacteristic of the body and should be viewed independently of arthritis or vertebral osteophytes (Oppenheimer, 1942). Oppenheimer then went on to introduce the term *spondylitis ossificans ligamentosa*, which he considered to be a secondary reaction to a particular unknown pathologic entity (Oppenheimer, 1942). It was around this time that spinal fusion began to be recognized using a routine posterior-anterior (PA) chest x-ray, a technique that continues to used to this day (Rothschild, 1988).
The next major step involved differentiation between two potentially different pathologic rheumatic entities. Forestier and Rotes-Querol participated in a clinical and radiological study to determine how one ankylosing disease (soon to be known as DISH) differs from that common in the contemporary literature: ankylosing spondylitis (1950). Forestier and Rotes-Querol examined nine male patients, six of whom were noted as being obese, by means of lateral spinal radiological screenings (1950). The main symptom described by the patients was a stiffness of the spine, not necessarily associated with pain or discomfort (Forestier and Rotes-Querol, 1950). The authors noted that peripheral joints were not involved, a view that has changed subsequently (Forestier and Rotes-Querol, 1950). The dorsal or thoracic region is shown to exhibit “A continuous but irregular flowing outgrowth alongside the anterior aspect” (Forestier and Rotes-Querol, 1950:322) which is found to be several millimeters to several centimeters thick. The authors go on to state that the growths are often discontinuous in the lumbar region and produce a “Candle flame [shape], the apex of which may reach far up in front of the vertebral body” (Forestier and Rotes-Querol, 1950:322). Several other descriptions helped to shape the qualifications for DISH (at this time it was termed ankylosing hyperostosis):

The anterior edges of the bodies are clearly outlined and may be clearly distinguished from the protuberance…The structure of the protuberances is [sic] fairly homogenous, but their texture is not apparent…The protuberances are not clearly visible on the lateral edges of the spine, but appear as little bridges, chiefly on the right side (Forestier and Rotes-Querol, 1950: 322-333).

Forestier and Rotes-Querol go on to explain that no peripheral arthritis was noted in the pelvis or hands and limbs, and the authors even mention that the disease appears to be limited only to the spine (Forestier and Rotes-Querol, 1950). This description is in stark contrast to the current view of DISH, which is essentially ankylosing hyperostosis with peripheral elements (Resnick et al.,
1975). Forestier and Rotes-Querol are credited with accentuating the differences between ankylosing hyperostosis and ankylosing spondylitis (1950). The first of these differences being the age at which the disease is first established: youth or middle age for AS and old age for AH (Forestier and Rotes-Querol, 1950). The next difference is the extent of ossification of the ALL: only intervertebral coverage for AS and complete intervertebral and vertebral body coverage for AH (Forestier and Rotes-Querol, 1950). The final difference was the presence (AS) or absence (AH) of sacroiliac fusion (Forestier and Rotes-Querol, 1950). Forestier and Rotes-Querol defined the new condition as senile ankylosing hyperostosis of the spine to accentuate the pathologic features as well as the clinical ones (Forestier and Rotes-Querol, 1950). Jacques Forestier was considered by many to be one of the founders of modern rheumatology, having established the first rheumatology clinic in France (Utsinger, 1985).

Rheumatologists began to take notice of ankylosing hyperostosis and soon population studies became an important aspect in the progression of terms and criteria associated with the disorder. Julkunen et al. (1971; 1975) published several papers in the 1970’s in which they conducted a clinical study of two Finnish populations to determine the presence of ankylosing hyperostosis. Julkunen et al. (1971) first examined 12,858 individuals: 6,151 men and 6,707 women, for ankylosing hyperostosis and found it to be present in 3.5 percent of men and 2.2 percent of women with a male to female ratio of 1.5:1 (Julkunen et al., 1971). It is important to note that due to the high preponderance of women in the study, the ratio may not be totally accurate. The results were then broken down by social class and it was determined that there was no occupational stress correlation with AH, an important addition to early ankylosing hyperostosis literature (Julkunen et al., 1971). Julkunen et al. (1971) also used a number of control patients to determine the significance of diabetes on hyperostotic subjects. They found
that 19.1 percent of men and 28.6 percent of women who were hyperostotic were also hyperglycaemic as compared to 7.4 percent of men and 12.8 percent of women in the controls (Julkunen et al., 1971). This study was the first to solidly establish the link between AH (DISH) and diabetes and was the starting point for many future studies on the topic.

An article several years later by Julkunen et al. examined another group of Finnish individuals (1975). Through x-ray analysis, Julkunen et al. determined that in the 8,993 person sample, 236 were diagnosed with hyperostosis (1975). They observed that AH was highly present in men between the ages 60 to 69, noting that it was about 1.5 to 2 times more common in men than women (Julkunen et al., 1975). Forestier and Rotes-Querol (1950) and Julkunen et al. (1971) both observed very few symptoms in patients with AH, even less so than in the control patients:

    Overall, hyperostosis appears to be a common condition, and the data have once again confirmed that the disease is more common in males and that the prevalence rises with increasing age (Julkunen et al., 1975:26).

Julkunen et al. support the previous statement with data showing that hyperostosis was present in 3.8 percent of men and 2.6 percent of women in their sample (1975). Trauma was also evaluated but there was nothing in the data to suggest AH being a result of trauma (Julkunen et al., 1975). Julkunen et al. conclude that hyperostosis is associated with aging, as are several of the suggestions as to the etiology of the disorder (mentioned later under Etiology) (1975).

In 1975, Resnick et al. conducted a clinical, radiographic and pathologic study of 21 men, 18 of whom complained of spinal stiffness. This study helped to further evaluate the criteria and qualifications for hyperostotic spinal fusion (Resnick et al., 1975). The research involved not only a spinal radiographic evaluation but also evaluation of the involvement of the following areas: pelvis, femora, knees, forelegs and ankles, heels, feet, humeri and shoulders, elbows,
forearms and hand/wrists (Resnick et al., 1975). Each of these major sites were examined (left and right) and graded on a three point scale (no abnormality, mild to moderate abnormality, moderate to severe abnormality) (Resnick et al., 1975). Some patients experienced a limited range of motion or mild pain in particular areas, the most common symptom being a decreased range of motion in the lumbar back region as described by 10 patients and decreased range of motion in the cervical region as described by 11 patients (Resnick et al., 1975). It was also noted that six patients’ glucose levels suggested the presence of diabetes mellitus (Resnick et al., 1975).

The hyperostosis was observed to be “varied from an ill-defined increase in density or well-defined triangular outgrowth in front of the disc to a more extensive flowing pattern of new bone formation” (Resnick et al., 1975). Resnick et al. also observed two cases in which “two abnormal segments were separated by an area of abnormality” (1975). Two more soon to be important criteria for DISH were noted through radiographic observations: the intervertebral space was always preserved despite the ossification of the ALL and the posterior aspect of the vertebral body was void of any extraneous ossification (Resnick et al., 1975).

It is important to mention the observations made concerning the extraspinal manifestations of hyperostosis, which had largely been ignored in previous studies (Resnick et al., 1975). Pelvic whiskering was the most common condition (present in all 21 patients), in which the ligaments attached to the iliac crest, the ischial tuberosity and the trochanters were ossified (Resnick et al., 1975). Calcaneal spurs, located on the posterior edge of the calcaneus at the location of attachment for the Achille’s tendon occurred in 16 of the 21 patients studied (Resnick et al., 1975). All six of the obese patients exhibited calcaneal spurs (Resnick et al., 1975). Outgrowths also occurred on certain bones of the foot: the talus, navicular, cuboid and
fifth metatarsal; however, outgrowths were not common (present on four patients) (Resnick et al., 1975). Olecranion spurs and patellar spurs were also seen, along with some ossification on the distal ends of the tibia and fibula (Resnick et al., 1975). Some exostoses were also present on the glenoid fossa of the scapula and proximal humerus (shoulder), phalanges and metacarpals (Resnick et al., 1975).

Ankylosing spondylitis is defined as a disorder that “produces squaring of the vertebral bodies, thin bony syndermophytes, and apophyseal and sacroiliac articular alterations” (Resnick et al., 1975: 523). The authors then go on to describe other rheumatological disorders that could possibly be confused with DISH: acromegaly, fluorosis, pachydermoperiostosis, and hypertrophic osteoarthopathy (Resnick et al., 1975). Confusion regarding AH and AS was soon cleared with the onset of criteria for DISH (Resnick and Niwayama, 1976).

The criteria for the axial manifestations for DISH were first settled upon by Resnick and Niwayama:

(a) The presence of “flowing” calcification and ossification along the anterolateral aspects of at least 4 contiguous vertebral bodies with or without associated localized pointed excrescences at the intervening vertebral body-disc junctions.
(b) A relative preservation of disc height in the involved areas and the absence of extensive radiographic changes of “degenerative” disc disease, including vacuum phenomena and vertebral body marginal sclerosis
(c) Absence of apophyseal joint bony ankylosis and sacro-iliac joint erosion, sclerosis or bony fusion (1976:559).

In this particular study, Resnick and Niwayama examined 100 patients, 96 men and 4 women, 97 of whom had thoracic spinal abnormalities (1976). Abnormalities were most commonly found in the 9th, 8th, 10th and 7th vertebrae respectively in 97 percent of those examined (Resnick and Niwayama, 1976). Similar to the situation seen in Resnick et al. (1975), 5 patients exhibited two
abnormal sections of the thoracic vertebrae separated by a segment of normality (Resnick and Niwayama, 1976). The ossification of the ALL varied from 1 to 20 mm in thickness in those patients examined (Resnick and Niwayama, 1976). The cervical spine was also affected by excrescences in 78 percent of patients (Resnick and Niwayama, 1976). These excrescences measured 11mm to 12mm and involved the 6th and 5th cervical vertebrae most commonly (Resnick and Niwayama, 1976). The lumbar vertebrae were abnormal in 93 percent of patients, affecting the 3rd lumbar vertebrae most commonly, with the largest outgrowths extending 19mm to 20mm (Resnick and Niwayama, 1976).

Despite all these several spinal abnormalities, only 12 percent of the 25 patients fulfilled the criteria for DISH, 4 of whom were diabetic (Resnick and Niwayama, 1976). The authors observed:

> These [fibrous tissue] disc extensions create an “umbrella” effect as they grow in and around the fibers of the ALL, which appeared stretched over protruding fibrous tissue. Ossification develops within the blended fibers of the annulus and the ALL (Resnick and Niwayama, 1976: 563-564).

Resnick and Niwayama conclude, based on their observations that:

> DISH may not represent a disease per se but rather a vulnerable state in which extensive ossification results in an exaggerated response of the body in some patients [sic] stimuli which produce only modest new bone formation in others. (1976: 567).

Accentuating the differences between AS and DISH once again, Resnick and Niwayama mention that AS cause an ossification of the ALL (as in DISH) but also the intervertebral annulus fibrosus and nucleus pulposus (in which the intervertebral space is not maintained) (Resnick and
Niwayama, 1976). As previously stated, the intervertebral space must be maintained in order for the ALL ossification to qualify as DISH.

A radiographic and laboratory evaluation was carried out in order to evaluate new changes in the knowledge concerning DISH (Utsinger et al., 1976). A total of 30 patients were examined, 23 of whom complained of spinal stiffness and 11 of whom exhibited peripheral joint pain (Utsinger et al., 1976). Every patient had some form of hyperostosis of the spine and each had at least one extraspinal manifestation (Utsinger et al., 1976).

Upon examination of the etiology of DISH, Utsinger et al. (1976) noted that acromegaly can cause the formation of osteophytes; however, none of the patients examined had features of acromegaly. Hypoparathyroidism can also cause bony spur growth, but again, no patients had a history of such a disorder (Utsinger et al., 1976). Fluoride poisoning can also cause formation of osteophytes, but clinical results showed that fluoride levels were normal in all patients (Utsinger et al., 1976). Utsinger et al. considered the etiology to be unknown, a debate which continues on to this day.

In the 1980’s, realizing that Resnick’s criteria (Resnick and Niwayama, 1976) lacked the crucial appendicular elements, P.D. Utsinger (1985) revised the criteria for DISH:

1. Continuous ossification along the anterolateral aspect of at least four contiguous vertebral bodies, primarily in the thoracolumbar spine. Ossification begins as a fine ribbon-like wave of bone but commonly develops into a broad, bumpy, buttress-like band of bone.
2. Continuous ossification along the anterolateral aspect of at least two contiguous vertebral bodies.
3. Symmetrical and peripheral enthesopathy involving the posterior heel, superior patella or olecranon, with the enthesal new bone having a well-defined cortical margin.

Categories of DISH according to the criteria are as follows:
A. Definite: 1
B. Probable: 2, 3
C. Possible: (i) 2 and 3
(ii) 2
(iii) 3 (particularly if calcaneal spurs occur together with olecranon or patella spurs)

Exclusions:
1. Abnormal disc space height in the involved areas
2. Apophyseal (AP) joint ankylosis (328-329).

Utsinger also discusses the early changes in vertebrae that lead to ligament ossification, dividing them into types (1985). He deems type I to be the formation of osteophytes on the border of the intervertebral discs on at least two bodies (Utsinger, 1985). Type II is when the bone forms a continuous band across two adjacent vertebrae but no annulus fibrosis calcification is seen (Utsinger, 1985). Lastly type III involves an ossification of the ALL, with four or more vertebrae consecutively fused; the spinal definition of DISH (Utsinger, 1985). Most of these ossifications occur between T4 and T11, and only one of the type III was seen in the lumbar region in Utsinger’s study (1985).

Utsinger et al. (1976) and Utsinger (1985) studies have shown that the ages of the patients establish the need for the creation of such diagnostic criteria. For example, of the 200 patients examined with Category A (definite DISH) the mean age is 63 years, whereas the 63 patients in Category B (probable DISH) exhibit a mean age of 60 years and the 22 patients in Category C (possible DISH) have a mean age of 56 years (Utsinger, 1985). Utsinger then goes on to claim that vertebrae may not even be necessary for early DISH:

Consequently, we feel that physicians may entertain a tentative diagnosis of DISH (Category C. iii) even in the absence of spinal abnormalities…(Utsinger, 1985:329)
This statement, which was generally dismissed by Resnick et al.’s (1976) and Utsinger’s (1985) own criteria, completely altered the accepted view of DISH. Utsinger supports the current view that DISH affects males more than females (71 percent of the 200 whom exhibited DISH) (1985). Utsinger also proposes that DISH affects whites more than blacks, but did not propose a reason (Utsinger, 1985). In this study, spinal stiffness and tenderness were common symptoms, along with stiffness and tenderness in particular appendicular areas (Utsinger, 1985). As a result of the described tenderness, it was revealed that 20 out of 56 patients had calcaneal spurs, and 46 out of 50 had olecranon spurs (Utsinger, 1985).

In terms of spinal manifestations, Utsinger states that: “Smooth, ribbon-like ossification resembling that seen in ankylosing spondylitis, is far less common than the presence of thick irregular chunks of ossification” (1985: 336). These particular ossifications vary from a 1mm to 23mm posterior protrusion in Utsinger’s sample (1985). The cervical vertebrae are less involved than the thoracic and lumbar, which are both equally as frequently affected (Utsinger, 1985). The vertebrae most commonly affected by DISH were C4-C7, T7-T11, and L1 and L3 (Utsinger, 1985). The most commonly affected appendicular sites were the tibial tuberosity, the calcaneus, the superior patella, the olecranon and the anterior patella (Utsinger, 1985). The hip is commonly involved but Utsinger does not report to what extent (1985). Utsinger’s study was an important one in establishing the most commonly involved spinal and extraspinal elements of DISH (1985).

DISH is not thought to cause back or joint pain, only the occasional spinal and peripheral stiffness. A group of papers from the late 1980’s and early 1990’s set out to determine if there was a correlation between pain, and extraspinal and spinal manifestations of DISH (Schlapbach et al., 1989; Beyeler et al., 1990; Beyeler et al., 1992; Schlapbach et al., 1992). Schlapbach and
Beyeler wrote papers with colleagues about DISH and associated back pain, and about pain in several peripheral areas associated with DISH: the shoulder, the elbow and the hands (Schlapbach et al., 1989; Beyeler et al., 1990; Beyeler et al., 1992; Schlapbach et al., 1992). Schlapbach et al. (1989) carried out a controlled study to clarify the relevance of DISH to back pain, using a structured questionnaire. The control group represented individuals with previously cited back pain but no DISH symptoms: spinal fusion or peripheral osteophytes (Schlapbach et al., 1989). DISH probands (another word for medical subjects) were graded 0 to III using the Resnick et al. (1975) grading criteria (Schlapbach et al., 1989). The results showed the lack of positive correlation between back pain and both DISH positive and DISH negative probands (Schlapbach et al., 1989). This was the first controlled study of this type carried out and is considered to be an accurate representation of European white Caucasians (Schlapbach et al., 1989).

A paper the following year examined shoulder pain associated with DISH along with two other objectives: to develop a radiological criteria for shoulder hyperostosis grading and to evaluate a relationship between shoulder osteophytes and DISH (Beyeler et al., 1990: 349). After analyzing 47 probands both with and without shoulder hyperostosis, the prevalence of pain was seen to be four times higher in individuals who exhibited vertebral hyperostosis (Beyeler et al., 1990). This study concluded that shoulder hyperostosis may predispose shoulder pain, but as previously seen, there was no correlation between vertebral hyperostosis and back pain (Schlapbach et al., 1989; Beyeler et al., 1990).

A similar study (with similar objectives) was carried out two years later involving the elbow (Beyeler et al., 1992). Although the difference was not significant, of the 85 probands examined, elbow pain was present one and a half times more frequently with elbow hyperostosis.
than in controls (Beyeler et al., 1992). Beyeler et al. (1992) also found that more than half the controls without vertebral hyperostosis exhibited elbow hyperostosis, in most cases bilaterally. This suggests that the ligament ossification was not limited to the right or left side of the individual based on their handedness (Beyeler et al., 1992). The final study in 1992 involved the possibility of a higher prevalence of palpable finger joint nodules in DISH probands than in controls (Schlapbach et al., 1992). Proximal and distal phalanges were examined for broadened and arrowhead distal tufts, increased cortical width of tubular bones and prominent exostoses and enthesopathies (Schlapbach et al., 1992: 531). It was determined that the prevalence of nodules was indeed, associated with DISH; they were twice as prevalent in those with DISH compared to controls (Schlapbach et al., 1992). Since the results are significant, the authors wonder whether DISH and phalange nodule formation share etiologies (Schlapbach et al., 1992). Further data and study was deemed necessary (Schlapbach et al., 1992). Mention of these studies is important because DISH is primarily studied in living individuals and finding markers that suggest DISH (like hand pain or shoulder pain, and of course, back stiffness) are crucial to accurately determining the prevalence of the disease today.

A 1989 editorial in the British Journal of Rheumatology questions whether DISH is a state rather than a disease (Hutton, 1989). Hutton states that the constraining nature of Resnick et al.’s (1976) criteria does not allow for a gradation, instead cuts off the disorder at a particular number of vertebrae (Hutton, 1989). Hutton uses Schlapbach et al.’s (1989) data to support the idea that, since back pain is not directly associated with DISH, DISH may not be a disease entity and asserts that it may be a protective reaction (Hutton, 1989). Hutton goes on to suggest that DISH may be a very severe osteoarthritis, concluding that it may be better to consider that DISH has a yet-to-be-known significance instead of continuing to follow the originally established
dogmas (Hutton, 1989). Several authors mentioned in the current thesis have, however, gone on record as disagreeing with Hutton, and conclude that DISH is in fact a distinct disorder (Mata et al., 1997; Kiss et al., 2002a).

Although DISH has gone through many name changes over the years, the disputes over the exact criteria, definitions and causes of the disease continue to this day. While some feel that the criteria presented by Resnick et al. (1976) and Utsinger (1985) among others, accurately describes the disease, there is still a debate surrounding the rigidity of the criteria and even whether DISH is in fact a state and not a disease (Rogers and Waldron, 2001; Hutton, 1989).

Take the following statement concerning the criteria for DISH:

> The use of rigid criteria will almost certainly lead to an under-estimation of the true prevalence of DISH, but this will not affect the validity of between-study comparisons as long as the same diagnostic criteria are used in each (Rogers and Waldron, 2001: 363).

A 2008 editorial comments on how far rheumatologists have come in their understanding of DISH, but reminds them of how much further there is to go (Mader, 2008). For instance, as of right now there is no way to diagnose DISH based only on peripheral (joint) osteophytes without the presence of at least three ALL fused vertebrae (Mader, 2008). Mader comments that there is still no knowledge of the metabolic, inflammatory and entheseal changes in the early phases of DISH; a crucial aspect of early diagnosis (Mader, 2008). Mader concludes:

> It is therefore important to establish new diagnostic criteria that will take into consideration not only the radiographic aspects of the thoracic spine, but will encompass the clinical manifestations, the distribution and features of peripheral joints and entheseal sites involved, and aspects of spinal involvement other than the T-spine [thoracic spine]. Until that happens, we will diagnose the condition in its fully developed and probably irreversible phase, rather than
study its early and hopefully manageable phases (Mader, 2008: online editorial).

In midst of all of the differing opinions about how DISH should be studied and analyzed, sometimes it is difficult to identify the criteria to use for DISH studies. The exact criteria used in this study will be examined in more depth later, but it is this author’s opinion that a combination of Resnick et al. (1975) and Utsinger’s (1985) criteria most accurately describe DISH (as seen in Julkunen et al., (1971; 1975) (but not properly explained) and later in Kiss et al., (2002b) with the title ‘Resnick 2’), with particular attention being paid to the following osteophytic areas: tibial tuberosity, olecranon (ulna), patella, iliac crest and calcaneus.

**Diffuse Idiopathic Skeletal Hyperostosis and Ankylosing Spondylitis**

There have been several cases of DISH and AS occurring together, even though they are clearly two distinct disorders. This is important to examine because the current data in this thesis from the MCIG cemetery shows several cases of AS and DISH together as well as a transitional case. The first case from the literature was that of a 72 year old man who had DISH present in his cervical spine but AS changes in his lumbosacral area (a fusion of the sacrum and auricular surface of the pelvis) (Williamson and Reginato, 1984). Several years later, another case arose: this was a 49 year old man with no history of diabetes mellitus or obesity (Olivieri et al., 1987). Although the lumbar and cervical radiographs showed a squaring of vertebral bodies, specific to AS, the thoracic vertebrae showed a continuous “flowing mantle” of new bone formation with the intervertebral space maintained (Olivieri et al., 1987). Most of the time the symmetry is what differentiates AS from DISH, with AS occurring on both sides of the ALL while DISH appears only on the right posterior region of the vertebrae. Two years later, three more cases were
brought forward of both DISH and AS present in the same individual (Rillo et al., 1989). The first was a 55 year old male complaining of pain since 29 in his dorso-lumbar region (Rillo et al., 1989). Rigidity and kyphosis soon took hold, limiting his cervical and hip movement (Rillo et al., 1989). Upon radiologic confirmation, the patient was determined to have three separate fusions of the spine, from C3 to C6, T1 to T12 and L3 to L5 as well as a sacroiliac fusion on both the right and left sides (very severe and moderate, respectively) (Rillo et al., 1989). The patient also had DISH-like osteophytes on the iliac crests, trochanters of the femur, the calcaneus, the patella and the tibial tuberosity (Rillo et al., 1989). The other two patients, a 58 year old male who began to experience lumbar pain at 25, and a 61 year old male who first experienced pain at 51, both exhibited spinal fusion (C3 to L4 in the first, and T5 to T12 and L1 to L2 in the second) (Rillo et al., 1989). Diabetes appears in one of the three patients in question (Rillo et al., 1989). Each individual in this case study experienced DISH-like fusion of the vertebrae and extraspinal manifestations common with the disorder but also experienced sacroiliac fusion, thought once to be solely attributable to AS (Rillo et al., 1989). A recent DISH-AS case was analyzed by Kozanoglu et al. (2002). A 58-year old man with no history of diabetes mellitus complained of joint and back stiffness (Kozanoglu et al., 2002). A radiographic screening revealed calcification of the ALL and PLL ligaments as well as enthesopathic changes on the calcaneus, patella and ulna (Kozanoglu et al., 2002). The patient also showed sacroiliac fusion, reminiscent of AS (Kozanoglu et al., 2002). This is another of many examples of DISH and AS occurring together without severely affecting the quality of life of the patient in whom they are found (Kozanoglu et al., 2002).
There have been a number of studies examining the presence of DISH in particular populations from around the world. To get a better idea of how the MCIG cemetery collection fits into the larger context of DISH research, it is first necessary to examine the other studies concerning the disease.

In 1984, Bloom examined the presence of ankylosing hyperostosis in a Jerusalem hospital population using radiographs taken in 1981 and 1982. Although described as AH, Bloom was actually describing DISH, with simply different terminology (1984). Bloom described an overall DISH presence of 22.4 percent of 624 male patients, 46 percent of whom were over the age of 80 years (1984). Bloom also noted a DISH presence of 13.4 percent in 612 females, 30 percent of whom were over 80 years of age (Bloom, 1984). The male to female ratio was 1.7:1 and no cases were seen in females under the age of 50 nor in males under the age of 40 (Bloom, 1984).

In 1985, 560 adult burials from various museums were examined for DISH (Rogers et al., 1985). The authors examined an Egyptian mummy, Saxon bishops from Wells Cathedral, and 19th century Romano-British citizens from an English cemetery, as well as some mediaeval and post-mediaeval burials (Rogers et al., 1985). DISH was seen in 2.3 percent of the total number of adult remains examined and ranged from 2 percent to 3.7 percent depending on the time period (Rogers et al., 1985). The importance of the study was not to establish a difference in geographic variation concerning the disease but to solidify the hypothesis that DISH has a wide temporal and geographic presence.
In 1990 the presence of DISH in indigenous African Blacks was documented (Cassim et al., 1990). Five hundred lateral chest radiographs from the King Edward VIII Hospital in Durban, South Africa, were examined for the Resnick and Niwayama (1976) DISH criteria (Cassim et al., 1990). DISH was found to be present in 3.9 percent of the population (3.8 percent in males and 4.2 percent in females) with a male to female ratio of 1:1.05 (Cassim et al., 1990). It was also found that 52.4 percent of the patients with DISH were diabetic (Cassim et al., 1990). Unfortunately the appendicular skeleton was not analyzed in this study, the authors simply state that certain individuals exhibited appendicular involvement, while others did not (Cassim et al., 1990).

A 1997 Minnesota Hospital study by Weinfeld et al. examined DISH in two large American Midwest metropolitan populations. This study constitutes the largest sample in the English language literature (2300 patients) (Weinfeld et al., 1997). It found a DISH prevalence of 25 percent in males over 50 and 15 percent in females over 50, placing the male to female ratio at 3:2 (Weinfeld et al., 1997). Most of these patients were of German or Scandinavian descent (an interesting fact considering the MCIG cemetery collection) (Weinfeld et al., 1997). The authors also found that it was rarely seen in black patients before 60 years; blacks as a group also have a lower DISH prevalence altogether (Weinfeld et al., 1997). An even lower prevalence was found in the 72 Native Americans studied, most of whom were from northern tribes like Chippewa and Sioux (Weinfeld et al., 1997). This study also showed a high prevalence of individuals with osteoporosis, which the authors thought may have affected the development of DISH (Weinfeld et al., 1997).

That same year, a controlled DISH study was carried out at Montreal General Hospital in Canada (Mata et al., 1997). DISH was found to be present in 3.5 percent of the men and 2.6
percent of the women studied (Mata et al., 1997). The male to female ratio was shown to be 1.94:1 (Mata et al., 1997). It was found that 83 percent of the DISH cases were exhibited in Caucasian individuals (Mata et al., 1997). There were seven cases of dysphagia included, and as seen in past studies, there was less pain and more stiffness associated with DISH than with ankylosing spondylitis (Mata et al., 1997). The authors also contest Hutton’s (1989) editorial asserted that DISH is a state rather than a disease (Mata et al., 1997). Mata et al. state:

Thus, we studied patients with DISH and contrasted them with lumber spondylitis and ‘healthy’ patients to evaluate the contention that DISH has symptoms, findings, and disability that justify that it be considered a disease. The present study provides strong support for the hypothesis that DISH is a distinct disorder (1997: 111).

Mata et al. also support the idea of DISH being associated with obesity (Mata et al., 1997).

In 2002, DISH was examined in a Hungarian population (Kiss et al., 2002b). The study screened 635 individuals for DISH, 52 percent of who were women (Kiss et al., 2002b). Instead of using the criterion of four continuous fused vertebrae as suggested in Resnick et al. (1975) or two continuous fused vertebrae as suggested in Utsinger (1985), the authors primarily used the Resnick 2 criteria (Kiss et al., 2002b). DISH was found in 84 of 307 (27.3 percent) men and 42 of 328 (12.8 percent) women according to the Resnick 2 criteria (bridging ossification of two vertebrae) and 19 cases (6.1 percent) based on the Resnick 3 criteria (bridging ossification of three vertebrae) in men and 4 cases (1.2 percent) in women (Resnick et al., 1975; Kiss et al., 2002b). The male to female ratio in this population study was 2.1:1 for the Resnick 2 criteria (Kiss et al., 2002b). The authors suggest that the disease is highly prevalent in males over 50 (27.3 percent) but slightly less so in females (12.8 percent) (Kiss et al., 2002b).

In 2004, a Korean population was examined for the prevalence of DISH (Kim et al., 2004). A total of 3,595 subjects from Eroul and Daegu were involved in this study with a mean
age of 64.25 and an overall male to female ratio of 1979 to 1616 (55 percent to 45 percent) (Kim et al., 2004). The authors reported 104 (2.9 percent) individuals as exhibiting DISH according to Resnick’s criteria (four continuous ALL ossified vertebrae) and 146 (4.1 percent) using Julkunen’s criteria (three continuous ALL ossified vertebrae) (Kim et al., 2004; Julkunen et al., 1971; Resnick et al., 1975). Using Resnick’s criteria, men were 7.1 times more likely to be diagnosed with DISH than women (Kim et al., 2004). The authors conclude that overall, DISH is much less prevalent in Korean populations than in Caucasian populations (Kim et al., 2004).

A female Italian population was examined for DISH prevalence in 2005 (Pappone et al., 2005). A total of 93 subjects was examined with radiographs and 14 (15.1 percent) were diagnosed with DISH (Pappone et al., 2005). The cases tended to increase with age (6 cases in individuals over 70) and DISH was not reported in individuals younger than 49 (Pappone et al., 2005). The authors make no inferences about potential genetic or environmental factors influencing DISH in their sample (Pappone et al., 2005).

A recent study of an outpatient population in the Netherlands yielded interesting results concerning the prevalence of DISH (Westerveld, 2008). Posteroanterior and lateral chest radiographs were examined from 501 individuals, 47.5 percent of which were male with a mean age of 66.6 (Westerveld, 2008). DISH was seen to be present in 17.0 percent of the total population, 22.7 percent of men and 12.1 percent of women (Westerveld, 2008). The male to female ratio was 1.85:1 (Westerveld, 2008). Table 12 at the end of Chapter VIII shows a summary of all of the important population studies involving DISH as well as the MCIG study.
Chapter V

Diffuse Idiopathic Skeletal Hyperostosis throughout History

DISH was certainly as common in our ancestors as it is now…” (Rogers et al., 1985: 119).

A thorough account of DISH throughout history is discussed in the following chapter. DISH is by no means a new disorder and has been identified in many human populations, from the Dutch and Egyptians to medieval monks and American Indians. DISH has even been identified in some animals, leading some researchers to speculate possible evolutionary advantages of the disease.

The Middle Paleolithic: Neanderthal

The Shanidar 1 late archaic human (Neanderthal) from Iraq is the first documented DISH case from the Pleistocene era (Crubézy and Trinkhaus, 1992). Although much of the skeletal remains were absent, crushed or too fragmentary to examine (the T2 to T12 vertebrae), there is some data to suggest the presence of DISH (Crubézy and Trinkhaus, 1992). There is a bony ‘candle-like’ ossification from L3 to L5 on the left antero-lateral surface, suggesting DISH-like fusion, even though DISH normally involves ossification of the right aspect of the ALL (Crubézy and Trinkhaus, 1992). There is also extraspinal evidence in the form of bony spurs seen on the left ulna, both left and right patellae, both left and right calcanei and the right femur (greater trochanter) (Crubézy and Trinkhaus, 1992). It is thought that the scapula and hip may have exhibited some hyperostosis, but the fragmentation did not allow for any analysis (Crubézy and
Trinkhaus, 1992). The Shanidar 1 partial skeleton is thought to fit criteria 2 and 3 presented by Utsinger (1985), placing it between ‘probable’ and ‘definite’ (Crubézy and Trinkhaus, 1992). Although no dietary or isotopic analyses were done on Shanidar 1, Crubézy and Trinkhaus think this first observed case of DISH in the fossil record is an example of the disease’s noninvolvement with diabetes mellitus (1992).

Egyptians

Some ancient Egyptian mummies are known to show evidence of DISH. Rogers et al. examined a 21st Dynasty mummy and concluded DISH presence based on spinal and joint radiographs (Rogers et al., 1985). Early Egyptians and Nubians from the historic record were also found to have ankylosing spondylitis, which some authors like Russell (2004) think may have been misdiagnosed (Brothwell, 1967; Chhem et al., 2004). Ancient Egyptian ruler Ramesses II was examined radiographically and was found to have ankylosing spondylitis based on the presence of an ALL ossification in the cervical and lumbar vertebrae, as well as bony spurs found on the hip and acetabulum (Chhem et al., 2004). The interpretation of the radiographic evidence from this particular case is, however, subject to debate as a letter to the editor the same year revealed Russell’s doubt of the diagnosis of AS instead of DISH (Russell, 2004; Chhem et al., 2004). The matter might have been settled with a proper radiograph of Ramesses II’s sacroiliac joint but the fragile state of the mummy did not allow such analysis to be done (Chhem et al., 2004; Russell, 2004).

An analysis of 134 adult Meroitic Nubians from Northern Sudan yielded some fascinating results about DISH thousands of years ago (dated 350 BCE to CE 350) (Arriaza et
al., 1993). A total of 18 cases were observed (13.4 percent) with a male to female ratio of 3.5:1 (Arriaza et al., 1993). Unfortunately due to fragmentation, age estimates could not be gathered (Arriaza et al., 1993). Arriaza et al. suggest that females are less affected by DISH due to “female bone gracility and postmenopausal hormonal imbalances that decrease the amount of bone formation” (1993: 246). The authors are also skeptical of the current affiliation of DISH with diabetes mellitus, which will be addressed later (Arriaza et al., 1993).

**Sixth Century Enotrian in Magna Graecia, Italy**

A skeleton of an adult woman was found in Basilicata, Southern Italy, and dated back to the Enotrian culture, present around the 6th century BCE (Canci et al., 2005). The age-at-death was placed between 50-60 based on incomplete skeletal remains (Canci et al., 2005). Vertebral hyperostosis was observed from T6-T10 and L2-L5 on the right portion of the ALL; criteria of DISH (Canci et al., 2005). Extraspinal spurs were also present on the left ulna, the left ischium, the right calcaneus and the right proximal femur; all common places for osteophytic buildup in cases of DISH (Canci et al., 2005). The authors also comment that this is the first reported case of DISH in coexistence with melorheostosis, a rare nonhereditary bone disorder (Canci et al., 2005).

**DISH and Monks**

Before examining the medieval studies, it may be important to establish a background of Monastic life as a prelude to its relevance to DISH. So far in this thesis, there has been brief mention of DISH as it relates to diabetes. The most common and strongest examples of DISH as
it relates to diabetes come from monks and higher status individuals from medieval England. It should be noted that disagreements with the current section will be considered later in the discussion of diabetes.

The medieval monks of England during the middle ages appeared to live very well, especially in terms of diet. Originally, European monks were prohibited from eating meat, but as time went on, those rules became more lenient and allowed for freshly trapped game (Waldron, 1985). Exceptions were also made for monks who had fallen ill (Waldron, 1985). Waldron cites author Morris Bishop as describing monastery dwellers as having a vice of gluttony (Waldron, 1985; Bishop 1983). Waldron goes on to list many of the foods consumed by monks on a daily basis:

Indeed, the staggering variety of the medieval monastic diet is impressive. Fish was always abundant...capon and ducks, chickens, geese, egret and herons, pheasants, partridge and pigeons, quail teal and swan...all washed down with plenty of wine or ale. (1985: 1763)

Although they tried their best to be abstemious, Waldron states that monks ate very well (1985). Morris Bishop described the monkish diet and lack of exercise as inviting coronaries, and placed the caloric intake outside of Advent and Lent at 6,207 per day (Bishop, 1983). Waldron then goes on to explain that this particular lifestyle may have influenced DISH (Waldron, 1985).

In 1985, Tony Waldron postulated that DISH may have been an occupational disorder particularly common to those with a religious lifestyle. The site in question is the Merton Priory in Surrey, England (Waldron, 1985). Founded in 1140, it is one of the earliest Augustinian houses (Waldron, 1985). There were 35 complete burials excavated, three of which had spinal changes and extraspinal enthesopathies consistent with hyperostosis (Waldron, 1985). There were an extra eight individuals with extraspinal ossifications present that lacked the spinal
requirements for DISH (Waldron, 1985). Although the collection was poorly preserved and highly fragmentary, the extraspinal hyperostosis (spurs on the calcaneus, olecranon, iliac crest etc.) presented by Resnick et al. (1975) were all present (except any on the hand/wrist) along with the spinal hyperostosis (Waldron, 1985). By discarding the one apparent female and assuming that the fragmented individuals were male, the (male) prevalence at Merton priory is 7.3 percent (Waldron, 1985; Julkunen et al., 1971).

Rogers et al. (1985) analyzed 560 skeletons from various time periods looking for those that match the DISH criteria as presented by Resnick et al. (1975). The authors studied 303 medieval burials, 8 of which matched the criteria for DISH (2.6 percent) (Rogers et al., 1985). The male to female ratio was not compiled in this study, the authors most likely assuming the presence of only males (Rogers et al., 1985). The authors go on to postulate:

Although we do not know the origin of all the skeletons with DISH, many of them are definitely from higher social backgrounds…[thus] Their standard of living and nutrition was probably better than that of the general population and they probably lived longer (Rogers et al., 1985: 117-118).

In the years following its publication, many authors have taken an opposing stance regarding the positive correlation between DISH and diabetes/obesity. This topic of DISH and diabetes/obesity will be examined a bit more closely in a later section.

A later study by Waldron and Rogers examined an 18th century skeletal collection from Christ Church, Spitalfields in east London (Waldron and Rogers, 1990). A total of 968 skeletal remains were recovered, forty one of whom (4.2 percent) experienced fused sacroiliac joints (by way of bridging osteophytes) (Waldron and Rogers, 1990). The authors went on to explain that this excess bone formation translated to osteoarthritis in the collection and seemed to be more common than DISH (Waldron and Rogers, 1990). Although ankylosing spondylitis and DISH
together are not mentioned as a possibility, the authors suggest that roughly 1.1 percent of the population had DISH; the etiology of which is considered to be unrelated to osteoarthritis (Waldron and Rogers, 1990).

A follow up article by the same authors appeared roughly a decade later further connecting DISH with diabetes (Rogers and Waldron, 2001). Rogers and Waldron examined several English cemeteries, including the Wells Cathedral and the Royal Mint site, dating from the 13th and 16th centuries (Rogers and Waldron, 2001). The two chapels at Wells Cathedral showed a high preponderance of DISH at Lady Chapel (2 of 15, 13.3 percent) and Stillington’s Chapel (3 of 13, 23.1 percent) (Rogers and Waldron, 2001). The Royal Mint site had similar results, with the churches and chapels showing a significant DISH presence (6/52, 11.5 percent) (Rogers and Waldron, 2001). Rogers and Waldron therefore conclude that the high prevalence of DISH is related to the diet of the monks at the time:

It is very likely that those who were predisposed to develop DISH selected themselves to become monks; thus, the explanation must lie in the day-to-day activities within the monastery, and the one which suggests itself most strongly [is] related to the monks’ diet (2001: 361).

The authors link the presence of DISH to the result of a monastic diet quite closely, but note that the presence of DISH should not always suggest a high status lifestyle (Rogers and Waldron, 2001).

A 2007 article examined isotopic data for four individuals with DISH from a Later Medieval (13th to early 16th century CE) cemetery from the Gilbertine Priory of St. Andrew, Fishergate in York, United Kingdom (Müldner and Richards, 2007). Four individuals with DISH were examined and it was revealed that these individuals had higher nitrogen and carbon isotopic readings than the average of the 155 individuals examined in this study (Müldner and Richards,
2007). Each of the four individuals diagnosed with DISH plotted above the -18.9 percent ($\delta^{13}$C) and 13.0 percent ($\delta^{15}$N) averages (Müldner and Richards, 2007). Although this isotopic data is not conclusive, these numbers suggest these individuals had a diet rich in animal protein (Müldner and Richards, 2007). The authors go on to say that some pathological conditions have effects on stable isotope analyses and that physiological factors rather than dietary cannot be ruled out as a cause of DISH (Müldner and Richards, 2007). Another 2007 study reported similar findings from Pandhof Abbey in Maastricht, Netherlands (Verlaan et al., 2007). Roughly 40 percent (17 adults) of the 51 buried in the cemetery (in use from 275 to 1795 CE) were diagnosed with DISH (Verlaan et al., 2007). The authors think these individuals were wealthier members of society, with an access to an abundant food supply, thus addressing the ‘monastic way of life’ hypothesis (Verlaan et al., 2007). The authors, like Müldner and Richards (2007) state that this link between obesity and DISH has not been proven, and further investigation is warranted (Verlaan et al., 2007).

A meta-analysis in 2006 of DISH studies associated with monastic diets replicated the known positive correlation between the two (Mays, 2006). Mays concludes that:

Firstly, it is debatable whether the link between high body mass and DISH is strong enough for the frequency of DISH to be used as an indicator of obesity in past populations. Secondly, although the link between DISH and monastic burials seems widely accepted, it is not one which bears rigorous scrutiny: there is no published statistically valid evidence for a higher rate of DISH among medieval monastic burials than among non-monastic medieval material (2006: 187).

Mays thinks that if a study comparing monastic DISH presence to nonmonastic DISH presence were to be carried out, the correlation would be negative (2006).
Unfortunately, at this time the author has been unable to locate a skeletal analysis study of villagers living at the time of the monks in England in which DISH was considered. A good deal of information about the commoner diet is known, and a future research project involving a comparison between monastic cemeteries and non-monastic Middle Ages villager cemeteries would yield interesting results. Medieval villagers appeared to eat well: “bread, pottage and ale…bacon or salt pork…nuts, berries and roots…vegetables and fruit,” but they had a very serious protein shortage and deficiencies of lipids, calcium and vitamins A, C and D (Gies and Gies, 1990: 96-97; Mollat, 1986). Would DISH be prevalent in a pauper population such as this? If the data reflects that of the MCIG pauper cemetery collection, the answer appears to be yes.

**Pima Indians**

The Pima Indians, an American Indian tribe situated in the Southwestern United States and areas of Mexico, have been cited as having a high prevalence of DISH with around 25 percent of the total population affected (Henrard and Bennett, 1973; Spagnola et al., 1978). In male Pima Indians over the age of 55 the prevalence of DISH was 48 percent; 50 percent of whom were afflicted with diabetes mellitus (Henrard and Bennett, 1973; Spagnola et al., 1978; Bennett et al., 1971). While diminished in females, the prevalence of DISH was higher than average at 12 percent (Henrard and Bennett, 1973; Spagnola et al., 1978).
DISH in Non-Human Subjects

DISH has also been seen in non-human subjects in the fossil record and in current studies. BM Rothschild analyzed DISH throughout a large number of mammal species and revealed some interesting insights about the disease (1987; 1988). DISH can be seen in contemporary mammals like horses, gorillas, whales and dolphins but the surprising aspect is its prevalence in the fossil record (Rothschild, 1988: 68). DISH has been found in camels, rhinoceri, saber toothed tigers, wolves, mastodons and whales (Rothschild, 1987). The most stunning example is that of dinosaurs, the fossil remains of which have survived for over 65 million years (Rothschild, 1988). Rothschild states that Iguanaodons, Hadrosaurs, Ceratopsians, Therassaurus and Ornithischians all exhibited longitudinal ligament calcification in some form (Rothschild, 1987). Apatosaurus and Diplodocus both exhibit vertebral fusion, thus supposedly allowing for greater stability for the creatures (Rothschild, 1988). Since it was discovered that particular dinosaurs walked bipedally with their tails in the air, it is now thought that small vertebral fusions helped them to use these tails as whip-like weapons (Rothschild, 1987). Due to its continued presence in the fossil record and the aforementioned explanations, Rothschild postulates that DISH itself is an advantageous adaptation for particular animal species (Rothschild, 1988).

In clinical studies involving mice and cats, vitamin A dosage creates extensive skeletal proliferation, both hyperostotic and enthesopathic formations (Seawright et al., 1965; Gerber et al., 1981). Although this does not cement excess vitamin A involvement in DISH related bone proliferation, it is something to keep in mind because vitamin A overdose in humans can alter longbones (Gerber et al., 1954; Utsinger, 1985). The presence of DISH in nonhuman animals as
presented here, further the case that DISH has a wide geographic and temporal presence on this planet.
Chapter VI

Etiology

DISH is a common disorder of unknown etiology, although genetic, metabolic, endocrinologic, anatomic, environmental, and toxic factors have all been suggested as playing a possible role in the new bone growth characterizing it (Sarzi-Puttini and Atzeni, 2004: 288).

The possible etiologies that have been presented for DISH are discussed in Chapter VI. Although at this time there is still no universally agreed upon cause of the disease, it has not stopped researchers from examining many possible explanations. A variety of research topics regarding possible causes of DISH are summarized and explained in this chapter.

When the disease was first labeled senile ankylosing hyperostosis of the spine in 1950 by Forestier and Rotes-Querol, no etiology was known or postulated (1950). In the 1960’s and 1970’s, Julkunen proposed several possible explanations for the presence of hyperostosis. Diabetes and obesity (Julkunen et al., 1966; Julkunen et al., 1971), hyperglycaemia (Julkunen et al., 1968; Julkunen et al., 1971), and acromegaly (Julkunen et al., 1966) were all suggested to be risk factors associated with hyperostosis, but more obviously, age was considered a primary factor. Resnick et al. (1975) agree that the etiology for DISH is obscure, especially the involvement of the ossification of appendicular tendon and ligament attachments. Resnick and Niwayama (1976) reiterate this statement a year later and mention the possible role of hypervitaminosis A and hypoparathyroidism in DISH, but conclude that the etiology is still unknown. However, some authors consider DISH to be a “multisystem hormonal disorder, which seems to be the most reasonable conclusion to date” (Rogers and Waldron, 2001: 360).
The role of the HLA gene loci have been suggested as causal factors for DISH (Shapiro et al., 1976; Spagnola et al., 1978) along with other genes (Tanaka et al., 2001). The strongest connection to DISH appears to be diabetes mellitus. Obesity is usually associated with abnormalities involving insulin metabolism, which may have growth factor-like activity causing DISH related abnormalities (Utsinger, 1985). As far as hazards associated with DISH, dysphagia and myelopathy appear to be the most common (Utsinger, 1985).

**Diabetes Mellitus and Obesity**

The discovery of insulin dates back to 1922, when Banting et al. examined the internal secretions of the pancreas (1922). Prior to this time, patients who suffered from diabetes were lucky to survive two years past the date of their diagnosis (King and Rubin, 2003). Diabetes mellitus (E10-E14) is located under the endocrine, nutritional and metabolic diseases (E00-E90) in the International Classification of Disease (ICD) (WHO, 2007). Diabetes and obesity, along with impaired glucose tolerance and prolonged hyperinsulinaemia have been suggested a number of times as one of the possible causes of DISH. Diabetes as discussed in this these refers to the nongenetic disorder. There are many authors who agree that diabetes is involved in DISH (Julkunen et al., 1971; Hájvková et al., 1964; Bennett et al., 1971; Waldron, 1985; Rogers et al., 1985; Utsinger, 1985; Littlejohn and Smithe, 1985; Waldron and Rogers, 1990; Kiss et al., 2002a; Ghosh et al., 2004; Müldner and Richards, 2007; Verlaan et al., 2007) but also quite a few who feel the connection is unjustified (Resnick et al., 1975; Cassim et al., 1990; Crubézy and Trinkhaus, 1992; Rothschild; 1993; Arriaza et al., 1993; Sencan et al., 2005). Studies tend to fall on both sides of this debate as to whether or not DISH is related to diabetes. An early study
by Hájvková et al. (before DISH was properly named and was referred to as hyperostotic spondylitis) revealed that out of 101 with diabetes, 40 individuals were diagnosed with DISH (1965). The authors state that the meaning of these results were inconclusive in terms of etiology, but still an important aspect to examine in the future (Hájvková et al., 1965). Rosenbloom’s study years later suggested something similar: that roughly one half of all patients with DISH will have diabetes (Rosenbloom, 2004). Utsinger cites hyperglycaemia as the most common laboratory abnormality associated with DISH (Utsinger, 1985). He mentions that the 16 percent of patients he studied were hyperglycaemic, while 10 percent suffered from diabetes mellitus (Utsinger, 1985). It is clear that this debate is not an easy one to resolve, with both sides showing solid data to support their claims. Arriaza et al. (1993) postulate that DISH could be an evolutionary response to increased longevity, suggesting that it is a response to excessive skeletal stress. The presence of DISH in the Nubian collection reveals that it should be more common in higher ranks of stratified societies more so than hunter gatherer societies, as postulated by Arriaza et al. (1993). The authors conclude: “DISH is not just a product of contemporaneous health disorders of modern human behavior; it has been present in the Old World for more than 2,000 years” (Arriaza et al., 1993: 247).

A 1981 study carried out by Littlejohn and Smythe studying 11 patients with DISH showed that there was a significant difference in glucose levels compared to a control population. Although the BMI did not differ significantly between the groups, the glucose levels were 164 percent higher, on average, in those patients affected with DISH, suggesting significant hyperinsulinemia (Littlejohn and Smythe, 1981). Although both authors agree that the metabolic changes and new bone growth may be affiliated with another undetermined condition, Littlejohn and Smythe conclude:
Thus patients with DISH may be those who exhibit obesity-induced insulin receptor changes with subsequent hyperinsulinemia and tendency to adult-onset diabetes. The hyperinsulinemia may directly or indirectly cause the new bone growth seen in DISH (1981:968).

Obesity (independent of diabetes) is sometimes considered to be related to DISH as well, as seen in monks (Waldron, 1985; Rogers et al., 1985; Waldron and Rogers, 1990). Mata et al. (1997) carried out a controlled study and interpreted the results to suggest that early weight gain may be a risk factor for DISH, but no conclusion was reached. Other authors think that adult onset diabetes, most particularly the monastic or high status way of life, contributes to DISH (Rogers and Waldron, 2001). The authors concluded the following regarding DISH and its possible connection with diabetes:

The evidence seems overwhelming, therefore, that obesity and type II diabetes were likely to be hazards for those living within the monastery walls, and it seems probable that this would predispose them to develop DISH (Rogers and Waldron, 2001: 362).

Although an agreement has yet to be reached concerning the connection between DISH and obesity, the present thesis suggests that DISH is not the result of high status lifestyle and the accompanying diet, but other factors altogether.

A case study from 2004 revealed that a type II diabetic woman underwent radiographic examination due to increased stiffness and pain in the back and general weakness (Ghosh et al., 2004). This 58-year old woman was revealed to have a melting candle wax buildup present on adjacent lumbar vertebrae (along the ALL), criteria of DISH (Ghosh et al., 2004). In addition to type II diabetes, the woman also suffered from obesity, hypertension and hyperlipidaemia (Ghosh et al., 2004). Thus it appears that Ghosh et al. are in favor of the diabetes-DISH correlation (2004).
A case-control study was carried out using patients who participated in a screening survey of vertebral osteoporosis, the European Vertebral Osteoporosis Study (EVOS) (Kiss et al., 2002a). The survey was a questionnaire regarding particular lifestyle choices of those individuals diagnosed with DISH (Kiss et al., 2002a). The study determined the average age of those afflicted with DISH to be 65 years and it was also noted that weight gain between 25 years and the patient’s current age was common to DISH sufferers (Kiss et al., 2002a). The EVOS questionnaire revealed a high presence of diabetes mellitus (19.8 percent) in DISH patients (Kiss et al., 2002a). An elevated serum uric acid level was also found in DISH patients but this did not appear to be connected with obesity (Kiss et al., 2002a). The authors agree with Mata et al. (1997) that obesity at an early age is a strong risk factor for DISH (Kiss et al., 2002a). But they are unsure about the association of DISH with insulin levels (Kiss et al., 2002a).

Another case-control study was carried out a few years later but along different lines than the one previously mentioned (Sencan et al., 2005). This study examined a group of diabetes mellitus patients for the prevalence of DISH instead of the opposite (Sencan et al., 2005; Kiss et al., 2002a). The study included 133 diabetes mellitus patients and 133 non-diabetic control patients and revealed that 16 of the diabetes mellitus patients (12 percent) were diagnosed with DISH compared to 9 (6.8 percent) within the control group (Sencan et al., 2005). There were not an equal number of males and females participating in the study so a male to female ratio could not be established (Sencan et al., 2005). These results were not statistically significant, suggesting no link between DISH and diabetes mellitus in this particular case study (Sencan et al., 2005). The authors also mention that insulin and Insulin-like Growth Factor-1 (IGF-1) levels were normal in the DISH patients suggesting no correlation between either and DISH in this particular study (Sencan et al., 2005).
The statistics and opinions for and against the involvement of diabetes with DISH, as seen previously, show that a consensus regarding the relation between the two has yet to be reached. Although there may never be complete agreement in this debate, the topic should not be dismissed but should continue to be studied in clinical and cemetery populations.

**HLA-B Gene Locus**

The HL-A system is the human form of the major histocompatibility system found in most vertebrates (Bodmer, 1972). Genes in this area have been shown to control immune response and thus, the susceptibility to disease, tumors and viruses (Bodmer, 1972). The HLA region is on chromosome six and the HLA-A, B and C loci code for antigens that are in a majority of human tissues (Bodmer, 1981). In higher eukaryotes, gene clustering is very common and the HLA system is one of the more complex clusters known (Bodmer, 1981).

Variation at the HLA-B gene locus is sometimes associated with ankylosing spondylitis, primarily the HLA-B27 allele. One of the first studies to address the prevalence of the HLA antigens in DISH was done by Shapiro et al. in 1976. Forty seven patients who were diagnosed with DISH were tested for the B27 antigen and compared with 1,205 control patients (Shapiro et al., 1976). Sixteen of the forty seven patients possessed the B27 antigen (34 percent) as compared to 96 (8 percent) in the controls, a highly significant difference (Shapiro et al., 1976). It then follows that at least 25 percent of the population with the B27 haplotype would be expected to have DISH (Shapiro et al., 1976). Shapiro et al. provide several possibly explanations for the role of HLA-B27 in ligament ossification and spondyloarthopathy creation:

a) The B27 gene is linked to specific immune response genes which are requisite for the development of disease; b) the B27
antigen, or closely linked gene, has cross-reactivity with a microorganism which causes the above conditions (“molecular mimicry”); and c) the B27 allele, or a closely linked gene, controls a cell-surface receptor for the pathogenetic microorganism. (1976: 7).

Although these hypotheses were neither supported or rejected with their research, Shapiro et al. are confident that B27 is linked closely with new bone formation, like that found in DISH (1976). A later study by Utsinger showed only 21 of 200 DISH individuals positive for the HLA-B27 allele, a weaker correlation than found by Shapiro et al. (1985; 1976).

A 1978 study of the Pima Indians, a population already known to have a high prevalence of DISH (Henrard and Bennett, 1973) examined the possible association of the HLA-B27 antigen and its potential role in vertebral ankylosing hyperostosis (Spagnola et al., 1978). Four Pima males were examined (between 55 and 90 years of age) and compared to thirty-three similarly aged control patients for the haplotype frequency of the A and B series HLA antigens (Spagnola et al., 1978). All of the patients had the criteria for ankylosing hyperostosis: three osteophytic bridged vertebrae (Spagnola et al., 1978). No statistically significant results were found, as the Pima group showed an 18 percent HLA-B27 prevalence and the control group showed a 20 percent HLA-B27 prevalence (Spagnola et al., 1978). The authors conclude these findings contradict earlier research by Shapiro et al. (1976) suggesting a correlation between ankylosing spondylitis and the HLA-B27 antigen (Spagnola et al., 1978). Several other HLA gene locus alleles are being examined for a DISH correlation: HLA-B5 (Ercilla et al., 1977), HLA-B8 (Rosenthal et al., 1977) and HLA-A11 (Brigode and Grancois, 1977).
Other Genetic Involvement

A 2001 study suggests the involvement of bone morphogenic protein-2 (BMP-2) in the ossification of the posterior longitudinal ligament (sometimes referred to as OPLL) (Tanaka et al., 2001). BMPs are genes that promote bone growth and are especially important in vitro, particularly pertaining to cell proliferation, alkaline phosphatase activity and collagen synthesis (Tanaka et al., 2001: 1163). The BMP-2 gene of five individuals with OPLL and OALL were examined through polymerase chain reaction techniques (Tanaka et al., 2001). The authors concluded that BMP-2 is expressed in spinal ligaments and is an important part of ontogenetic differentiation between the ligaments and the bones (Tanaka et al., 2001). A study several years later suggests that Matrix Gla protein (MGP) may work to inhibit BMP-2, and a deficiency in MGP may be the reason for excess BMP-2 expression (Rutsch and Terkeltaub, 2003). The exact circumstances around which MGP is expressed, however, is still unknown (Rutsch and Terkeltaub, 2003).

A case study of a family with DISH gives more weight to the argument that the disease itself is due to genetic factors instead of environmental ones (Gorman et al., 2005). A 52-year old father and his 23-year old son and 24-year old daughter all suffered from stiffness of the neck and radiographic analyses revealed cervical osteophytes in all three cases (Gorman et al., 2005). HLA-B27 presence was negative in all three cases as well, thus suggesting that the relationship between genes and particular ligament ossifications still needs to be uncovered (Gorman et al., 2005).
Ossification of the Posterior Longitudinal Ligament (OPLL)

The ossification of the posterior longitudinal ligament (OPLL) is sometimes associated with DISH and usually occurs in the cervical vertebrae with resulting symptomatic dysphagia. OPLL is genetically linked and sometimes seen in families, as the previous section illustrated (Gorman et al., 2005). OPLL is sometimes known as “Japanese disease” due to its prominence in that area of the world (Koga et al., 1998; Gorman et al., 2005). Studies attempted to link OPLL to the HLA gene locus (particularly the COL11A2 allele) had, as of 2001, been unsuccessful (Havelka et al., 2001)

Myelopathy

Myelopathy refers to extra pressure or pinching of the spinal cord or nerve roots by the vertebrae (NASS, 2006). Myelopathy can sometimes be found in individuals that exhibit ankylosing hyperostosis of the spine and some extraspinal osteophytes. Myelopathy can sometimes cause increased reflexes (hyperreflexia), changes in normal walking and loss of balance, and the loss of sensitivity in the hands and feet (NASS, 2006). DISH related ligament ossifications can cause neurological abnormalities like myelopathy, in which basic motor functions may be disrupted (Utsinger, 1985). Myelopathy is often attributed to ossification of the PLL sometimes including the ligamentum flavum (Utsinger, 1985). Hukuda et al. examined the extraspinal manifestations in 58 patients who underwent surgery for cervical myelopathy between 1964 and 1980 (1983). Ossification of the PLL along their cervical vertebrae was quite frequent (although the number was not recorded) and extraspinal manifestations were present in
a number of individuals as well: 86 percent hip involvement, 80 percent knee, 63 percent ankle and 46 percent elbow (Hukuda et al., 1983). These extraspinal involvements clearly coincide with those criteria set forth by Resnick and Niwayama, and Utsinger (1976; 1985). Hukuda et al. oppose current literature by concluding that ossification of the ligamentum flavum in addition to the PLL is a crucial aspect of DISH (Hukuda et al., 1983). In 1983, DISH was estimated to be present in 20 million individuals in Japan with a male to female ratio of 7:3 (Hukuda et al., 1983).

The first account of a case of DISH affecting normal peripheral nerve function was reported in 1988 (Haskard and Panayi, 1988). A 61-year old patient diagnosed with DISH suffered from the compression of nerves as a result of the ossification associated with DISH (Haskard and Panayi, 1988). This patient complained of stiffness of the joints and exhibited a general muscle weakening of the hands (Haskard and Panayi, 1988). Although nerve damage is occasionally seen axially, there had been no previous accounts of peripheral nerve damage as a result of DISH (Haskard and Panayi, 1988). Another study discussed nerve entrapment affecting peripheral limbs, and out of 56 patients with DISH, carpal tunnel syndrome was seen in eight cases, ulnar entrapment was seen in one, and tarsal tunnel syndrome was also seen in one individual (Mata et al., 1997). Myelopathy and peripheral nerve entrapment although common, have been known to occasionally occur as a result of DISH ossifications.

**Dysphagia**

Dysphagia, an interruption in swallowing, is thought to occur in 17 percent of all DISH cases (Utsinger, 1985). Ankylosing hyperostosis of the spine (as it was known in the 1970’s
before the DISH nomenclature became more widespread) was first associated with dysphagia in Meeks and Renshaw (1973; Huang and Laha, 1978). However, the first case was observed (though not named) in 1905, and the first surgery occurred in 1926 (Zahn, 1905; Mosher, 1926). Like the thoracic and the lumbar portions of the spine, arthritic osteophytes can also occur on the cervical vertebrae and sometimes interfere with the surrounding soft tissue. Huang and Laha explain: “Occasionally, a huge cervical osteophyte may impinge upon the esophagus, trachea or adjacent soft tissue producing dysphagia” (1978: 273). Several possibilities have been proposed as to how DISH affects dysphagia: a large osteophyte can cause mechanical obstruction, smaller osteophytes can impinge on esophagus mobility, inflammation can cause oesophageal obstruction, spasms that can affect swallowing, and nerves could be damaged by hyperostosis (Coelto, 1995).

In the Huang and Laha case report, a 52 year-old man cited difficulty swallowing and hoarseness of voice along with the inability to swallow solid food (1978). A roentgenogram, laryngogram, and esophagogram showed a large osteophyte bridge present on the C5 and C6 anterior vertebral bodies (Huang and Laha, 1978). The bridging was then surgically excised and no further symptoms were cited (Huang and Laha, 1978). As Forestier and Rotes-Querol described, with ankylosing hyperostosis immobility of the spine and pain are uncommon symptoms, however, when the ankylosing hyperostosis extends to the cervical area, movement restriction and pain become quite common (1950; Huang and Laha, 1978). Huang and Laha recommend that when dysphagia is determined to be caused by cervical osteophytes, further dorsolumbar and joint surveys may be important in diagnosis (1978). A 2003 case study cited a 56-year old man with a diagnosis of DISH, who had difficulty swallowing fluids (Clark et al., 2003). A lateral radiograph showed a large osteophyte on the C3-C4 vertebrae, limiting neck
mobility to 10 percent of normal (Clark et al., 2003). A simple operation was performed and the patient’s dysphagia was eliminated (Clark et al., 2003).

One particular report suggested a thoracic hyperostosis involvement in dysphagia (Cai et al., 2003). A 73 year old man was having difficulty swallowing and pain that he described as “[like] being thumped by a truckload of watermelons,” a radiographic scan was conducted (Cai et al., 2003: 1575). Vertebral osteophytes were found low on the thoracic vertebrae, at T9 and T10 (Cai et al., 2003). It was suggested that the weight of the diaphragm and other organs in the thoracic cavity were compressing the esophagus into the large osteophytes causing dysphagia (Cai et al., 2003).

In conclusion, dysphagia is a somewhat common side effect of DISH and is particularly difficult to determine in a skeletal population. As seen from Cai et al., the lack of cervical osteophytes does not guarantee that a patient did not suffer from dysphagia (2003). Dysphagia in the MCIG collection will not be mentioned in the results and discussion section because in the absence of soft tissue, there is no way to be sure a particular individual actually suffered from dysphagia.

**DISH Detection**

When dealing with DISH in living populations, stiffness and lack of mobility suggest the presence of DISH, however the only way to properly diagnose it is through extensive radiographic examination (Mata et al., 1993). Posteroanterior and lateral chest radiographs of the cervical, thoracic and lumbar vertebrae, and the sacroiliac area are very helpful in diagnosing vertebral hyperostosis and “radiologists experienced in reading radiographs can use chest radiographs to diagnose DISH in a highly consistent manner” between 76 percent and 75 percent
of the time (Mata et al., 1993: 1908). Radiographs of the patellae, ulnae, calcanei, femora, tibiae and scapulae help to detect the presence of osteophytes and are crucial for diagnosing DISH in living populations (Mata et al., 1993). Computed tomography (CT) scans can help to distinguish a hyperostotic spine and be used to determine any inflammatory components of extraspinal osteophytes (Cammisa et al., 1998). Bony coating associated with DISH (osteophytes) can be distinguished using magnetic resonance imaging (MRI) (Cammisa et al., 1998). Other authors suggest that MRI analysis has also opened horizons for the early detection of joint damage and synovial inflammation (Boutry et al., 2007).
Chapter VII
Methods and Materials

This purpose of this chapter is to explain the analysis of the skeletal remains in the MCIG cemetery collection. Through analysis of individuals with extensive vertebral enthesophytes or vertebral fusion, conclusions regarding the presence of DISH or DISH-like cases can be reached. If DISH is in fact present in a percentage of the cemetery population, this data can then be used to support the hypothesis that DISH is not directly caused by dietary factors, most particularly those associated with diabetes.

The author’s preliminary analysis of diffuse idiopathic skeletal hyperostosis in the Milwaukee County Institution Grounds cemetery began in October of 2006. The author worked with the MCIG collection in the fall of 2006, the spring of 2007 and the summer of 2008. The collection was housed in Lalumiere Language Hall, 526 N 14th Street, on the south end of Marquette University’s campus. Since 1993, Norman Sullivan, Associate Professor of Anthropology at Marquette University, and his osteology students, have been compiling inventory, metric data, nonmetric data, age/sex data and paleopathologic data for the 1,649 skeletal remains recovered from the excavated cemetery. Unfortunately, many of those burials were too fragmented to properly analyze, which is the case for several individuals that have some evidence of DISH. These fragmented burials will be mentioned later in the thesis. The data was compiled and recorded using the criteria found in the Standards for Data Collection from Human Skeletal Remains (SDCHSR) (Buikstra and Ubelaker, 1994). The SDCHSR forms have been completed over the years following the acquisition of the collection under the guidance and
supervision of Sullivan, so it can be said with confidence that the data found within these forms is reliable.

The first step in analysis was identifying which of the burials could potentially have DISH or a similar disease like AS. Due to time restrictions, the author could not inspect every burial in the MCIG collection for DISH, so the SDCHSR forms were consulted to determine the individuals with the greatest chance of exhibiting the disease. For each burial in MCIG a form from SDCHSR was filled out recognizing the paleopathologies present (Buikstra and Ubelaker, 1994). Each bone and pathology is giving a number based on its location and severity. The first area of interest is the vertebrae, particularly conditions 7.2 (osteophytes) and 7.5 (spondylitis) as indicated in Buikstra and Ubelaker (1994). If sections of the vertebrae were marked as having curved spicules (7.2.3) or fusion present (7.2.4) the burial number was marked down for a later thorough analysis. In addition to vertebral bone formation, severe arthritic buildup on peripheral limbs was also noted. This is indicated by Buikstra and Ubelaker as (8.1), arthritic lipping (1994). The forms consulted for this aspect of the analysis can be seen in Appendix A (Buikstra and Ubelaker, 1994).

Each of these burials was then examined for the presence of vertebral fusion in the cervical, thoracic, lumbar and sacroiliac areas. The criteria sheet created and used by the author can be seen in Appendix B. This criteria sheet instructs the examiner to mark each corresponding vertebra to better distinguish its involvement in DISH. Heavy enthesophytes, “puzzle piece kissing” (a term coined by the author and described in the discussion section) and fusion are the possible descriptions of arthritic vertebrae. Each of the five extraspinal elements were also analyzed and placed into three categories based on osteophytic presence (Figure 29 to Figure 35). The first was a small osteophyte, totaling less than 3mm, the second was a medium
osteophyte between 3mm and 5mm and the third was a large osteophyte extending over 5mm. Due to their location on the bone, some of these spurs were difficult to measure with a calipers so a small ruler was used to designate the amount of protrusion. The results were then compared with the present study criteria (described below) and the individual was classified as exhibiting no DISH, DISH-like conditions or clinical DISH. Criteria for extraspinal grading was first established by Resnick et al. (1975) but simply described as mild to moderate and moderate to severe abnormality. Another extraspinal grading system, presented by Beyeler et al., (1990) was also deemed inadequate. The author thinks the criteria presented here is the best way to describe DISH. Through a numerical grading system that involves numerical measurements, the researcher is able to describe an ossification point more accurately than a vague “moderate” or “severe” verbal description. Resnick et al. (1975) mentioned a number of other extraspinal areas that may be affected by DISH but only five of these were examined for the present study: anterior patella, tibial tuberosity, posterior calcaneus, iliac crest and proximal olecranon of the ulna.

The differences among the three phases on the extraspinal elements examined can be seen in Figure 29 to Figure 35. The author thinks that the role of the extraspinal manifestations in DISH should not be considered a large part of the criteria in number. Two extraspinal areas are mentioned in the criteria used in this thesis. The author thinks the definitions of DISH should not rely solely on the presence of these areas, but the extraspinal factors should act as a status level indicator on the progression of the disease itself. Although this project only analyzes DISH and DISH-like skeletal cases, this does not mean that particular DISH examples do not express more features of DISH than others.
Figure 29: Burial 9926. Left ulna. A 3-5mm buildup occurring on the olecranon.

Figure 30: Burial 9303. Right ulna. A >5mm buildup occurring on the olecranon.
Figure 31: Burial 9354. Right tibia. A 3-5mm tibial tuberosity buildup.

Figure 32: Burial 9303. Right tibia. A >5mm tibial tuberosity buildup.
Figure 33: Burial 9345. Right patella. A >5mm anterior buildup.

Figure 34: Burial 9302. Right Pelvis. A >5mm iliac buildup.
Figure 35: Burial 8196. Left calcaneus. A 3-5mm buildup on the posterior area.
Lastly, each burial was aged and sexed using all of the possible methods described in SDCHSR (Buikstra and Ubelaker, 1994). Since many of the burials were fragmentary, it was sometimes difficult to determine age and sex of each individual. The Suchey-Brooks and the Todd Pubic methods were used to determine age from the pubis (when present) (Buikstra and Ubelaker, 1994). The auricular surface of the pelvis was also graded (when present). The SDCHSR grading system for skull sutures was also utilized to determine age (when full skulls were available). Since many of those individuals examined had fragmentary skulls, little weight was given to skull sutures (Buikstra and Ubelaker, 1994). The established age and sex of each individual was then recorded on the DISH recording form shown in Appendix B.

Present Study Criteria

In this study, the criteria used to designate DISH in a particular individual was one of my own design, adding to a collaboration of several past criteria (Resnick et al., 1975; Resnick and Niwayama, 1976; Utsinger, 1985). The criteria were:

1. The osteophytic bridging or “puzzle piece kissing” of three contiguous vertebral bodies, along the right anterolateral ligament of the spine.

2. The intervertebral space was maintained, meaning the annulus fibrosus and the nucleus pulposus were not ossified.

3. Absence of sacroiliac fusion, general bone erosion, posterior longitudinal ligament ossification and sclerosis.
4. The presence of any number of extraspinal manifestations (of whatever degree of severity), but most particularly: the proximal ulna (olecranon), the anterior patella, the posterior calcaneus, the iliac crest and the tibial tuberosity.

The following are the requirements for the three stages of DISH as used in this study:

- **Complete DISH:** An osteophytic bridging or “puzzle piece kissing” of three contiguous vertebrae along the anterolateral longitudinal ligament and the presence of two or more extraspinal manifestations of any degree.

- **DISH-Like:** An osteophytic bridging of two vertebrae with “puzzle piece kissing” vertebrae or extensive osteophytic vertebrae adjacent to the bridging, along with the presence of two or more extraspinal manifestations.

- **Potential DISH:** The presence of extensive osteophytic vertebrae (but no fusion or “puzzle piece kissing”) and one or more extraspinal manifestations. Potential DISH is not examined in this study.

**Statistics**

The data was then tabulated and organized into charts, tables and graphs. These results were analyzed using Microsoft Excel. Two Chi square tests were utilized in order to determine significance of sex in DISH and DISH-like cases (Grimm, 1993). The results are reported below.
Chapter VIII

Results

The results of the skeletal analysis of the MCIG collection are presented in Chapter VIII. A total of 74 internments were examined for this thesis. Each of the burials was selected for examination based on a previous primary paleopathological diagnosis by Norman Sullivan and was determined to have extensive vertebral osteophytes or fusions according to SDCHSR criteria (Buikstra and Ubelaker, 1994). DISH was exhibited in 12 cases, and a DISH-like condition or possible DISH, was seen in 14 cases of the total 74 examined. A more thorough description of these individual burials can be found in Appendix C. The thesis analysis results are presented in Table 1.

Non-DISH cases

Thirty nine of the individuals examined did not possess any DISH or DISH-like pathologies. This does not mean that no vertebral enthesophytes or extraspinal manifestations present in these cases, but simply that these individuals did not show symptoms that warranted any further analysis. As seen in Appendix C, the 39 individuals who exhibited no DISH or DISH-like pathologies are left blank (represented by a 0) and were not aged and sexed. An example of heavy enthesophytes without the presence of DISH can be seen in Figure 36 in which the two lower thoracic vertebrae are “kissing” but not in the “puzzle piece” fashion that most likely concerns DISH. There is no guarantee that this individual would eventually exhibit DISH (if they
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Table 1: Study results. A (0) indicates no presence or not examined. NA indicates not aged and NS indicates not sexed. These apply to cervical fusion and AS cases.
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Table 1 (cont): Study results
Figure 36: Burial 3042. An example of a spine with very little right anterolateral ligament buildup and ossification. This is a non-DISH case.
continued living), but at the time of death, with only two lower thoracic vertebrae affected, the criteria of DISH are not met. It should be mentioned that the individuals examined that did not exhibit DISH varied greatly in age (although the sex and age were not recorded). Thus it cannot be claimed that DISH affected every late age person examined because many of the 39 non-DISH individuals examined would have been aged as 50+ years.

**Ankylosing Spondylitis**

Of those 74 individuals from MCIG examined, 5 of the individuals exhibited ankylosing spondylitis. Ankylosing spondylitis was for the most part, unless it existed with DISH, not examined in this thesis. The individual seen in Figure 37 can be said to exhibit AS. As previously described, AS involves intervertebral ossification and an all encompassing fusion of the ALL, usually including the PLL. Unlike DISH, AS does not require extraspinal features and a majority of the cases do not have any extraspinal ossifications at all.

**DISH and AS**

The presence of both DISH and AS in the same individual occurs twice in the MCIG population and is cited several times in this thesis (Williamson and Reginato, 1984; Olivieri et al., 1987; Rillo et al., 1989; Kozanoglu et al., 2002). Figure 38 demonstrates the DISH type fusion that occurred in this individual, including a “puzzle piece kissing” fusion. Although not featured in Figure 38, the individual from burial 5075 exhibited the extraspinal manifestations of DISH as well as the fused sacrum seen in AS. At this time, there is no data regarding the percent
Figure 37: Burial 5073. An example of ankylosing spondylitis of thoracic vertebrae. The intervertebral space is not maintained and the ALL ossification appears to fully cover the vertebrae and connect with PLL ossification.
Figure 38: Burial 5075. The present photo (T6-T12) shows extensive lateral osteophytes from T6-T10, however, the bones are not completely fused but appear to “puzzle piece kiss” in which the arthritic areas fit together with the adjacent vertebrae.
of individuals diagnosed with DISH and AS, but it appears to be very rare in current populations as compared to the presence of each disease by itself.

**DISH-like and AS-like**

There is one individual in the MCIG collection that exhibits both DISH-like and AS-like features. The individual does not have enough vertebrae fused to be considered DISH and the sacrum is only fused to the pelvis completely on one side of the body, thus suggesting that this individual be considered DISH-like and AS-like. At this time, there has been nothing in the literature showing the presence of both DISH and AS in transitional forms, but this individual, burial 9348, clearly shows that it is possible. The author found no references as to the percentage of individuals affected by transitional DISH and AS simultaneously.

**DISH cases**

As seen in Table 2, there were 12 cases of DISH present in the MCIG collection. All of these cases were determined to be males, using sexing methods from SDCHSR (Buikstra and Ubelaker, 1994). Seven individuals fell within the 40 to 50 year age range after aging methods were applied, and five individuals were deemed to be over 50 years of age (Table 3). Figure 39 is an example of one of the DISH fusions seen in the collection. In DISH cases, the thoracic spine was involved in fusion or showed enthesophytes in every individual (100 percent), whereas the cervical spine showed involvement in only one case (8.3 percent) and the lumbar region was involved in four cases (33.3 percent).
<table>
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<th>Vertebrae</th>
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<th>Illiac Crest</th>
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Table 2: DISH cases. The number in the vertebrae section indicate the number of fused and enthesophytic vertebrae present. F represents sacro-iliac fusion. The extraspinal numbers indicate the grade of that area for that individual.
Figure 39: Burial 3068. T6-T12 vertebrae shown here, with extensive buildup along the right ALL. “Puzzle piece kissing” can be seen here.
Table 3: DISH age.

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Table 4: The number of DISH burials with cases of extraspinal involvement.

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Table 5: Number of patients exhibiting particular DISH manifestations.

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<tr>
<td>Tibia</td>
<td>7</td>
</tr>
</tbody>
</table>
All of these individuals except one (burial 5040) show the presence of at least three extraspinal ossifications even though only two are required in the current criteria of DISH. Table 4 shows the number of extraspinal areas affected across all of the individuals with DISH. It is clearly skewed toward the higher end, with three individuals showing at least one ossification on all five of the extraspinal areas, six individuals exhibited ossification on four areas, and three showing three ossified areas. Table 5 shows the most common extraspinal areas affected in DISH: the calcaneus, followed closely by the ulna. Table 6 shows the number of times each grade is exhibited for each of the extraspinal areas. There appears to be no correlation between DISH individuals and the side on which the extraspinal ossifications are present.

Table 2 shows the number of vertebrae involved in each case, including both fusions and extensive enthesophytes; these burials are thoroughly described in Appendix C. Table 2 also presents the age and sex of each individual and the grade of both the left and right extraspinal areas according to the criteria. If one of the boxes in the table is blank, this indicates that the area was too fragmented to examine.

**DISH-Like Cases**

DISH-like cases are covered in Table 7. There were 14 of these present in the MCIG collection, including two in females. The types of fusions and number of extraspinal areas involved vary and are selectively discussed in Appendix C. Four individuals were aged between 30 to 40 years, six aged between 40 to 50 years and four determined to be over the age of 50 (Table 8). Two individuals failed to show any evidence of extraspinal areas of ossification but the results of Table 9 were, overall, much more evenly dispersed than that of Table 4, the DIS
<table>
<thead>
<tr>
<th></th>
<th>Ulna</th>
<th>Iliac Crest</th>
<th>Tibia</th>
<th>Patella</th>
<th>Calcaneus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
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<td>1</td>
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<tr>
<td>Grade 2</td>
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<td>3</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>2</td>
<td>2</td>
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<tr>
<td>Totals</td>
<td>7</td>
<td>8</td>
<td>8</td>
<td>7</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 6: Occurrence of extraspinal manifestations in DISH.
<table>
<thead>
<tr>
<th>Individual</th>
<th>Burial #</th>
<th>Cervical</th>
<th>Thoracic</th>
<th>Lumbar</th>
<th>Pelvis</th>
<th>Vertebrae</th>
<th>Ulna</th>
<th>Iliac Crest</th>
<th>Tibia</th>
<th>Patella</th>
<th>Calcaneus</th>
<th>Sex</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3026</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>M</td>
<td>40-50</td>
</tr>
<tr>
<td>2</td>
<td>3071</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>F</td>
<td>30-40</td>
</tr>
<tr>
<td>3</td>
<td>5041</td>
<td>-</td>
<td>3</td>
<td>2</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>F</td>
<td>30-40</td>
</tr>
<tr>
<td>4</td>
<td>5048</td>
<td>-</td>
<td>6</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>M</td>
<td>40-50</td>
</tr>
<tr>
<td>5</td>
<td>5094</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>M</td>
<td>50+</td>
</tr>
<tr>
<td>6</td>
<td>5243</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>M</td>
<td>50+</td>
</tr>
<tr>
<td>7</td>
<td>6250</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>F</td>
<td>40-50</td>
</tr>
<tr>
<td>8</td>
<td>7112</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>M</td>
<td>50+</td>
</tr>
<tr>
<td>9</td>
<td>7224</td>
<td>-</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>M</td>
<td>50+</td>
</tr>
<tr>
<td>10</td>
<td>8196</td>
<td>-</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>M</td>
<td>30-40</td>
</tr>
<tr>
<td>11</td>
<td>9226</td>
<td>-</td>
<td>4</td>
<td>4</td>
<td>-</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>M</td>
<td>50</td>
</tr>
<tr>
<td>12</td>
<td>9237</td>
<td>-</td>
<td>6</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>M</td>
<td>30-40</td>
</tr>
<tr>
<td>13</td>
<td>9295</td>
<td>-</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>M</td>
<td>30-40</td>
</tr>
<tr>
<td>14</td>
<td>9348</td>
<td>-</td>
<td>5</td>
<td>2</td>
<td>F</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>M</td>
<td>40-50</td>
</tr>
</tbody>
</table>

Table 7: DISH-like cases. The number in the vertebrae section indicate the number of fused and enthesophytic vertebrae present. F represents sacro-iliac fusion. The extraspinal numbers indicate the grade of that area for that individual.
Table 8: DISH-like age.

<table>
<thead>
<tr>
<th>Age</th>
<th># of Individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-40</td>
<td>4</td>
</tr>
<tr>
<td>40-50</td>
<td>6</td>
</tr>
<tr>
<td>50+</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 9: Number of DISH-like burials with cases of extraspinal involvement.

<table>
<thead>
<tr>
<th># of Extraspinal Areas</th>
<th>Burials With</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 10: Number of patients exhibiting particular DISH-like manifestation.

<table>
<thead>
<tr>
<th>Site</th>
<th>Individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spine-C</td>
<td>0</td>
</tr>
<tr>
<td>Spine-T</td>
<td>14</td>
</tr>
<tr>
<td>Spine-L</td>
<td>4</td>
</tr>
<tr>
<td>Spine-SI</td>
<td>1</td>
</tr>
<tr>
<td>Calcaenus</td>
<td>8</td>
</tr>
<tr>
<td>Ulna</td>
<td>9</td>
</tr>
<tr>
<td>Patella</td>
<td>4</td>
</tr>
<tr>
<td>Iliac Crest</td>
<td>6</td>
</tr>
<tr>
<td>Tibia</td>
<td>6</td>
</tr>
</tbody>
</table>
extraspinal areas. One individual had all five areas affected, while three individuals exhibited ossifications at four areas.

In DISH-like cases, the thoracic spine was involved in every individual (100 percent) and the lumbar was involved in four individuals (28.5 percent). The cervical vertebrae were not involved in any DISH-like cases. Table 10 shows this data, as well as the most common extraspinal areas affected in DISH-like individuals: the ulna, followed closely by the calcaneus. Table 11 shows the number of times each grade is exhibited for each of the extraspinal areas. There appears to be no correlation between DISH-like individuals and the side on which the extraspinal ossifications are present.

Cervical Fusion

There are four burials noted as exhibiting cervical fusion (5152, 9215, 9304, 9342) but not considered to be DISH. An ALL (and PLL) fusion can be seen between C1-C2 and C3-C4 (Figure 40). No extraspinal manifestations of these burials were examined due to the author’s knowledge at the time concerning the criteria for cervical DISH. There is also no way to be sure if these burials could be considered AS. These burials may be important enough to warrant a reexamination in the future, but for this thesis, they are only included in the examined burials and considered not to be DISH.
Fragmentation

Fragmentation was a common and problematic issue regarding the MCIG cemetery collection. Three burials examined were deemed too fragmented to be classified as DISH and were not regarded as such. Fragmentation is an issue when dealing with historic and prehistoric burials and can be caused by everything from excavation methods to soil content to site drainage.

Chi Square

The total number of DISH cases present in the collection was 12 males, 0 females (1.23 percent of the total population, 1.39 percent of males). There was a statistically significant difference between males and females with DISH ($p=1.73$ at $p<0.05$). In examination of the DISH results, it does not appear that the disease increases with age, but fragmentation and the broad age categories may have something to do with this: Age 40-50 (58.3 percent), Age 50+ (41.7 percent). Unfortunately there are no non destructive techniques for establishing age after an individual reaches 50-60 years.

The total number of DISH-like cases totaled 14, with 12 males and 2 females involved (males 1.39 percent, females 1.65 percent). There was a statistically significant difference between males and females with DISH ($p=0.04$ at $p<0.05$). The age range for the DISH-like category proved to be slightly different than that of DISH cases, with more individuals of a younger age bracket present (30-40 years: 28.6 percent, 40-50 years: 42.8 percent, 50+ years: 28.6 percent).
<table>
<thead>
<tr>
<th></th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Ulna</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Iliac Crest</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Tibia</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Patella</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Calcaneus</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 11: Occurrence of extraspinal manifestations in DISH-like cases.
Figure 40: Burial 5152. Cervical fusion shown between C1-C2 and C3-C4.
If the DISH and DISH-like data is combined, DISH appears to have a 12:1 male to female ratio and is present in roughly 2.67 percent of the adults in the collection. This male to female ratio does not reflect that of the MCIG cemetery which has an approximate 7:1 male to female ratio. The data presented here as compared to other DISH studies can be seen in Table 12.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Pop Type</th>
<th>Total Pop</th>
<th>Male %</th>
<th>Female %</th>
<th>Total %</th>
<th>M:F Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Julkunen et al.</td>
<td>1975</td>
<td>Finland - H</td>
<td>8993</td>
<td>3.80%</td>
<td>2.60%</td>
<td>2.62%</td>
<td>1.5:1</td>
</tr>
<tr>
<td>Resnick &amp; Niwayam</td>
<td>1976</td>
<td>USA - A</td>
<td>250</td>
<td>NA</td>
<td>NA</td>
<td>12.00%</td>
<td>NA</td>
</tr>
<tr>
<td>Henrard &amp; Bennett</td>
<td>1973</td>
<td>Pima Indians - H</td>
<td>NA</td>
<td>25.00%</td>
<td>4.70%</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Bloom</td>
<td>1984</td>
<td>Jerusalem - H</td>
<td>1456</td>
<td>22.40%</td>
<td>13.40%</td>
<td>15.25%</td>
<td>1.7:1</td>
</tr>
<tr>
<td>Rogers et al.</td>
<td>1985</td>
<td>Various - S</td>
<td>560</td>
<td>NA</td>
<td>NA</td>
<td>2.30%</td>
<td>NA</td>
</tr>
<tr>
<td>Waldron</td>
<td>1985</td>
<td>Merton Priory - S</td>
<td>35</td>
<td>8.60%</td>
<td>NA</td>
<td>8.60%</td>
<td>NA</td>
</tr>
<tr>
<td>Cassim et al.</td>
<td>1990</td>
<td>African Blacks - H</td>
<td>1000</td>
<td>3.80%</td>
<td>4.20%</td>
<td>3.90%</td>
<td>1:1.07</td>
</tr>
<tr>
<td>Kiss et al.</td>
<td>2002</td>
<td>Hungary - H</td>
<td>635</td>
<td>27.30%</td>
<td>12.80%</td>
<td>19.84%</td>
<td>2.1:1</td>
</tr>
<tr>
<td>Arriaza et al.</td>
<td>1993</td>
<td>Nubian - S</td>
<td>134</td>
<td>18.00%</td>
<td>7.00%</td>
<td>13.40%</td>
<td>3.5:1</td>
</tr>
<tr>
<td>Weinfeld et al.</td>
<td>1997</td>
<td>Midwest - H</td>
<td>1363</td>
<td>25.00%</td>
<td>15.00%</td>
<td>NA</td>
<td>3:2</td>
</tr>
<tr>
<td>Rogers &amp; Waldron</td>
<td>2001</td>
<td>Monastic - S</td>
<td>272</td>
<td>6.25%</td>
<td>NA</td>
<td>6.25%</td>
<td>NA</td>
</tr>
<tr>
<td>Kim et al.</td>
<td>2004</td>
<td>Korea - H</td>
<td>3595</td>
<td>7.10%</td>
<td>1.60%</td>
<td>4.10%</td>
<td>7:1</td>
</tr>
<tr>
<td>Pappone et al.</td>
<td>2005</td>
<td>Italy - H</td>
<td>93</td>
<td>NA</td>
<td>15.10%</td>
<td>15.10%</td>
<td>NA</td>
</tr>
<tr>
<td>Westerveld et al.</td>
<td>2008</td>
<td>Netherlands - H</td>
<td>501</td>
<td>22.70%</td>
<td>12.10%</td>
<td>17.00%</td>
<td>1.6:1</td>
</tr>
<tr>
<td>Ozga</td>
<td>2009</td>
<td>Midwest - S</td>
<td>973</td>
<td>2.78%</td>
<td>1.65%</td>
<td>2.67%</td>
<td>12:1</td>
</tr>
</tbody>
</table>

Table 12: Notable DISH studies. H-Hospital, S-Skeletal, A-Autopsy
Chapter IX
Discussion

Several important ideas concerning DISH were supported in this thesis. Likewise, several other commonly accepted ideas regarding the disease were refuted. Before summarizing the conclusions from this thesis, the results of the study are examined and new research questions will be proposed involving the spinal column, the extraspinal ossification areas and the issues of dealing with a fragmentary collection. The new terminology, “puzzle piece kissing” used when dealing with fusion in skeletal collections, will also be defined and explained in this chapter.

There are several important points to be gained from this study. The first is the need for reorganization of the fusion classification proposed many years ago by Resnick and Niwayama (1976) and Utsinger (1985). This study proposes the inclusion of “puzzle piece kissing” as a type of criterion comparable to fusion. This may not be easily visualized in x-ray studies, or hospital studies, but it is clear that in skeletal samples with DISH, classifying a fusion is not as easy as simply stating its “presence” or “absence.” Secondly, a three grade classification system for extraspinal manifestations is proposed. In skeletal populations it is easy to clearly measure the extent to which extraspinal elements occur and this three stage system using millimeter measurements. Based on the data analyzed for this thesis, it is proposed that a three grade system is quite adequate to accurately describe extraspinal involvement in DISH. Thirdly, the MCIG collection included one particularly interesting burial which expressed a previously undocumented pathology: transitional AS and DISH (Burial 9348). The MCIG cemetery collection showed two cases of DISH and AS together. It also provided one case of early DISH and early AS together which has not been previously reported. This particular case firmly
supports the idea that both AS and DISH are progressive disorders and do not simply develop suddenly and unexpectedly in individuals. Lastly, and most importantly, DISH cases found in the MCIG collection strongly question the current hypothesis that obesity and diabetes cause DISH.

**Spinal Column**

The spinal column is the most important area of examination when dealing with DISH. The presence of extraspinal ossifications means nothing without the vertebral fusion required to diagnose DISH. Resnick and Niwayama (1976) stated that the thoracic was involved 97 percent of the time, coinciding with the observations of this thesis, in which every DISH and DISH-like individual exhibited a thoracic DISH presence. Resnick and Niwayama (1976) also note that the lumbar spine is involved 93 percent of the time, and the cervical is involved 78 percent. As stated in the results; the lumbar and cervical were involved very little in this study of DISH. The cervical was involved in only one case in DISH individuals and not involved at all in any DISH-like cases. The lumbar spine was involved in four individuals with DISH and four individuals that exhibited DISH-like features. Although the number of DISH and DISH-like cases in the MCIG collection was small compared to those in Resnick and Niwayama’s (1976); the current findings suggest several conclusions. It appears that the lumbar spine is involved in roughly one third of the MCIG DISH and DISH-like cases, but was present in 90 percent of those individuals examined by Resnick and Niwayama, thus suggesting that the lumbar spine may become involved in DISH after the ossification of the ALL in thoracic vertebrae. It seems that the individuals in MCIG, due to their low status and poor health, died young, thereby suggesting that a right ALL fusion of DISH of the lumbar vertebrae occurs later in the course of the disease.
Also, due to the lack of cervical vertebrae seen in the DISH and DISH-like cases in the MCIG collection, it seems that cervical fusion, the fusion that sometimes causes dysphagia, may be a different disease altogether. Without genetic analysis, there is no way to know if the DISH that occurs in the cervical vertebrae is the same as the DISH that occurs in the thoracic and lumbar. At this point in time, these questions regarding DISH are speculative, but may lead to interesting considerations regarding the disease.

An issue that became apparent when dealing with the MCIG collection is the manner in which the extent of ALL ossification be measured. This thesis does not attempt to measure the onset or extensiveness of the vertebral fusion of DISH, but throughout the current research it was clear that some fusions were more developed than others. Because the vertebral body is essentially blocked by the ALL fusion itself, measuring the posterior projections of the ossification proves to be very difficult if not impossible. An MRI or x-ray analysis of DISH in living patients may present the possibility of ossification measurement, but at this point, the measurement of DISH-like ossification protrusion in skeletal material proves rather difficult.

**Extraspinal Involvement**

The involvement of extraspinal features is an extremely important aspect of diagnosing DISH in skeletal collections. In this thesis only five extraspinal ossification areas were examined: pelvis (iliac crest), ulna (olecranon), tibia (tibial tuberosity), patella (anterior region), and calcaneus (posterior region). There are several other areas of the body that may exhibit involvement in DISH: pelvis (ischium), femurs (greater and lesser trochanters) and feet (tarsals and metatarsals) and hands (carpals and metacarpals) (Resnick et al., 1976). As seen in Table 5
and Table 10, there seems to be particular areas more commonly involved than others in DISH and DISH-like individuals. In both DISH and DISH-like individuals the ulna and the calcaneus were most commonly involved. It seems that due to their constant use, the calcaneus and the ulna appear to be the most common areas affected. The question of the impact environmental influences have on these areas is still being asked, but it is clear that these two extraspinal areas are the most common extraspinal ossification areas of DISH.

The grade to which the extraspinal areas affect DISH and DISH-like individuals can be seen in Table 6 and Table 11. When the number of extraspinal areas, both left and right, are tallied by grade, the numbers do not appear to provide any information. In DISH cases, there are 29 cases of grade one, 26 cases of grade two and 21 cases of grade three. This clarifies the idea that even when DISH is exhibited in the spinal column the extent to which particular extraspinal areas are involved varies greatly. One might expect to see mostly grade three involvement present in Table 6 but instead we see a fairly even distribution across all grades. These findings appear to suggest that extraspinal ossification areas can be used as clues to better understand how the disease progresses in individuals. Since certain extraspinal areas are more commonly affected than others, it seems as though the ulna and calcaneus areas should ossify first, and as they progress to grade two or grade three, the involvement of other extraspinal areas will begin to be seen. The number of extraspinal areas involved in DISH can be seen in Table 4 and clearly show that five, four or three present ossification areas are the norm when dealing with DISH individuals. It should be mentioned that some of this variation in DISH and DISH-like extraspinal involvement may reflect the kind of work load exercised by particular individuals.

Some interesting conclusions can also be gathered from Table 11, which examines the grade of DISH-like extraspinal presence in individuals in the MCIG collection. The totals for the
extraspinal grades of DISH-like individuals are as follows: 33 for grade one, 15 for grade two and 8 for grade three. It appears that grade one extraspinal ossifications are by far the most common grade in DISH-like cases. This further suggests that these extraspinal ossifications act as markers for the progression of the disease and that both the extraspinal areas and the vertebral fusions exist in transitional, elementary forms. The presence of 8 grade three ossifications also shows the variability of the disease among individuals, further emphasizing how difficult it is to quantify and describe the criteria for the disease. As seen in Table 9, there are no commonalities between DISH-like individuals and the number of extraspinal ossification areas, which are somewhat evenly distributed.

**Sex and Age**

DISH is a disease that usually affects males more often than females and the results of MCIG study confirm this data. No females exhibited DISH and only two exhibited DISH-like traits (Table 2 and Table 7). Despite the male to female ratio being very high in the MCIG collection, we still see a female presence in this study. I think if the male-female ratio were closer to one to one, we would see a much higher female DISH presence than we do currently.

Although age is sometimes difficult to establish in skeletal collections, each individual with DISH or DISH-like presence was aged using SDCHSR methods (Buikstra and Ubelaker, 1994). The results of skeletal aging are arranged in Table 3 and Table 8. In DISH cases, seven individuals were estimated to be between the age of 40 and 50 and five individuals were estimated to be over 50. Unfortunately, due to the author’s training and the inability to use invasive means of aging, the individuals were not aged as accurately as they could have been.
The estimated ages of DISH individuals may not seem important but when compared with the data found in Table 11 from DISH-like individuals, it seems that DISH-like cases happen earlier on average. This supports the conclusion that DISH is a progressive disease and that younger individuals should be seen exhibiting DISH-like criteria instead of clinical DISH criteria. The results show that four individuals were aged between 30 and 40 years and exhibited a very early form of the disease (Table 7 and Appendix C). As seen in Table 7 and table 9, the number of extraspinal areas and the number of vertebrae involved still vary greatly for these young individuals with DISH-like evidence. Two of the four cases exhibit only one extraspinal ossification area while another exhibit three and the last exhibit four. Aside from one case with grade three calcanei spurs, these individuals usually exhibit grade one ossification criteria. Unfortunately there does not seem to be any patterns based on age in DISH and DISH-like cases regarding the presence or grade of extraspinal areas.

**Fragmentation**

One of the greatest challenges when dealing with a skeletal collection like MCIG was the issue of fragmentation. Fragmentation was extremely common in the MCIG collection and several individuals with fused vertebrae could not be properly examined due to the extent of fragmentation in the burial. It was mentioned earlier that Resnick et al. (1976) suggested a number of other extraspinal areas of interest related to DISH, but due to the fragmentation, some of these had to be left out of the thesis (most particularly the investigation of hands and feet). There was also an issue with cervical vertebrae in the MCIG collection, due to their particularly fragile nature and their difficult excavation removal. Vertebrae fragmentation make analysis
especially difficult in cases where spinal fusion is interrupted by a period of vertebral normality. The fragmentation of the collection may have actually caused the final numbers for DISH and DISH-like presence to be lower than they were in reality. Overall, the fragmentation of the MCIG collection did somewhat impede the analysis of DISH, but not enough to jeopardize or invalidate the current study.

**Definition of New Terminology**

In the MCIG cemetery collection, there are many examples of vertebral fusion in which one enthesophytic vertebra appears to fit together with an adjacent enthesophytic vertebra but they do not fuse. This phenomenon has been deemed “puzzle piece kissing” between vertebrae and it is suggested that the vertebrae that present this type of interaction be considered as fused (Figure 38). The author suggests that “puzzle piece kissing” is unique to analysis of skeletal populations (and may not be visible in living populations) and should be considered fused. In order for vertebrae to be “puzzle piece kissing” the vertebrae must completely connect with each other along the ALL enthesophytic area, suggesting that in a short time (if the individual were to have continued living) the development of DISH related fusion was inevitable. It is predicted that radiographic analysis may not detect these small spaces between adjacent vertebrae ALL ossification and that these vertebrae would act as fused vertebrae in clinical studies, limiting mobility and promoting back stiffness.
Fusion

According to the Resnick and Niwayama (1976) criteria, four contiguous vertebral fusions are required for DISH, but Utsinger (1985) requires only a three vertebrae. After examining firsthand the manifestations of DISH in a skeletal sample, it is clear that qualifying a spinal fusion is not a straightforward criterion. It is proposed that Utsinger’s (1985) criteria be used for examination of DISH in skeletal populations—with one amendment: the addition of “puzzle piece kissing” as an equivalent to vertebral fusion. There were several cases in the MCIG collection in which enthesophytic buildup occurred so closely with adjacent vertebrae that it may well have acted as a fusion in the living individual by creating spinal stiffness and limiting mobility. This phenomenon may be incredibly difficult to see in radiographic studies, and since this population only involves skeletal remains, there is no way to be completely sure what this phenomenon looks like in an x-ray. Magnetic resonance imaging; however, may eliminate this problem. It is proposed that some leniency be granted in the category of strict fusion of three vertebrae, especially in skeletal populations, because nearly fused vertebrae may have produced similar if not identical symptomatic manifestations in living individuals with DISH.

Extraspinal Manifestations: A Three Grade System

Another proposed addition to the current DISH literature is the use of a revised three grade system. As stated several times in the literature, measuring the severity of extraspinal manifestations involved with DISH is extremely difficult if not impossible. However, in skeletal populations, a firsthand examination yields some interesting results regarding this system.
As previously mentioned, there was a series of studies in the late 1980’s and early 1990’s involving DISH: spinal fusion, some of the peripheral elements, and pain (Schlapbach et al., 1989; Beyeler et al. 1990; Beyeler et al., 1992; Schlapbach et al., 1992). To coincide with Resnick et al. (1976), Schlapbach and Beyeler created a grading system for determining the extent of shoulder and elbow hyperostosis:

Grade 0: none or only one attached ossification of less than 2 mm;
Grade I: two or more ossifications of less than 2 mm or one ossification of 2-3 mm;
Grade II: two or more ossifications of more than 2 mm or one ossification of more than 3 mm;
Grade III: two or more ossifications of more than 3 mm. (Beyeler et al., 1990:350; Beyeler et al., 1992:320).

This categorical system is, in this author’s opinion, inadequate. Although Schlapbach and Beyeler make some suggestions and comments about bilaterality of the hyperostosis, their reports do not include analysis of right and left shoulder and elbow X-rays (Beyeler et al., 1990; Beyeler et al., 1992). In addition, ligament ossification is usually only seen in one spot on the head of the proximal ulna, ruling out the possibility of having more than two ossifications at the areas specified as important to a proper critique of the disease.

The reason for mentioning Beyeler et al. (1990; 1992) is that when dealing with a skeletal population, the left and right manifestations of each extraspinal area can be examined and measured with a high degree of accuracy. As previously stated, this study incorporated a three grade system for the examination and measurement of these extraspinal manifestations. The first grade was a small osteophyte (<3mm), the second was a medium osteophyte (3-5mm) and the third was a large osteophyte (>5mm). This proposed system accurately describes the variation in DISH related osteophytes. There is no need for more than three stages, but two stages would definitely be inadequate when dealing with DISH. The main differences between the criteria
created by the author and those criterion originally established by Beyeler et al. (1990; 1992) is the absence of two osteophytic spurs involved. Of all of the extraspinal manifestations examined and graded in this thesis, an area exhibiting two spurs related to DISH was never encountered (for example, there was never two spurs on the right posterior calcaneus). Although this thesis did not examine the scapula or the femur, which may have manifestations in two areas, it is argued that for the five extraspinal areas examined in this thesis, a three grade system is more than adequate.

**DISH and AS**

Burial 9348 in the MCIG collection is a particularly interesting case because it so clearly shows that both DISH and AS can coexist in transitional stages. Obviously it is assumed that both disorders needed a transitional period at some point, but it seems, at least in this case, that both AS and DISH developed together, instead of one before the other.

**DISH in Early Milwaukee**

The most important part of this thesis is its overall ramifications for the proposed association between DISH and obesity and diabetes. The background of Milwaukee as seen in this thesis and the data presented by Richards (1997) made the case that during the period in which the MCIG cemetery was in use, the general health and wellness of the inhabitants was less than adequate. As proposed by Waldron (1985) and later Waldron and Rogers (1990) DISH was hypothesized to be involved with high status living, due to its overwhelming presence in medieval monastic populations. Although DISH is present in 1.23 percent of the adult population
and 2.78 percent when DISH-like symptoms were included, the author thinks that based on knowledge of the time period during which these individuals were buried, the MCIG collection is a case against a biochemical causal connection between DISH and diabetes.

As described in the background section, many of those buried in the MCIG cemetery were first or second generation immigrants, struggling to make a living to provide food for themselves and their families. The results of Richards’ (1997) analysis of the MCIG revealed that most of the occupants were considered to be low-status individuals. It then follows that their diet would not have been as rich and healthy as those from Waldron’s (1985) monastic studies (1985). The cemetery itself was sometimes referred to as the Milwaukee Pauper Cemetery (Richards, 1997). Richards’ analysis of the burial records confirmed a very small number of cases of diabetes related deaths at the time, and although this argument does not hold much concreteness, it should be mentioned. The inhabitants of the almshouse who are buried in the MCIG cemetery, including the hospital and the mental asylum most likely were fed adequately (regulations encouraged this, but how strictly they were followed is open for debate) but probably never to the point that would result in adult diabetes or obesity of particular individuals.

What exactly caused DISH in the MCIG cemetery collection if it is not the result of diabetes or obesity? Many have suggested that DISH is a genetic, age-affiliated disease, which seems to be the most likely description. Unfortunately, many of the individuals from the MCIG did not live into their later years, so the complete progression of the disease could not be fully viewed. Noninvasive skeletal aging methods also make it almost impossible to determine, with accuracy, exact ages past fifty years. The HLA-B locus studies seem to be inconclusive, but it appears that researchers have simply been unable to locate the alleles that correlate with ligament
ossification. No genetic tests were conducted with the MCIG collection. It may be an interesting experiment in the future which leads to clues regarding the involvement of new genetic loci.

Table 12 presents some of the major population studies of DISH including the MCIG cemetery sample. The MCIG cemetery study is included in this table with both the DISH and DISH-like cases contributing to the final percentage. In the MCIG cemetery collection there were particular circumstances which most likely caused DISH to be underrepresented in this analysis. Fragmentation was a huge factor in inhibiting the determination of the extent of DISH in particular cases and sometimes did not allow for extraspinal examination. The underrepresentation of women in the MCIG collection is also something to keep in mind. If the male to female ratio in the cemetery were closer to 1:1, DISH would be seen much more often in females, but as previously mentioned, the ratio is roughly 7:1. Despite these drawbacks, the author is convinced that the data and conclusions formed in this study are as accurate a portrayal as possible of DISH in the MCIG cemetery collection.
Chapter X

Conclusion

The term diffuse idiopathic skeletal hyperostosis and the criteria involved in its identification have developed under the watchful eyes of rheumatologists, anthropologists and physiologists and orthopedists for the past century. Although the name may have expanded from its early association with a simple ligament ossification, DISH still continues to be a difficult to explain pathologic skeletal condition. For all the things we do know about DISH, there are even more things we do not know. The etiology is still a mystery although many have postulated an enormous number of genetic, dietary and environmental factors. The way in which DISH progresses continues to be a mystery as well. Extraspinal manifestations help to better qualify the disease, but they are by no means uniform or predictable. The total percentage of the population afflicted with DISH also remains a mystery. The average is thought to be between 6 percent and 10 percent but as seen in Table 12, the numbers among studies vary greatly ranging from 3.8 percent to 27.3 percent.

A background was provided in this thesis about the origins of the criteria of DISH as well as the studies undertaken regarding it. The excavation of MCIG was mentioned to explain the origins of the MCIG collection and how it came to Marquette University. The city of Milwaukee was also discussed in detail in order to solidify and establish the point that the DISH present in the MCIG collection was not the result of high status and a hearty diet. Methods and materials were presented in this thesis in order to better explain the process by which the DISH investigation in the MCIG collection took place. The results section summarized the findings of
the study and the discussion section attempted to make sense of the data and arrive at general conclusions regarding it.

This study has arrived at several conclusions regarding DISH. First, there is no uniform way in which DISH exists or progresses. Through examination of the data presented in this thesis, it is clear that establishing criteria for when DISH begins and when it ends is a difficult task. Extraspinal ossification areas provide us with clues about the extent and progression of the disease, but vary among individuals, as seen in this thesis. Secondly, when dealing with skeletal collections, the “puzzle piece kissing” of two adjacent vertebrae should be considered as fusion. As documented in this thesis, the author thinks that simply because the vertebrae do not completely attach to each other does not mean they should not be considered fused in order to establish the presence of DISH. Lastly, the grading system for extraspinal ossifications presented in this thesis should be used in all future skeletal DISH studies. This criterion is much more accurate than a simple verbal categorization system describing an extraspinal area as “moderate” or “severe.” The author thinks that by keeping these three conclusions in mind when dealing with DISH in skeletal collections, results from future studies will be much more accurate and informative.

This thesis also attempted to establish DISH as more likely a hereditary disorder rather than a disease related to diet, diabetes and obesity. The history Milwaukee during the time in which the MCIG cemetery was in use tried to establish a link between the status and health of Milwaukee people at the time and those housed in the MCIG cemetery. At the turn of the century Milwaukee was undergoing massive health reforms and many immigrants, like those buried in the MCIG cemetery, struggled to stay healthy and well fed. Most of the individuals buried in the MCIG cemetery were known as paupers and shown to be in the lower economic strata of society
thus making it almost impossible for them to be healthy and obese, a feature that some deemed to be the cause of DISH itself. It seems that those individuals from MCIG who exhibit DISH did not arrive at such a state by way of diet but rather other factors. Although no genetic analysis was performed on this collection, this thesis makes a good case that DISH is a hereditary disorder.

It is clear that there is no easy answer for what causes DISH and to what extent it effects populations, but that does not mean its study should be abandoned. A few characteristics are certain, however: it is a global phenomenon, it almost always occurs more in males, and the differences in individual fusions and extraspinal manifestations vary almost as much as the number of people in which they are found. DISH is seen in many vertebrates, not only humans, and some are beginning to consider it to be an evolutionary advantage for some vertebrates, since it results in heightened stability (Rothschild, 1987). The same cannot, at this time, be said for humans with DISH since as clinical studies show, many afflicted with it experience stiffness and at least some pain. Those who choose to study DISH are aiding a significant percentage of the global population. Many scholars are confident that in the coming years, more will be understood about the etiology and possible preventative measures relating to DISH.

Further Studies

The MCIG collection refutes the suspected correlation between DISH and diabetes but this should not mean a halt on studies regarding their connection. Obviously, the more studies conducted, the more data available for comparison, thus leading to the presence of new trends. An interesting investigation, mentioned briefly in the history section, would be a comparison
between a high status (Monastic) cemetery and that of a low status medieval cemetery. If DISH is present in both cemeteries equally, it would further support the conclusion that DISH is not directly related to diet and lifestyle, but most likely hereditary in origin.

Another important area of examination is the genetic realm. Honing in on a particular locus that is involved in DISH is the first step to developing treatments for out of control ligament ossification. Advancements have been made concerning the HLA-B gene locus and our understanding of the role of the BMP in excess bone growth is rapidly increasing as well. Continued study of these genes and their alleles in laboratory mice would help us better understand their involvement in DISH. The origins and reasons for DISH elude researchers at this time, but the more we understand about the disease, the more we may be able to apply the findings to other rheumatological disorders and skeletal pathologies.

Further Applications

An important understanding of the way in which DISH forms and progresses might help in its treatment and maybe one day prevent the disease. Clinical studies of DISH have established the disease’s presence over thousands of years in humans and across the entire planet. DISH is not a deadly disease but it is an important one to examine, limiting mobility and decreasing the standard of living in those that suffer from it. Although very few DISH cases involve serious health concerns, the most common of which involve the pinching of nerves, further investigations of DISH should not be pushed aside. Continuing research into the origins and treatments of DISH will aid not only those that suffer from it, but will also benefit our understanding of the ways in which arthritis takes form throughout the body.
Chapter XI

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Appendix A

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Appendix B

DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS

RECORDING FORM

Site Name/Number_________________________________________ Name__________
Feature/Burial Number____________________________________ Date__________
Burial/Skeleton Number____________________________________

Vertebral Pathologies

Key: Blank – No pathology, VE – Vertical Enthesophytes, PPK – Puzzle Piece Kissing, F – Fusion, X (Over vertebra) – Not Present/Fragmented

Cervical
C1______C2______C3______C4______C5______C6______C7______T1

Thoracic
T1______T2______T3______T4______T5______T6______T7______T8
______T9______T10______T11______T12______L1

Lumbar
L1______L2______L3______L4______L5______S1

Sacrum
Left Auricular Surface_______Sacrum_______Right Auricular Surface

Final Analysis Too Fragmented/Incomplete ______
Check One No DISH ______
DISH-Like ______
DISH ______
Extraspinal Pathologies

*Key: Grade 0 – No Buildup, Grade 1 – Buildup between 0-1mm, Grade 2 – Buildup between 3-5mm, Grade 3 – Buildup greater than 5mm, X (Over side) – Not Present/Fragmented*

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Age Sex Determination (From SDCHSR)

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Final Age and Sex Estimation:
Appendix C

Non-DISH cases

An example of heavy enthesophytes without the presence of DISH can be seen in (Figure 36) in which the two lower thoracic vertebrae are “kissing” but not in the “puzzle piece” fashion that most likely concerns DISH. There is no guarantee that this individual will eventually exhibit DISH (if they continued living), but at the time of death, with only two lower thoracic vertebrae affected, the criteria of DISH are not met. This is a great example of the complexities of the DISH categorizing system and how important it is to recognize the sequence in which DISH first appears; so that living populations can take precautionary measures to halt the progression of the disease.

Ankylosing Spondylitis

Ankylosing spondylitis was for the most part, not examined in this study, but several of the burials studied had AS-like features.

Burial 5073

Burial 5073 (Figure 37) exhibited an ossification of the right and left sides of the ALL along with a PLL fusion and a sacroiliac fusion. Vertebral space was not maintained and no extraspinal features were found. No further examination was done on this burial once it was determined to be AS.

Burials 8057, 8148, 8150, 8174

Several other burials thought to show ankylosing spondylitis were examined but no notes were taken because they were not directly related to the thesis. Although the number of ankylosing spondylitis cases are reported here, it should be noted that this is not an accurate representation of AS in the MCIG cemetery collection, since it was not the disease this thesis set out to examine.

DISH and AS

Several cases appear to exhibit a combination of DISH and AS as seen in several articles presented in this thesis (Williamson and Reginato, 1984; Olivieri et al., 1987; Rillo et al., 1989; Kozanoglu et al., 2002).

Burial 5075

This burial exhibited three fused vertebrae (T9-T11) along with “puzzle piece kissing” vertebrae (T12) and one with medium enthesophytic buildup (T8) (Figure 38). This burial also
exhibited sacral fusion, reminiscent of ankylosing spondylitis, along with varying degrees of extraspinal involvement at all five examined sites. This case appears to be an example of DISH exhibited through the occurrence of extraspinal factors and vertebral fusion (right ALL) but the fused sacrum (not shown in figure) is a hallmark of AS.

**Burial 9302**

Burial 9302 is the most extensive case of DISH in the MCIG cemetery collection and appears to be a case of DISH and AS. The burial is very fragmented which prevents a fusion of the PLL from being seen, but it appears that the intervertebral space is maintained in the ALL fused areas. The fusion begins in the cervical vertebrae (C6-C7), is separated by a period of normality, then begins again in the thoracic vertebrae (T3-T12). The sacrum is fused to both sides of the pelvis, but the extent of this fusion could not be determined due to the fragmentation of the pelvis. Extraspinal osteophytes are present at all five sites varying from less than 3mm to over a centimeter. Most of the osteophytes would be considered grade 3 according to the present criteria. The sacroiliac fusion was somewhat fragmented on either side, so much so that the extent of the fusion could not be determined. This is most likely the second case of DISH and AS occurring together in the MCIG cemetery collection.

**DISH-like and AS**

**Burial 9348**

Burial 9348 appears to be a case in which DISH, although not fully developed, coexists with AS, also not fully developed. The sacroiliac area is partially fused on the left side but not the right. Three of the five extraspinal areas of interest are affected at varying degrees. There are two fused thoracic vertebrae and three other enthesophytic thoracic vertebrae. The sex estimation of the individual was determined to be 30-40 and this particular case would most likely have developed into a combination of DISH and AS in the future.

**DISH cases**

**Burial 2068**

Burial 2068 has no associated photos but the extent of extraspinal manifestations of DISH are severe. Heavy enthesophytic bridging was visible on the lower thoracic vertebrae. There was a small bit of fragmentation that made the exact thoracic vertebrae unknown, but it appears that with these extraspinal manifestations present, this case can safely be assumed to be DISH.

**Burial 3068**

Although burial 3068 did not present any complete fusion between vertebrae, extensive enthesophytes on T6-T12 and again from L2-L4 suggest the clear presence of DISH. Burial 3068
is a perfect example of the “puzzle piece kissing” DISH indicator in which T8-T11 are so closely oriented, it is only a matter of time before they fuse together (Figure 39). The extent of extraspinal manifestations suggest the presence of DISH.

Burial 5040

Burial 5040 is a particularly interesting example in that, although fragmented, the individual clearly exhibits a DISH fusion along the right aspect of the ALL extending from T9-L1. The peculiar condition is the noninvolvement of extraspinal factors. Despite the fragmentation of the material, it is clear that bony spurs on the ulnae, iliac crests, calcanei, tibiae and patellae do not exist. The individual was presumed to be in his early forties at time of death, which may or may not have had an influence on extraspinal involvement.

Burial 5049

This burial is another highly fragmentary case that most likely exhibits DISH based on several thoracic vertebrae present and the extraspinal manifestations. Three thoracic vertebrae (the exact vertebrae could not be reliably identified) exhibited heavy enthesophytes and suggested right ALL fusion. Extraspinal manifestations were found on four out of the five indicators with heavy bony spurs occurring on both iliac crests and the right calcaneus.

Burial 7006

This particular burial exhibited a right ALL fusion involving 5 thoracic vertebrae. However, the neural arches of the vertebrae (and many of the surrounding vertebrae) were missing or too fragmented to determine the exact vertebrae number. The fragmentation also influenced the extraspinal identification of the state of the left tibia, calcaneus and iliac crest and the right ulna and iliac crest. This burial appears to have DISH based on the presence of the five fused vertebrae. Unfortunately the fullest amount of information could not be gathered due to its fragmentary nature.

Burial 7107

Burial 7107 is yet another case in which DISH can be considered present despite heavy fragmentation. Five lower thoracic vertebrae exhibit right ALL fusion, but the surrounding vertebrae could not be examined due to their degenerated state. The same goes for the extraspinal manifestations in which all of the extraspinal areas present can be seen to have osteophytic buildup.

Burial 7144

Burial 7144 was examined for DISH and found heavy ‘candle-wax’ buildup along several thoracic and lumbar vertebrae. Although the vertebrae were not completely fused together T8-L3 exhibited “puzzle piece kissing” with extensive vertical enthesophytes on the right ALL. This burial also had several large extraspinal osteophytes. Some buildup was present but nothing
extending vertically between vertebrae, only laterally. This case exhibited a >1cm spur on the right anterior patella and also showed a large spur on the left iliac crest. Small spurs were also seen on both calcanei, and a medium one was present on the right iliac crest as well. It should be mentioned that this case was very fragmented and other vertebrae, most specifically the cervical, could not be examined properly.

Burial 7234

Burial 7234 is a good example of how DISH may progress in a middle aged individual. The individual is thought to be between 40 and 50, but exhibits spinal fusion and extraspinal involvement in four out of the five main areas. The vertebrae of burial 7234 are highly fragmented but it appears that two separate fusions of two vertebrae occur in the thoracic area. Due to the fragmentation, discerning the exact identity of the vertebrae involved was not possible but the first fusion most likely occurred in the region between T4 and T7 and the second somewhere between T8-T11.

Burial 9269

Burial 9269 included four right ALL fused thoracic vertebrae, according to the criteria used. There was no question as to whether it should be considered DISH. There was some enthesopathic buildup on T5 and T11 that could possibly have developed into hyperostosis. Extraspinal manifestations involved three of the five extraspinal areas with a large osteophyte on the left iliac crest. Small osteophytes were also found on the left ulna, the left tibia and the left calcaneus.

DISH-Like Cases (Possible DISH)

Burial 3071

Burial 3071 is an example of how DISH could possibly progress into clinical DISH. The individual in question most likely died in his late 30’s, and exhibited early enthesophytes on his lower thoracic vertebrae which appear to be developing into a fusion. The presence of small bone spurs on the iliac crests and on the right posterior calcaneus with a medium spur on the left calcaneus, suggests this individual had an early form of DISH.

Burial 5040

Burial 5040 exhibited severe enthesophytes on the right ALL on four vertebrae (T8-T11) and medium build up on the two surrounding vertebrae, T7 and T12. Although only one small extraspinal manifestation was found on the left ilium, it is possible that the calcanei may also have been afflicted, which were unfortunately not recovered during the original excavation.
**Burial 5094**

This burial exhibited a DISH-like fusion on T10-T11, however, the adjacent vertebrae were too fragmentary to determine any other ALL fusion. There were several extraspinal manifestations that suggest if the burial were complete, it would be DISH-like (if not DISH). Bony spurs on three of the five extraspinal focal points suggest the influence of ligament ossification as related to DISH. Although very few vertebrae are available, the type of enthesophytes present and the presence of extraspinal factors suggest an early form of DISH.

**Burial 5243**

Burial 5243 is another fragmentary burial that exhibits several features that would qualify it as potentially exhibiting DISH. Three thoracic vertebrae (T8-T10) showed heavy enthesophytic buildup but the surrounding vertebrae were far too fragmented to analyze. However, this burial exhibited extraspinal manifestations of DISH on four of the five areas of interest in varying degrees of severity.

**Burial 7112**

Burial 7112 is another heavily fragmented case, but two fused vertebrae can be seen. No osteophytes were seen on the ulnae or calcanei and the rest of the extraspinal areas of interest were too fragmentary to grade. This is a case, based on the right ALL fusion, that can be deemed DISH-like, especially amidst the lack of surrounding vertebrae to analyze.

**Burial 7224**

Due to the extraspinal fragmentation, burial 7224 is difficult to diagnose as DISH but it does have one right ALL fused vertebrae with 3 other adjacent enthesophytic ones. Although this burial has no extraspinal manifestations, it should not be thrown out of consideration for DISH because of the lack of vertebral fusion. The enthesophytic buildup is seen in the burial, but it is not as prominent as in the previous cases, thus suggesting an early form of the disease.

**Burial 8196**

Burial 8196 exhibits a particular case in which the vertebral enthesophytes are less prominent but the presence of many extraspinal factors suggest DISH. Enthesophytic buildup occurs on four vertebrae T7-T10 in varying degrees of severity, and extraspinal manifestations are present in all five of the areas. The young age of this individual (30’s) suggests the early presence of DISH, a disorder that usually does not show itself until after age 40.

**Burial 9226**

Burial 9226 exhibits small enthesophytes on four thoracic vertebrae and four lumbar vertebrae as well as extraspinal manifestations on four of the five critical areas. Although it may be easy to consider this DISH at first glance, the lack of heavy vertical vertebral enthesophytes shows that this burial does not meet the clinically described criteria for DISH.
Burial 9237

Although burial 9237 has two separate right ALL fusions (T8-T9; T11-T12) and four surrounding vertebrae with small enthesophytes, it should be considered possible DISH due to its lack of extraspinal manifestations and the young age of the individual (30’s). Burial 9237 exhibits two large osteophytes on each calcaneus but nowhere else outside of the spine. It is clear that this burial cannot be dismissed as developing into DISH in the near future.

Burial 9295

Burial 9295 contained a T1-T2 fusion along the ALL and a T8-T9 fusion with several small vertebral buildup areas between and outside, but none was significantly large. The extraspinal manifestations were present in all extraspinal areas except the patella, to varying degrees. Burial 9295 is another case in which DISH might have been expected to progress if the individual had not died at a young age (30’s).

Burial 9345

Burial 9345 is an extensive DISH case with a right ALL fusion from T7-L1 with extensive enthesophytes on two other lumbar vertebrae. Even though the tibial tuberosities were not involved, each of the other four extraspinal areas were affected to a high degree (most were grade 3). This individual in his late 40’s clearly exhibited DISH.

Cervical Fusion

Burial 5152, 9215, 9304, 9342

Cervical fusion cases was not examined in this thesis, but may warrant a reanalysis, due to its possible presence in cervical DISH (sometimes resulting in dysphasia in living patients)

Fragmentation

Burial 3048

Burial number 3048 exhibited a lower thoracic fusion along the PLL, but was too fragmented to observe any such fusion along the ALL. Suggestion of sacroiliac fusion was also present but the extent could not be determined, thus, the individual was deemed too fragmented to diagnose any possible DISH. Ankylosing spondylitis should not be ruled out, but the fragmentary nature of the burial makes the diagnosis inconclusive.

Burial 8119

Burial 8119 showed one enthesophytic lumbar vertebrae and exhibited extraspinal osteophytes in four out of the five areas of interest. The vertebrae could not be properly analyzed to their fragmentation. Small osteophytes were found on the right ulna, the right and left iliac crests, and the left calcaneus; while medium osteophytes were found on both the tibial
tuberosities and the right calcaneus. This case is important to mention because it would most likely be considered DISH or DISH-like were it in a better preserved state.

*Burial 8143*

Burial 8143 is similar to burial 8119 in that it exhibits some extraspinal manifestations on the right ulna, the right tibia and the left calcaneus but only two enthesophytic vertebrae were available to be analyzed. Another lumbar vertebrae may be affected with right ALL buildup but the adjacent vertebrae were too fragmentary to reach any conclusions.