MORPHOLOGICAL ASSESSMENT OF DISEASE AND METABOLIC DISORDERS IN A WESTERN CAPE SKELETAL POPULATION

by

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DECLARATION

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Date: December 2016

ABSTRACT

Amongst others, disease, pathology, metabolic disorders and other traits, can be investigated after death by examination of skeletal remains. The evaluation of lesions resulting from disease and metabolic disorders in the Kirsten Skeletal Collection will allow for a better understanding of the effects of disease on skeletal material and of the social development and adaptation of a 20th century population group who, prior to death, inhabited the Western Cape region. The aim of this research was to describe and evaluate the presentation of skeletal pathology resulting from disease and metabolic disorders in the Kirsten Skeletal Collection at Stellenbosch University.

A total number of 300 skeletons were studied. The male to female ratio for the study was 2:1, and the majority derived from the mixed population/Cape Coloured group (n=209). Three different examination methods were used in order to identify traits of diseases or disorders on the skeletal material. Macroscopic evaluation of skeletal material was done by examining each skeletal element under a magnifying lamp. Microscopic analysis was done by using dry bone histological techniques to create bone sections which were examined under a light microscope with POL contrast. Lastly, full body x-rays from each skeleton were taken using the Lodox® Statscan® imaging system and radiographs were examined with the help of a musculoskeletal radiologist.

Congenital and acquired malformations occurred in 45.7% (n=137) of skeletons. These included sacralisation (11.9%), lumbarisation (7.3%), spina bifida (14.0%), scoliosis (4.7%), kyphosis (17.0%), and spondylolysis (2.7%). Infectious diseases presented mostly as a periosteal reaction on skeletal elements. Visually recognisable periostitis occurred in 60.7% of skeletons with 29.3% of skeletons showing visceral periosteal rib lesions. Metabolic disorders were observed in 72.0% of skeletons and included porotic hyperostosis (10.7%), cribra orbitalia (35.6%), enamel hypoplasia (43.8%), Harris lines (24.3%) and osteoporosis (41.3%). The males in the study population showed a statistically significantly higher prevalence for cribra orbitalia than the females. Signs observed for degenerative bone disease included vertebral osteophytes (81.0%), peripheral osteophytes (43.0%), Schmorl's nodes (9.3%), and diffuse idiopathic skeletal hyperostosis (5.7%). Neoplasms were observed in 23.3% of the skeletons examined and included primary benign bone tumours (17.7%), primary malignant bone tumours (1.0%), and secondary skeletal metastases (5.3%). Neoplasms observed showed a similar prevalence as previous studies. Paget's disease occurred in four skeletons.

An important finding in the present study was the high prevalence of periostitis in the mixed population group which was ascribed to a variety of factors including unsanitary living environments, malnutrition, alcohol abuse and lack of effective medical treatment. Pulmonary infections such as tuberculosis (TB) contributed to a high prevalence of visceral rib lesions; however, this study did not find visceral rib lesions to be pathognomonic of TB. The present study also showed metabolic disorders indicating periods of stress throughout life such as malnutrition and infectious diseases. Results on cribra orbitalia (males affected more than females) contradicted previous literature and the iron deficiency anaemia theory, suggesting that other factors contributed to the presentation of cribra orbitalia. To the author's best knowledge, this was the first in depth study using a combination of three different methods to evaluate disease presentation of a skeletal collection representative of the inhabitants of the Western Cape, therefore, giving a unique interpretation of the health status of this population.

OPSOMMING

Siektes, patologie, metaboliese afwykings en ander toestande kan na dood bestudeer word deur die skeletmateriaal te ondersoek. Die evaluering van beenletsels wat weens siektetoestande en metaboliese versteurings op die skeletmateriaal in die Kirsten Skeletversameling voorkom, sal bydra om die sosiale ontwikkeling en aanpassing van ‘n 20ste eeu populasiegroep wat voor dood in die Wes-Kaap gewoon het, beter te verstaan. Die doel van die navorsing is om die voorkoms van skelet patologie weens siektes en metaboliese versteurings in die Kirsten Skeletversameling by Stellenbosch Universiteit te evalueer en beskryf.

‘n Totaal van 300 skelette is ondersoek. Die verhouding tussen mans en vrouens in die studiepopulasie was 2:1, met die meerderheid van die studiepopulasie wat vanaf die gemengde populasiegroep/Kaapse Kleuringroep afkomstig is (n=209). Drie verskillende metodes is gebruik om die voorkoms van siektes en/of afwykings op die skeletmateriaal te identifiseer. Makroskopiese evaluasie van die skelette is gedoen deur elke skelet element onder ‘n lamp met vergrootglas ondersoek. Mikroskopiese analise van beensnitte is met behulp van droë been histologiese tegnieke voorberei en onder ‘n ligmikroskoop met POL kontras ondersoek. Laastens, is heelliggaam x-strale van elke skelet geneem met die Lodox® Statscan® beeldingstelsel, en radiografiese opnames is met die hulp van ‘n muskuloskeletale radioloog bestudeer.

Aangebore - en verworwe abnormaliteite het in 45.7% (n=137) van skelette voorgekom. Dit het ingesluit sakralisasie (11.9%), lumbalisasie (7.2%), spina bifida (14.0%), skoliose (4.7%), kifose (17.0%), en spondilolise (2.7%). Die effek van infektiewe siektes kon meestal as ‘n periostale reaksie op die skelet waargeneem word. Visueel waarneembare periostitis het in 60.7% van die skelette voorgekom, en 29.3% het visserale periostale ribletsels getoon. Letsels weens metaboliese afwykings is in 72.0% van skelette waargeneem en het porotiese hiperostose (10.7%), cribra orbitalia (35.6%), emalje hipoplasie (43.8%), Harris se lyne (24.3%) en osteoporose (41.3%) ingesluit. Mans in die studiepopulasie het ‘n statisties beduidende hoër voorkoms van cribra orbitalia as die vrouens getoon. Tekens van degeneratiewe beensiektes wat waargeneem is het vertebrale osteofiete (81.0%), perifere osteofiete (43.0%), Schmorl se nodes (9.3%) en diffuse idiopatiese skeletale hiperostose (5.7%) ingesluit. Neoplasmas is in 23.33% van skelette wat ondersoek is waargeneem en het primêre nie-kwaadaardige gewasse (17.7%), primêre kwaadaardige gewasse (1.0%) en sekondêre skeletuitsaaings (5.3%) ingesluit. ‘n Soortgelyke voorkoms soos aangedui in

vorige studies, is waargeneem vir neoplasmas. Paget se siekte is in vier skelette geïdentifiseer.

‘n Belangrike ontdekking van die huidige studie was die hoë voorkoms van periostitis in die gemengde populasie groep wat toegeskryf was aan verskeie faktore insluitend onhigiëniese lewensomstandighede, wanvoeding, alkohol misbruik en ‘n tekort aan effektiewe mediese behandeling. Pulmonale infeksies soos tuberkulose (TB) het tot die hoë voorkoms van viserale ribletsels bygedra, alhoewel hierdie studie nie viserale ribletsels as kenmerkend van TB gevind het nie. Die huidige studie het ook metaboliese afwykings getoon wat dui op stres tydperke tydens lewe soos wanvoeding en aansteeklike siektes. Die resultate van cribra orbitalia (mans meer as vrouens beïnvloed) weerspreek vorige literatuur en die yster tekort anemie teorie, en dui sodoende op ander faktore wat kan bydra tot die voorkoms van cribra orbitalia. Tot die skrywer se kennis, is hierdie die eerste in diepte studie wat ‘n kombinasie van drie metodes gebruik om die siektes van ‘n skeletversameling, verteenwoordegend van Wes-Kaap inwoners, te evalueer en gee sodoende ‘n unieke interpretasie van die gesondheids status van hierdie populasie.

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RESEARCH OUTPUTS

International Conferences:

Conference: ICMMA 2015: 17th International Conference on Microscopic and Macroscopic Anatomy (Barcelona, Spain)

Title: Radiological Analysis of Skeletal Metastases from Cervical Cancer

Participation: Poster presentation

Conference: ICAP 2016: International Conference on Anatomy and Physiology (Birmingham, UK)

Title: Tuberculosis and visceral rib lesions in the Kirsten Skeletal Collection

Participation: Oral presentation

National Conferences:

Conference: ASSA (2016): 44nd Annual Conference of the Anatomical Society of Southern Africa

Title: Congenital Malformations in the Kirsten Skeletal Collection

Participation: Oral presentation

Annual Academic Year Day at the Faculty of Medicine and Health Sciences, Stellenbosch University:

Conference: AAD 2015

Title: Radiological Analysis of Skeletal Metastases from Cervical Cancer

Participation: Poster presentation

Conference: AAD 2016

Title: Tuberculosis and visceral rib lesions in the Kirsten Skeletal Collection

Participation: Poster presentation

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ABBREVIATIONS

AIDS:	Acquired Immune Deficiency Syndrome
AS:	Ankylosing spondylitis
BMD:	Bone Mineral Density
BO:	Button Osteoma
CO:	Cribra orbitalia
CT:	Computerized tomography
COD:	Cause of death
DISH:	Diffuse idiopathic skeletal hyperostosis
DJD:	Degenerative joint disease
EH:	Enamel hypoplasia
etc.:	Et cetera
HIV:	Human immunodeficiency virus
HL:	Harris lines
PH:	Porotic hyperostosis
RA:	Rheumatoid arthritis
TB:	Tuberculosis
VRL:	Visceral rib lesions

Chapter 1 INTRODUCTION

Pathology, malformations and variations in the skeleton can be the result of or influenced by multiple factors including genetic variation, environmental influences, culture, nutrition and socio-economic status. Congenital malformations occur between fertilization and birth and can be indicative of a genetic influence, and/or malnutrition, infection and other environmental stimulus that affected the mother. Acquired malformations could give insight into external influences during life such as occupation or trauma. Signs of infectious diseases could reflect differences in living conditions, socio-economic status, and access to medical treatment in a population. Metabolic disorders can indicate malnutrition or periods of stress and, together with signs of infectious diseases, could provide a better understanding of the life history and socio-economic status of a group. Degenerative bone diseases can be reflective of an aging population. Information regarding neoplastic conditions obtained after death could improve the screening and diagnosis of these conditions in the clinical setting. By examining all these types of pathologies, metabolic disorders, and malformation after death, insight can be gained on the health and living conditions of a population during life.

The Kirsten Skeletal Collection consists of skeletonised cadavers received into the medical program at Stellenbosch University and is representative of three population groups in the Western Cape, namely, black, mixed, and white groups. Documentation of these skeletons includes information regarding the Cause of Death (COD). This, however, does not illustrate the extent of malformations or diseases present throughout life, and in many instances the COD is non-specific. Studying diseases and metabolic disorders present on these skeletons would add to the current knowledge of the Kirsten Skeletal collection and improve the understanding of the lifestyle of the population.

The literature review summarized the current information regarding the Kirsten Skeletal collection and gives an overview of basic anatomy of the skeleton. Furthermore, it gives information on the diseases and disorders that was examined in the present study. This information includes different characteristics of diseases and factors that could cause or influence disease presentation. The literature review will allow the reader so get a basic understanding of the normal anatomy and pathologies needed to understand the results and discussion.

In the present study, skeletal material was examined using a combination of three methods (macroscopically, microscopically and radiologically) for signs of diseases or metabolic

disorders. The materials and methods section gives a detailed description of how these methods were applied. It also includes information regarding the diagnostic criteria used for each disease or abnormality. Grading methods were used where available and all findings were documented.

Results are reported according to types of diseases and statistical analyses were done between age, sex, and population groups. Percentages and statistical significance for comparisons are given in tables for each type of disease followed by a more detailed description and analysis for each disease. Special attention was given to the presentation of periostitis in general, and specifically on the visceral surface of ribs.

To the author's best knowledge, this is the first study using a combination of three methods to examine the overall presentation of diseases and metabolic disorders in the Kirsten Skeletal Collection which provides a unique view on the life history and socio-economic status of the population groups represented by this collection. This study also contributes to some current theories on the interpretation of certain skeletal lesions such as visceral rib lesions (VRL) and cribra orbitalia (CO).

Chapter 2 LITERATURE REVIEW

2.1 KIRSTEN SKELETAL COLLECTION

The skeletons of the Kirsten Skeletal Collection are processed from cadavers used in the teaching program of medical students at Stellenbosch University (Tygerberg campus) in the Western Cape, South Africa. The skeletonising of cadavers started from the year 1957 (still continues presently) with 54.0% of all cadavers used in dissection between the years 1957-1996, being skeletonised (Labuschagne & Mathey, 2000). Approximately 64.0% of skeletons in the Kirsten Skeletal Collection were received from known public hospitals within the Western Cape region with Tygerberg, Karl Bremer and Grootte Schuur hospitals contributing the majority (Table 2.1). For the remaining 36.0%, the sources were either undocumented or cadavers were received from undertakers and private bequeathments. The last known residence was documented for approximately 76.0% of skeletons in the Kirsten Skeletal collection. Table 2.2 gives the percentage of skeletons received from each province of South Africa as well as Namibia. Of all the skeletons for which the last residence is known, 92.4% lived in the Western Cape with 67.8% of all skeletons being specifically from the Cape Peninsula (Table 2.2). From this data it can be assumed that the majority of the individuals in the Kirsten Skeletal collection lived in the Western Cape region for some period of time before death.

Table 2.1: Percentage contribution of cadavers from different hospitals in the Western Cape

Hospital	Contribution
Tygerberg Hospital	53.7%
Karl Bremer Hospital	13.7%
Grootte Schuur Hospital	13.4%
Paarl Hospital	4.4%
Conradie Hospital	3.4%
Stikland Hospital	2.4%
Brooklyn Chest Hospital	1.9%
Somerset Hospital	1.9%
Stellenbosch Hospital	1.7%
Valkenberg Hospital	1.7%
Other	1.9%

Table 2.2: Percentage of skeletons from each province in South Africa and Namibia

Province	District	Percentage of donors
Western Cape:	Cape Peninsula	67.8
	Cape Winelands	14.9
	West Coast	2.9
	Overberg	2.4
	Breede River Valley	2.1
	Garden Route	1.5
	Central Karoo	0.6
	Klein Karoo	0.3
	All	92.4
Northern Cape:	All	3.6
Eastern Cape:	All	1.3
Gauteng Province:	All	1.0
KwaZulu-Natal:	All	0.3
North West Province:	All	0.1
Namibia:	All	1.4

During apartheid in South Africa, enforced from 1948 to 1994, individuals were officially classified as either "black" (predominantly of Bantu descent), "white" (European descent), or "coloured" (a heterogeneous group with descent from Khoesan, Bantu, European and Indian) and were separated according to their racial classification (Pfeiffer *et al.*, 2016). This classification was indicated in the South African identification document which increased accuracy of documentation of cadavers received at Stellenbosch University (Pfeiffer *et al.*, 2016). A study by Daya *et al.* (2013) illustrates that the ancestry proportion distribution of the coloured population group in Cape Town consists mostly of African San, followed by African non-San, European, South Asian and East Asian. Table 2.3 illustrates the regional and national composition of the contributing population groups in South Africa as well as the population composition of cadavers received at Stellenbosch University (Labuschagne & Mathey, 2000). The population composition of the donors closely resembles that of the Western Cape but vastly different from that of South Africa (see Table 2.3). It can, therefore, be suggested that the population composition of the Kirsten Skeletal Collection is representative of the Western Cape.

Table 2.3: Population Composition: Regional, National and Donors (%)

	Cape Peninsula				Western Cape	South Africa	Donors
Population	**1960**	**1970**	**1980**	**1991**	**1991**	**1991**	**1956-1996**
Black	9.3	9.8	12.7	19.3	16.4	75.4	15.3
Coloured	51.8	54.7	53.6	53.5	58.3	8.7	62.6
White	37.8	34.5	32.6	26.1	24.5	13.3	22.1
Indian	1.1	1.0	1.1	1.1	0.8	2.6	<0.1

Source: Adapted from Labuschagne & Mathey (2000)

Between the years 1957-1996, approximately twice as many male cadavers (68.4%) were received into the teaching program as female cadavers (31.6%) (Labuschagne & Mathey, 2000). Labuschagne & Mathey (2000) looked at the sex distribution for each population group separately which showed that the black population group had the highest percentage males (83.1%) while the white population group had the lowest (57.9%). The coloured population group (which forms the majority of cadavers) consisted of 68.5% males (Labuschagne & Mathey, 2000).

The mean age of death for cadavers received between the years 1957-1996, was 55.4 years (range 15-98 years) (Labuschagne & Mathey, 2000). Table 2.4 illustrates the mean age at death for each population group and sex group separately. From this table it can be observed that the white group generally contained older individuals compared to the coloured and black groups while, with regards to the male and female groups, both had a similar mean age at death.

Table 2.4: Mean age at death of cadavers (years)

	Black	Mixed	White	Total
Males	52.2	52.7	68.6	55.6
Females	44.8	47. 9	71.6	54.8
Combined	51.0	51.2	69.9	55.4

Source: Adapted from Labuschagne & Mathey (2000)

Labuschagne & Mathey (2000) suggested that the educational levels for the cadaver population were low (especially that of the black and coloured groups). The authors based this assumption on the occupations listed in the donor files which included that of homemaker, domestic servant, casual worker or labourer. This supports the assumption that the Kirsten Skeletal Collection is representative of a low socio-economic community (Labuschagne & Mathey, 2000; Pfeiffer *et al*., 2016). The following sections will discuss the anatomy of the skeleton and describe diseases or disorders that could be present in the Kirsten Skeletal collection.

2.2 MACROSCOPIC ANATOMY OF BONE

2.2.1 Functions of the skeleton

The function of the skeletal system is to support the body, protect the internal organs, and facilitate muscle action and movement of the body through muscle attachments and ligaments (Nordin & Frankel, 2001; Brits, 2009; White *et al*., 2012). It also serves as a production site

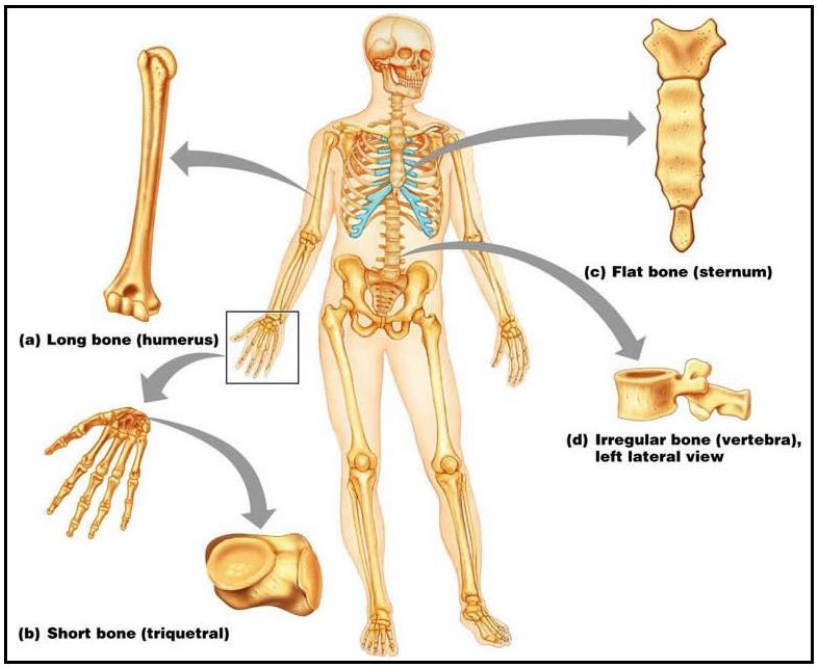
for blood cells as it contains bone marrow, and serves as a reservoir for essential minerals, including phosphate and calcium (Nordin & Frankel, 2001; Hall, 2005; White *et al*., 2012).

2.2.2 Types of bone tissue

Bone can macroscopically be divided into two types: cortical or compact bone and cancellous, or trabecular bone (Nordin & Frankel, 2001; Hillier & Bell, 2007; White *et al*., 2012). Cortical bone is hard and forms the external surface, or shell, of bones and provides a surface for muscle attachment (Nordin & Frankel, 2001; Hillier & Bell, 2007; White *et al*., 2012). Cancellous bone consists of a loose network of bony spicules known as trabeculae and is located on the interior of the cortical layer (Ortner, 2003; Hillier & Bell, 2007; White *et al*., 2012). The spaces between the trabeculae are filled with red bone marrow (Nordin & Frankel, 2001; White *et al*., 2012).

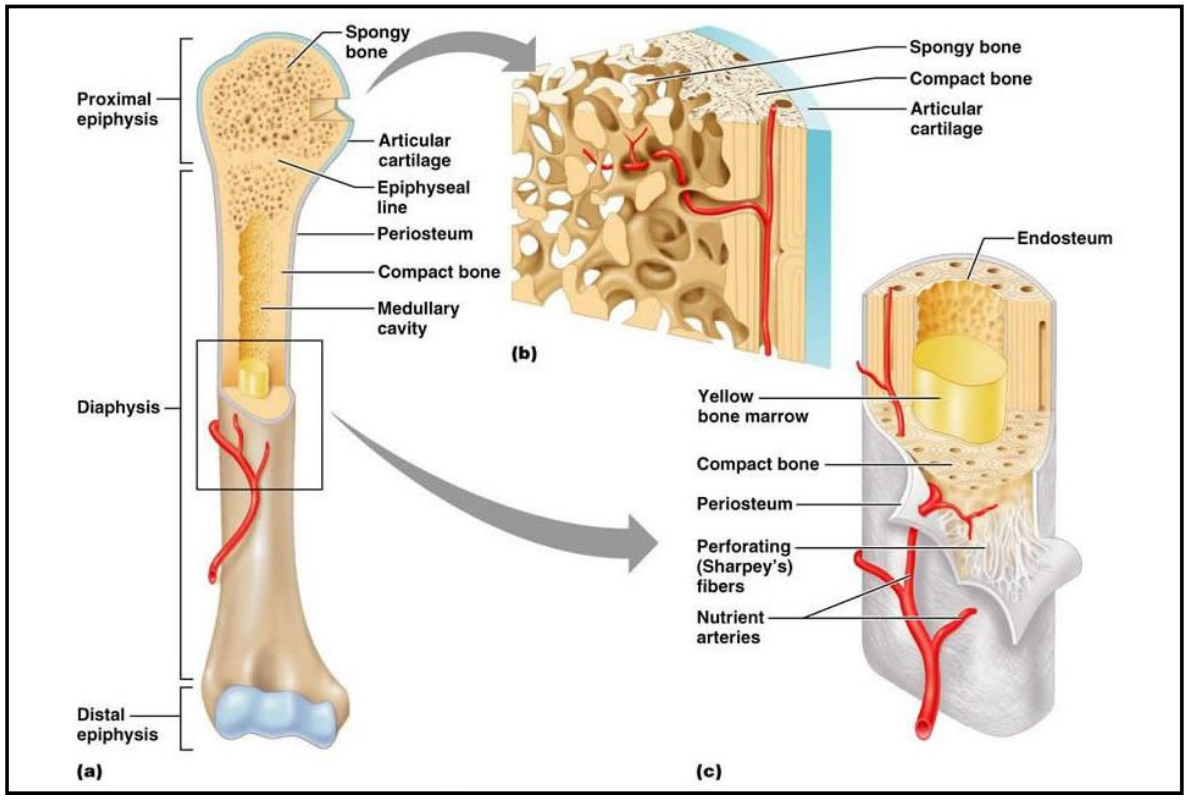
2.2.3 Typical bone forms and structure

Bones of the human body can be categorized into different types according to their shape and structure (Figure 2.1). These are long bones, short bones, flat bones, irregular bones, and sesamoid bones (Moore & Dalley, 2006). Long bones consist of a diaphysis, or shaft, and the epiphyses which form the two ends of the bone (Figure 2.2a). The diaphysis contains the medullary cavity which is surrounded by a thin layer of cancellous bone and a thick layer of compact bone (Figure 2.2c). The epiphyses consist of cancellous bone enclosed in a thin layer of cortical bone (Figure 2.2b) (Ross *et al*., 1995). Short bones are found in the ankle and wrist and have a cuboidal shape. Flat bones consist of two compact bone layers with a spongy bone layer in between (Figure 2.3). In areas where a flat bone is very thin, it can consist of only a compact bone layer. The term sesamoid bone refers to bones that develop in tendons where they cross between two long bones, e.g. the patella (Moore & Dalley, 2006). Irregular bones are those that do not fit in any of the other groups and may have various shapes.



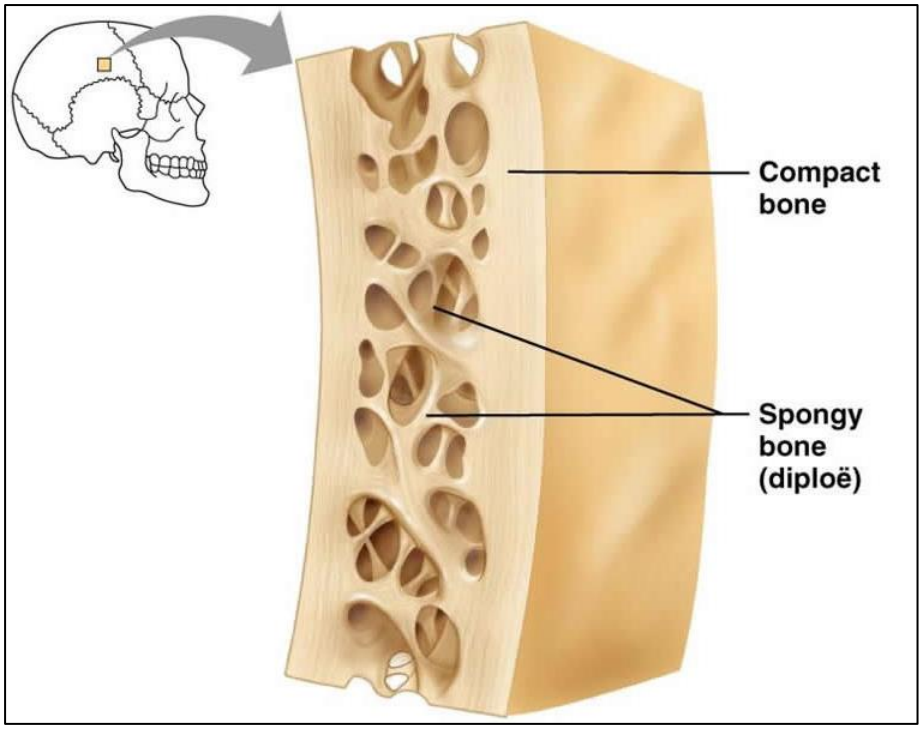
Source: Marieb and Hoehn (2007)

Figure 2.1: Typical bone structures
Different forms and structure include (a) long bones e.g. humerus; (b) short bones e.g. triquetrum; (c) flat bones e.g. sternum; and (d) irregular bones e.g. vertebra.



Source: Marieb and Hoehn (2007)

Figure 2.2: Structure of long bones
Long bones consist of a diaphysis (shaft) and epiphyses at the ends of the long bone (a). The epiphysis consists of cancellous bone enclosed in a thin layer of cortical bone (b). The diaphysis consists of a medullary cavity surrounded by a thin layer of cancellous bone and a thick layer of compact bone (c).



Source: Marieb and Hoehn (2007)

Figure 2.3: Structure of flat bones

2.3 MICROSCOPIC ANATOMY OF BONE

2.3.1 Primary bone

Primary bone refers to new bone being laid down during primary growth and can be found on the endosteal and periosteal circumferences of bone on a cross section (Martin *et al*., 2015). Woven bone, also known as immature bone, is the first mineralized form of connective tissue and forms rapidly compared to other types of bone (Pfeiffer, 1996; White *et al*., 2012). Woven bone is found during initial growth of the skeleton in a foetus and immediately after birth (Pfeiffer, 1996; Nordin & Frankel, 2001; White *et al*., 2012). It is replaced by another type of bone, called lamellar bone, by the age of four or five years (Nordin & Frankel, 2001; Martin *et al*., 2015). Woven bone is also found within a fracture callus, adjacent to local inflammatory processes, or in pathological conditions (Pfeiffer, 1996; Martin *et al*., 2015). This bone type is poorly organized with the collagen fibres oriented randomly and contains large vascular spaces (Pfeiffer, 1996; Martin *et al*., 2015).

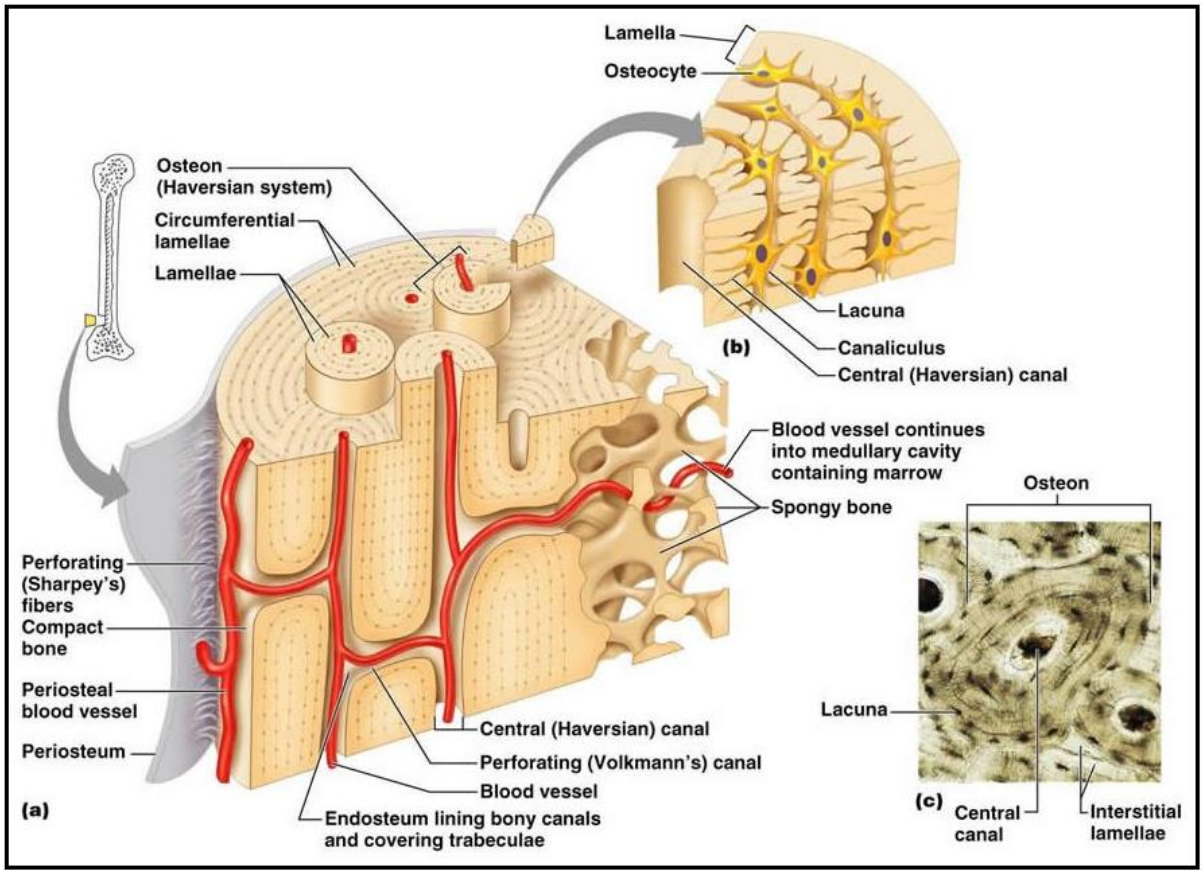
When tissue displays a highly organized arrangement, it is termed lamellar bone (White *et al*., 2012). Lamellar bone takes longer to form than woven bone and consists of layers of bone tissue called lamellae which lie parallel to the bone surface or are concentrically arranged around a vascular canal (Pfeiffer, 1996; Hillier & Bell, 2007; White *et al*., 2012).

These concentrically arranged lamellae form an osteon with collagen fibres of consecutive lamellae arranged at different angles (Pfeiffer, 1996; Hillier & Bell, 2007; White *et al*., 2012). A primary osteon usually has fewer concentric lamellae and a smaller vascular canal than a secondary osteon and lacks a cement line (Pfeiffer, 1996).

2.3.2 Secondary bone

New bone that is deposited after resorption of older bone can be termed secondary bone (Martin *et al*., 2015). Secondary bone can be divided into different categories including secondary osteons, interstitial bone, and endosteal and periosteal circumferential lamellar bone (Pfeiffer, 1996).

Secondary osteons can be referred to as Haversian systems which possess a central canal containing blood vessels and nerve fibres (Figure 2.4) (Nordin & Frankel, 2001; White *et al*., 2012). This canal is commonly known as the Haversian canal and is surrounded by concentric layers of lamellar bone similar to the primary osteon, and surrounded by a cement line not present in a primary osteon. Bone cells, or osteocytes, are contained in small cavities on the borders of lamellae called lacunae (Nordin & Frankel, 2001; White *et al*., 2012). Small channels called canaliculi connect these lacunae with each other as well as with the Haversian canal (Nordin & Frankel, 2001; White *et al*., 2012). The cement line cannot be crossed by the canaliculi (Nordin & Frankel, 2001). In long bones a longitudinal parallel arrangement of Haversian systems are found with Volkmann's canals connecting the Haversian canals with each other and extending to the cancellous bone (Nordin & Frankel, 2001; White *et al*., 2012).



Source: Marieb and Hoehn (2007)

Figure 2.4: Microscopic structure of compact bone
Compact bone consists of a collection of osteons or Haversian systems. (a) Organization of Haversian systems in compact bone. (b) Haversian system with osteocytes in lacuna. (c) Microphotograph of an osteon showing the lacuna and central canal.

Between secondary osteons, remnants of primary osteons, lamellar bone and older secondary osteons may be found (Pfeiffer, 1996). These remnants form part of the interstitial bone and is produced by the resorption and separation of pre-existing primary bone tissue from the bone surface and vascular canals by cement lines (Pfeiffer, 1996).

2.3.3 Bone cells

Three types of bone cells are responsible for the formation, maintenance and resorption of bone: osteoblasts, osteocytes and osteoclasts. Another type of bone cell is an osteogenic cell which is the precursor of an osteoblast (Ortner, 2003).

Osteoblasts are responsible for the production of the bone matrix (inorganic and organic components of bone) (Ortner, 2003; White *et al*., 2012). It produces organic matter including type 1 collagen, proteoglycans and glycoproteins, and also plays an important role in the formation of the inorganic component (Ortner, 2003; White *et al*., 2012). They are mono-

nucleated cells that develop from osteogenic cells and are located at the surface of developing bone tissue (Ortner, 2003). As the osteoblasts secrete bone matrix, they become enclosed by the bone matrix and become known as osteocytes (Ortner, 2003; White *et al*., 2012).

Osteocytes occupy the lacunae and have cytoplasmic processes that extend through the canaliculi to connect with other osteocytes (Ortner, 2003; White *et al*., 2012). This allows for cell communication and the diffusion of nutrients to all the cells. Osteocytes are responsible for maintaining the bone matrix and are less active than osteoblasts (White *et al*., 2012). Resorption is initiated at the cell death of osteocytes.

Osteoclasts are large multinucleated cells located in cavities in the bone known as Howship's lacunae (Ortner, 2003; Brits, 2009). These cells are responsible for resorption and remodelling of bone (Ortner, 2003; White *et al*., 2012).

2.4 PATHOLOGY

Trauma, disease and other lifestyle traits, such as musculoskeletal markers, can be investigated after death by examining bone and teeth. All pathological changes observed on bone are the result of an imbalance between bone formation and bone resorption, as well as growth-related diseases (White *et al*., 2012).

Various causes exist for the imbalance between the formation and resorption of bone. While different authors use different categories to divide the diseases (Aufderheide & Rodríguez-Martin, 1998, Ortner, 2003; Komar & Buikstra, 2008; White *et al*., 2012), the categories that will be discussed include congenital and acquired malformations, infectious diseases, metabolic disorders, degenerative bone disorders, neoplastic conditions, and lastly miscellaneous conditions.

2.4.1 Congenital and acquired malformations

Congenital malformations refer to pathological changes that take place during normal development between fertilization and birth (Aufderheide & Rodríguez-Martin, 1998; White *et al*., 2012). It can be the result of genetic influence, an environmental stimulus or infection, or maternal malnutrition during developmental stages when the foetus is vulnerable (Warkany, 1944; Masni ková & Beňuš, 2003; Ortner, 2003; White *et al*., 2012). These malformations can be observed prenatally, at birth, during childhood, or in adulthood and the severity of anomalies range from insignificant to fatal (Masniková & Beňuš, 2003).

Congenital malformations can affect any organ or structure, with skeletal malformations accounting for approximately 40.0% of all congenital malformations (Aufderheide & Rodríguez-Martin, 1998). As mentioned, a large variety of congenital malformations can occur in the skeletal system, the result of which might be observed in a skeletal population (Aufderheide & Rodríguez-Martin, 1998; Ortner, 2003; White *et al*., 2012). Individuals with severe malformations may have a decreased life expectancy (Aufderheide & Rodríguez-Martin, 1998) and for this reason, severe malformations will not be observed as frequently as less severe malformations in adult skeletons.

Congenital malformations are common in the axial skeleton, with preference to the vertebral column due to its complex embryology and structure (Kaplan *et al*., 2005). During embryology, the vertebral structures are formed by mesenchyme and the development of bone itself is induced by the notochord (Kaplan *et al*., 2005). Abnormalities of the mesenchyme, notochord, or any other influence on the signalling for bone formation, may cause defects in the vertebral structures (Kaplan *et al*., 2005).

Acquired malformations in this section will refer to changes in the form or structure of skeletal elements as a result of external influences such as occupation, trauma, and other pathological conditions. Congenital and acquired malformations that will be discussed in more detail include spina bifida, sacralisation and lumbarisation of vertebrae, scoliosis, and lastly, kyphosis.

2.4.1.1 Spina bifida

Incomplete midline closure of the two halves of the neural arches in vertebrae is known as spina bifida. It occurs mostly in the lumbosacral region of the vertebral column but may occur at any spinal segment from the atlas to the sacrum (Groza *et al*., 2012). Spina bifida can be divided into two types, namely, spina bifida occulta, and spina bifida cystica or aperta. In spina bifida occulta, the neural tissue and meningeal structures do not protrude through the opening and may go unnoticed (Aufderheide & Rodríguez-Martin, 1998; Ortner, 2003). On the skeleton, spina bifida occulta is characterized by a slit between the two halves of the unfused neural arches and is most commonly seen on the sacrum (Figure 2.5) (Groza *et al*., 2012). In spina bifida cystica, the meningeal structures and/or neural tissue protrude through the defect resulting in a more severe type of spina bifida, which can be fatal (Aufderheide & Rodríguez-Martin, 1998; Ortner, 2003). Spina bifida cystica can further be divided into three grades of severity depending on the structures that protrude through the defect: meningocele

(meninges and nerve roots protrude), myelomeningocele (spinal cord and meninges protrude), and myelocele (skin and dura fail to close) (Aufderheide & Rodríguez-Martin, 1998).

Source: Groza *et al.* (2012)

Figure 2.5: Spina bifida occulta of sacrum
Sacrum of a 55-60 year old male with open S1-S5 neural arches.

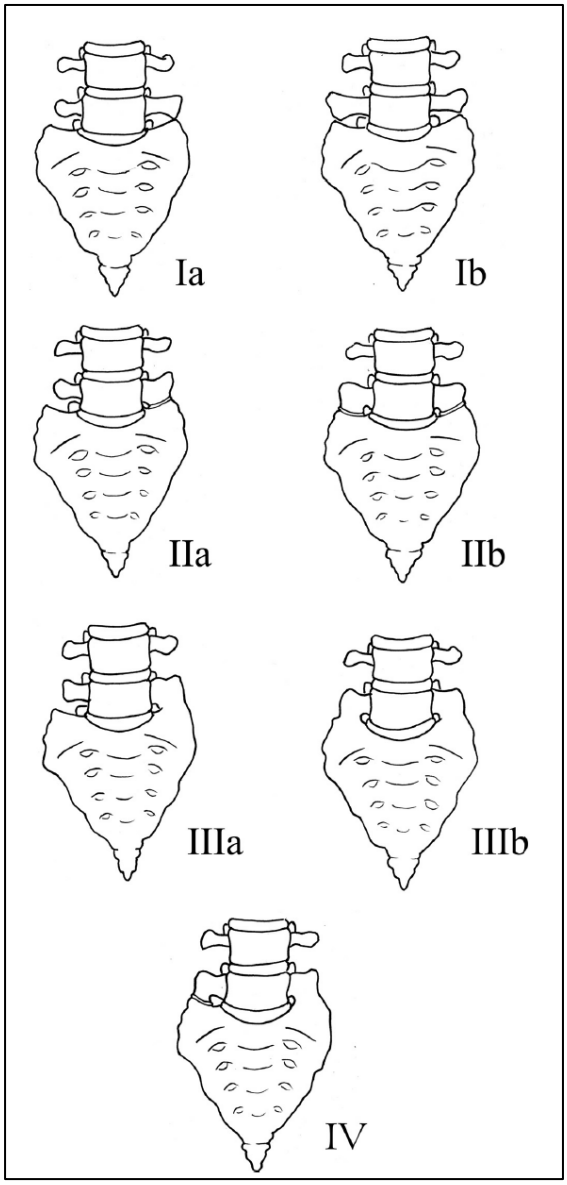
2.4.1.2 Sacralisation/lumbarisation

Sacralisation refers to complete or incomplete fusion of the fifth lumbar vertebra to the sacrum. With lumbar sacralisation the fifth lumbar vertebra becomes part of the superior aspect of the sacrum resulting in an additional segment to the sacrum and the lumbar region losing a segment (Figure 2.6). Konin & Walz (2010) outlines different types of sacralisation adapted from Castellvi *et al*. (1984): Ia) unilateral dysplastic transverse process (>19mm width), Ib) bilateral dysplastic transverse process (>19mm width), IIa) unilateral diarthrodial joint between the transverse process and sacrum, IIb) bilateral diarthrodial joint between the transverse process and sacrum, IIIa) unilateral fusion between the transverse process and sacrum, IIIb) bilateral fusion between the transverse process and sacrum, and IV) unilateral

diarthrodial joint with transverse process and sacrum fusion on the collateral side (Figure 2.7). Incomplete fusion of the first sacral segment to the sacrum is termed lumbarisation and can be divided into the same types as sacralisation. When the first sacral segment is completely separated from the sacrum, it results in six lumbar vertebrae and only four sacral segments.

Source: Groza *et al.* (2012)

Figure 2.6: Sacralisation of L5 (type IIIb)



Source: Konin & Waltz (2010)

Figure 2.7: Castellvi's classification of lumbosacral transitional vertebrae

2.4.1.3 Scoliosis

The term scoliosis is used when the vertebral column shows an abnormal lateral curvature, giving it an S-shaped appearance. Different types of scoliosis include congenital, idiopathic, and paralytic scoliosis (Aufderheide & Rodríguez-Martin, 1998). Congenital scoliosis can either be caused by a failure in segmentation of the embryological precursors of vertebrae, or congenital defects such as hemivertebrae (only one half of the vertebra is formed), in individual vertebrae (Kilgore & Van Gerven, 2010). Idiopathic scoliosis is an acquired malformation and appears mostly at puberty with the vertebral column deformities increasing

during growth spurts (LeBlanc *et al*., 1997). Since this type of scoliosis forms the majority of cases, scoliosis will further be considered an acquired malformation.

2.4.1.4 Kyphosis

Kyphosis specifically refers to curvature of the vertebral column with the convexity directed posteriorly (Roaf, 1960). A natural kyphosis of 20-40 degrees is found in the thoracic regions of the vertebral column, however, in paleopathology the term kyphosis is used for excessive posterior convexity (hyperkyphosis) in these regions (Roaf, 1960; Schneider *et al*., 2004). This deformity can be caused by a variety of congenital spinal malformations, Scheuermann's disease, or trauma (Roaf, 1960). It can also be the result of aging, with occupation and lifestyle also contributing (Fon *et al*., 1980).

2.4.2 Infectious diseases

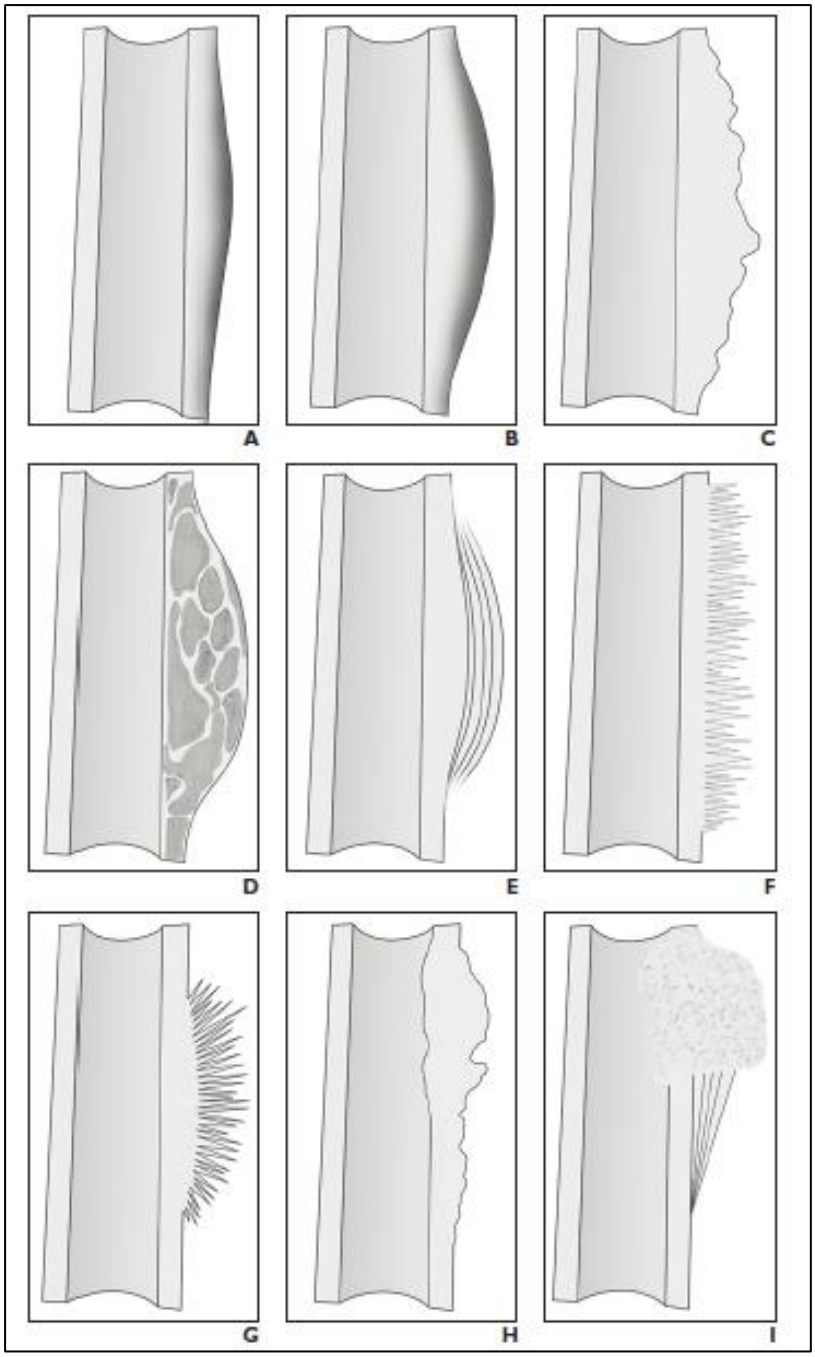
Most infectious diseases do not leave direct evidence of the disease on the skeletal remains as they are not present for extended periods of time, which would have enabled them to elicit an inflammatory response in bone (Ortner, 2003; White *et al*., 2012). These can include acute, lethal infections, or infections that are easily eliminated by the immune system or other treatments; the duration of these infections are not long enough to cause inflammation of bones (Aufderheide and Rodríguez-Martin, 1998). The infectious diseases that do leave signs on the skeleton are usually subacute chronic diseases that produce similar responses, which make differential diagnosis difficult (Ortner, 2003; White *et al*., 2012). Inflammation caused by infection has different terms (periostitis, osteitis, or osteomyelitis) according to the primary site of inflammation (Ortner, 2003). Infectious diseases can also be classified into different categories according to the type of infectious agent causing the disease (Aufderheide and Rodríguez-Martin, 1998). These groups include bacterial, viral, fungal, and parasitic infections; however, only bacterial infections will be discussed in more detail. Tuberculosis (TB) is a common infectious disease and a major problem in the Western Cape (Yach, 1988) and, therefore, will be discussed further.

2.4.2.1 Periosteal reactions

Periostitis affects the outer surface of the bone through inflammation of the periosteum, while inflammation within compact bone is termed osteitis (White *et al*., 2012). Both periostitis and osteitis may be caused by a variety of insults including infectious diseases, trauma, malignancies, metabolic, or arthritic conditions (Golding, 1985; Rana *et al*., 2009; Yao *et al*.,

2009). Periostitis can occur as a localized reaction in an area where the adjacent tissue is inflamed, or as a systemic reaction towards systemic infections that reaches the different bones via the circulatory system (Golding, 1985; Rana *et al*., 2009). The distribution of lesions throughout the skeleton is therefore important for differential diagnosis. An example of a localized periosteal reaction includes periostitis that occurs on the visceral surface of ribs in response to pulmonary diseases (Matos & Santos, 2006). On the other hand, systemic infections would, in most cases, affect the tibiae and fibulae bilaterally (Epstein *et al*., 1979; Lambert, 1993; Bourbou, 2003; Christensen *et al*., 2013).

The appearance of a periosteal reaction can differ depending on the underlying cause as well as the duration and severity of the insult (Pineda *et al*., 1987; Rana *et al*., 2009). Rana *et al*. (2009) described the different types of periosteal reactions, as seen radiologically, which included thin, solid, thick irregular, septated, laminated (onionskin), perpendicular (hair-on-end), sunburst, disorganized, and Codman's triangle, or a combination of any of these (Figure 2.8). The different types of periostitis can also be used for differential diagnoses. A solid periosteal reaction, for example, usually occurs in response to a nonaggressive, slow process whereas a speculated periosteal reaction can be caused by aggressive insults such as Ewing's sarcoma (Rana *et al*., 2009).



Source: Rana *et al*., (2009)

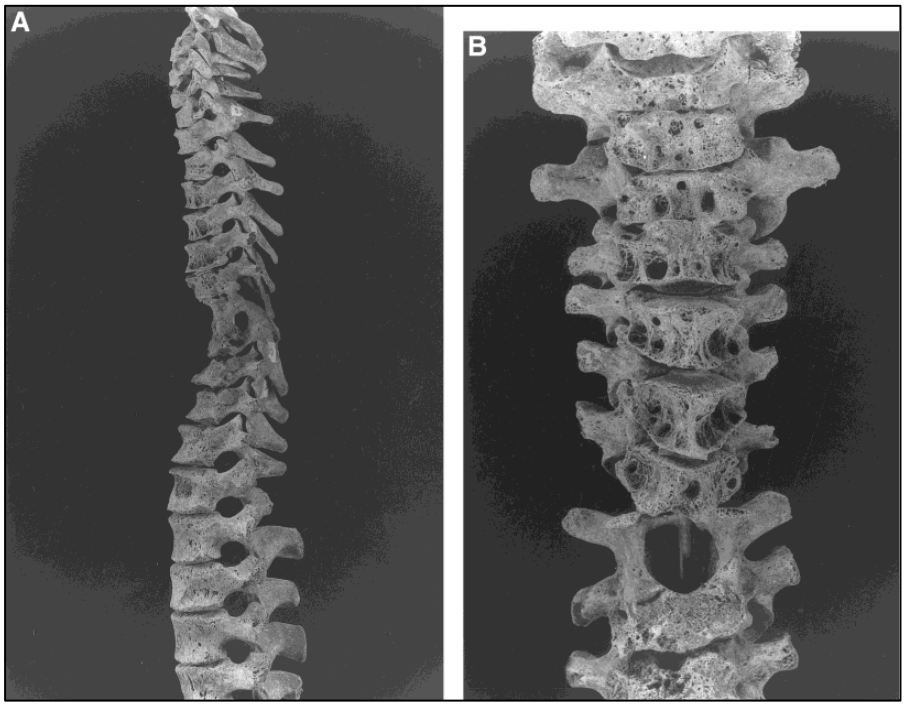
Figure 2.8: Different types of periosteal reactions
Diagram illustrates A) thin, B) solid, C) thick irregular, D) septated, E) laminated (onionskin), F) perpendicular (hair-on-end), G) sunburst, H) disorganized, and I) Codman's triangle periosteal reactions.

2.4.2.2 Tuberculosis

Tuberculosis, an acute or chronic infectious disease caused by the bacterium *Mycobacterium tuberculosis*, will further be referred to as TB. It may infect any organ with pulmonary TB (infection of the lungs) being the most common. This is due to transmission of the bacteria from person to person through inhalation of droplets (Mays *et al*., 2001b). Factors

contributing to the spread of the disease include population density, environmental influences such as air ventilation, as well as other infectious diseases such as the human immunodeficiency virus (HIV) (Manchester, 1984). HIV inhibits the host's immune system's ability to defend against *M. tuberculosis* resulting in an increase in TB in populations affected by HIV (Roberts *et al.*, 1998). Other factors allowing for an increase in TB is the growing resistance of bacteria against antibiotics due to crowded living conditions, poor healthcare access and patients failing to complete treatment (Steyn *et al.*, 2013).

The skeleton becomes involved as a result of haematogenous spread of the TB bacterium from soft tissue (Mays *et al.*, 2001b). Previously, the diagnosis of TB from skeletal material relied primarily on spinal lesions (Figure 2.9) with hip and knee lesions also being an important diagnostic factor (Roberts *et al.*, 1998; Mays *et al.*, 2002). These lesions are mostly destructive causing cavities to form within the cancellous bone (Mays *et al.*, 2001b). Characteristics of spinal TB (also known as Pott's disease) include the region of the vertebral column affected (lumbar and thoracic vertebral bodies), destruction of the cancellous bone forming cavitation, collapse of the affected vertebral body, loss of intervertebral disc space, and kyphosis (Mays *et al.*, 2001b).



Source: Santos and Roberts (2001)

Figure 2.9: Spinal TB
Destruction of thoracic vertebral bodies is shown from a lateral (A) and frontal (B) view of the vertebral column.

Studies have shown that chronic infection resulting from pulmonary TB can cause a periosteal reaction on the visceral surface of ribs in contact with pleura of the infected lung areas (Figure 2.10) (Roberts *et al*., 1998; Guttentag & Salwen, 1999; Matos & Santos, 2006). These lesions can present as subperiosteal growth (porosity and striation of bone), proliferative lesions, or pleural plaque formation (Geldenhuys, 2014). These lesions affect mostly the vertebral ends of the fourth to sixth ribs on the left which corresponds with the most prevalent sites in the lungs for pulmonary TB (Santos & Roberts, 2006). Matos & Santos (2006) found that individuals with non-TB pulmonary diseases are more likely to have woven bone lesions at the sternal ends of inferior ribs rather than lamellar bone at the vertebral ends of ribs as seen in individuals with pulmonary TB. These criteria can be used to aid differential diagnosis between TB and other pulmonary diseases. However, rib lesions are not pathognomonic to TB and other skeletal lesions must be present as well to make a diagnosis (Roberts *et al*., 1998; Santos & Roberts, 2006; Steyn *et al*., 2013).

Source: Steyn *et al.* (2013)

Figure 2.10: Visceral rib lesion
New bone formation on the visceral surface of the vertebral end of rib due to pulmonary TB

2.4.3 Metabolic disorders

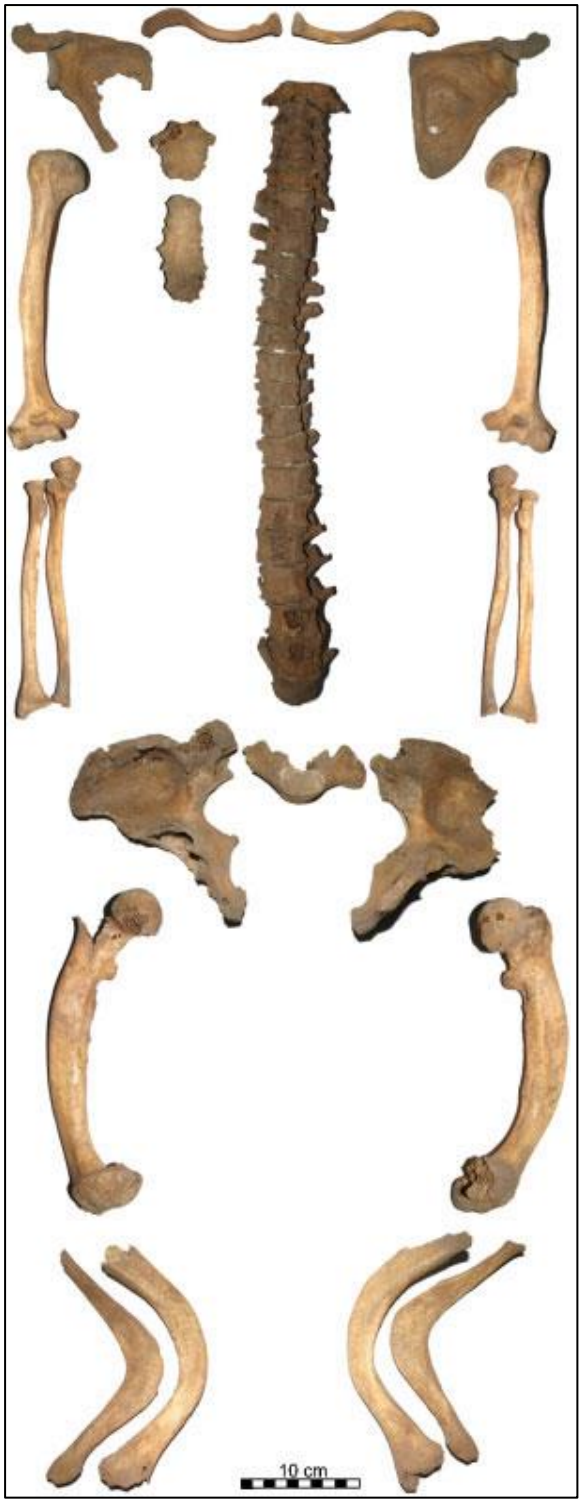
Disorders in which reduced osteoid production or decreased mineralization occurs, results in a loss of bone mass and can be termed metabolic disorders (White *et al*., 2012). These include pathological conditions resulting from nutrient deficiencies, or changes in endocrine function (Huss-Ashmore *et al*., 1982; White *et al*., 2012). Nutritional deficiencies may result from either an inadequate intake of nutrients or inadequate absorption of ingested nutrients (Ortner, 2003). Differentiating between specific nutrient deficiencies may be difficult as malnutrition usually involves the deficiency of more than one specific nutrient (Huss-Ashmore *et al*., 1982). A general interpretation can be made on the nutritional status of an individual by examining skeletal elements, but a specific diagnosis can only be made when a distinctive characteristic of a specific deficiency, such as seen in severe vitamin C deficiency, is present. Diseases caused by a specific nutrient deficiency that will be discussed in more detail include rickets/osteomalacia, porotic hyperostosis (PO) and CO. Osteoporosis, which is more the result of age-related changes in endocrine secretions than nutritional deficiency, will also be discussed in detail. General indicators of a stress period during childhood, such as malnutrition or infections, that will be discussed include Harris lines (HL) and enamel hypoplasia (EH).

2.4.3.1 Rickets/Osteomalacia

One of the important requirements for the metabolism of phosphorus and calcium and therefore the mineralization of osteoid is the pro-hormone, vitamin D (Ortner, 2003; Holick, 2005; Mays *et al*., 2006). Vitamin D can be produced by the body when the skin is exposed to ultraviolet light and can also be acquired through dietary intake (Ortner, 2003; Brickley *et al*., 2005; Holick, 2005; Waldron, 2009). Rickets and osteomalacia are metabolic diseases caused by a vitamin D deficiency (Waldron, 2009; White *et al*., 2012). This deficiency can be caused by a lack of sunlight exposure, insufficient or lack of vitamin D dietary intake, intestinal malabsorption, or a combination of these (Ortner, 2003). In both children and adults vitamin D deficiency is characterized by inadequate mineralization of new bone formed in skeletal material (Huss-Ashmore *et al*., 1982; Ortner, 2003; Reginato & Coquia, 2003; Brickley *et al*., 2005; Waldron, 2009; White *et al*., 2012). However, the severity and type of bone deformation due to the lack of mineralization differs between children and adults as children still have growing long bones (Ortner, 2003; Reginato & Coquia, 2003; Brickley *et al*., 2007; White *et al*., 2012). The disease can, therefore, be classified as either rickets or

osteomalacia depending on whether the deficiency occurs during childhood or adulthood respectively (Huss-Ashmore *et al*., 1982; Waldron, 2009).

Rickets is a childhood disease influencing primarily the cartilage growth plate; therefore, the most pronounced changes are observed in parts of the skeleton with the most rapid growth rates (Huss-Ashmore *et al*., 1982; Ortner, 2003; Schamall *et al*., 2003; Mays *et al*., 2006; Mays *et al*., 2007; Waldron, 2009). Ortner & Mays (1998) provides a table with skeletal features found in infants with rickets. These features include porosity of the skull and bone adjacent to the growth plates of post-cranial bones (Ortner, 2003). Several bones can be deformed including the mandibular ramus which can change shape due to activity of the muscles of mastication during chewing (Waldron, 2009). The upper limb and lower limb bones can also bend in different directions due to weight bearing, such as during crawling and walking (Figure 2.11) (Ortner, 2003; Waldron, 2009; White *et al*., 2012). Flaring occurs on growing bone ends including the long bones and sternal rib ends (Huss-Ashmore *et al*., 1982; Ortner, 2003; Holick, 2005; Waldron, 2009). Mays *et al*. (2006) found the same features in a study on young children and also described rib deformities with an increase in the acuteness of the rib angle. The authors also found that the skeletal material present with flattening of bone beneath the femoral head and *coxa vara*, or a reduced angle between the head and shaft of the femur (Ortner, 2003). The vertebrae can also be deformed by weight bearing leading to kyphosis, lordosis, or scoliosis (Aufderheide and Rodríguez-Martin, 1998; Ortner, 2003).



Source: Adapted from Haduch *et al*. (2009)

Figure 2.11: Residual rickets
Post-cranial skeleton of individual with residual rickets.

Osteomalacia affects primarily the mechanically stressed areas of the skeleton or where bone remodelling occurs the most (Ortner, 2003; Schamall *et al*., 2003; White *et al*., 2012). One of the more common characteristics of osteomalacia is Looser's zones, or pseudofractures

(Reginato & Coquia, 2003; Brickley *et al*., 2005; Waldron, 2009). Where an accumulation of osteoid occurs, they appear as radiolucent areas on radiographs (Waldron, 2009). Looser's zones possibly result from stress fractures in weakened bone that fail to heal. If the bone experiences trauma, it can become a full fracture (Brickley *et al*., 2005). Pseudofractures can occur at the inferior and superior pubic rami, lateral border of the scapula, medial femoral neck and sub-trochanteric region, as well as the ribs, and are usually symmetrical (Francis & Selby, 1997; Ortner, 2003; Reginato & Coquia, 2003; Brickley *et al*., 2005; Brickley *et al*., 2007; Haduch *et al*., 2009; Waldron, 2009).

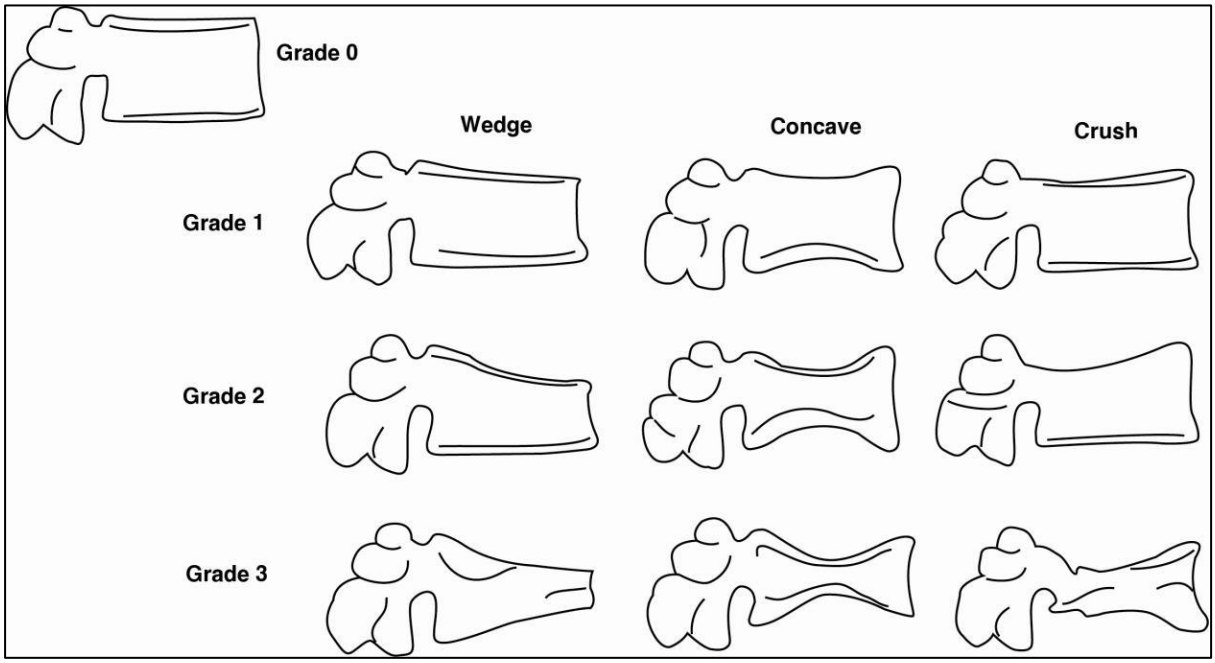
Several other skeletal characteristics can be used to identify osteomalacia. The scapulae of an individual with osteomalacia can present with increased posterior curvature of the scapula body or folding of the superior border (Brickley *et al*., 2005). Weakened vertebral bodies cannot withstand weight-bearing and results in a concavity at the inferior and superior surfaces of the vertebral body giving it a 'biconcave codfish appearance' (Francis & Selby, 1997; Ortner, 2003; Brickley *et al*., 2005; Brickley *et al*., 2007). This can result in kyphosis and scoliosis in the thoracic and lumbar regions of the vertebral column (Ortner, 2003: Reginato & Coquia, 2003; Brickley *et al*., 2005). Viewing a cranio-caudal projection of a vertebra on a radiograph shows vague, rounded, thin-walled trabeculae (Schamall *et al*., 2003). An increased angle of the sacral body can occur (Brickley *et al*., 2005). Folding of the iliac crest and a decrease in the antero-posterior length of the ilium may be observed, including anteriorly facing acetabulae (Ortner, 2003; Brickley *et al*., 2005). Long bone bending deformities such as anterolateral bending of the femur may also occur, however not as severely as in rickets (Ortner, 2003; Brickley *et al*., 2005). Histological examination of an affected bone may show enlarged lacunae with inadequately mineralized walls (Schamall *et al*., 2003; Brickley *et al*., 2007). Bone adjacent to cement lines may also be defective where fragments of new bone do not connect to pre-existing bone, resulting in open ring-like areas in bone (Brickley *et al*., 2007).

2.4.3.2 Osteoporosis

Osteoporosis refers to the loss of total bone mass without changing the ratio of bone mineral to bone matrix (Ortner, 2003). Two types of osteoporosis are described. Type 1 refers to osteoporosis observed mostly in post-menopausal women, which is characterised mainly by trabecular bone loss (Aufderheide and Rodríguez-Martin, 1998). Type 2 is found in both sexes and usually has a later onset age than type 1, and is characterized by the loss of both

cortical and trabecular bone (Aufderheide and Rodríguez-Martin, 1998). Bone density is generally measured from the vertebral bodies, distal radius or femoral neck through X-ray or computerized tomography (CT) scans (Aufderheide and Rodríguez-Martin, 1998).

Vertebral compression can be the result of pathology but is generally associated with increased age and decreased bone density such as in osteopenia or osteoporosis (Genant *et al*., 2000). It could be observed as either a wedge (anterior compression), concave (middle compression), or crush (posterior compression) appearance of the vertebral body (Curate *et al*., 2014; Genant *et al*., 2000). Figure 2.12 illustrates a semi-quantitative scoring method developed by Genant *et al*. (1993), as illustrated by Curate *et al*. (2014), which shows the different types of compression as well as the severity of compression.



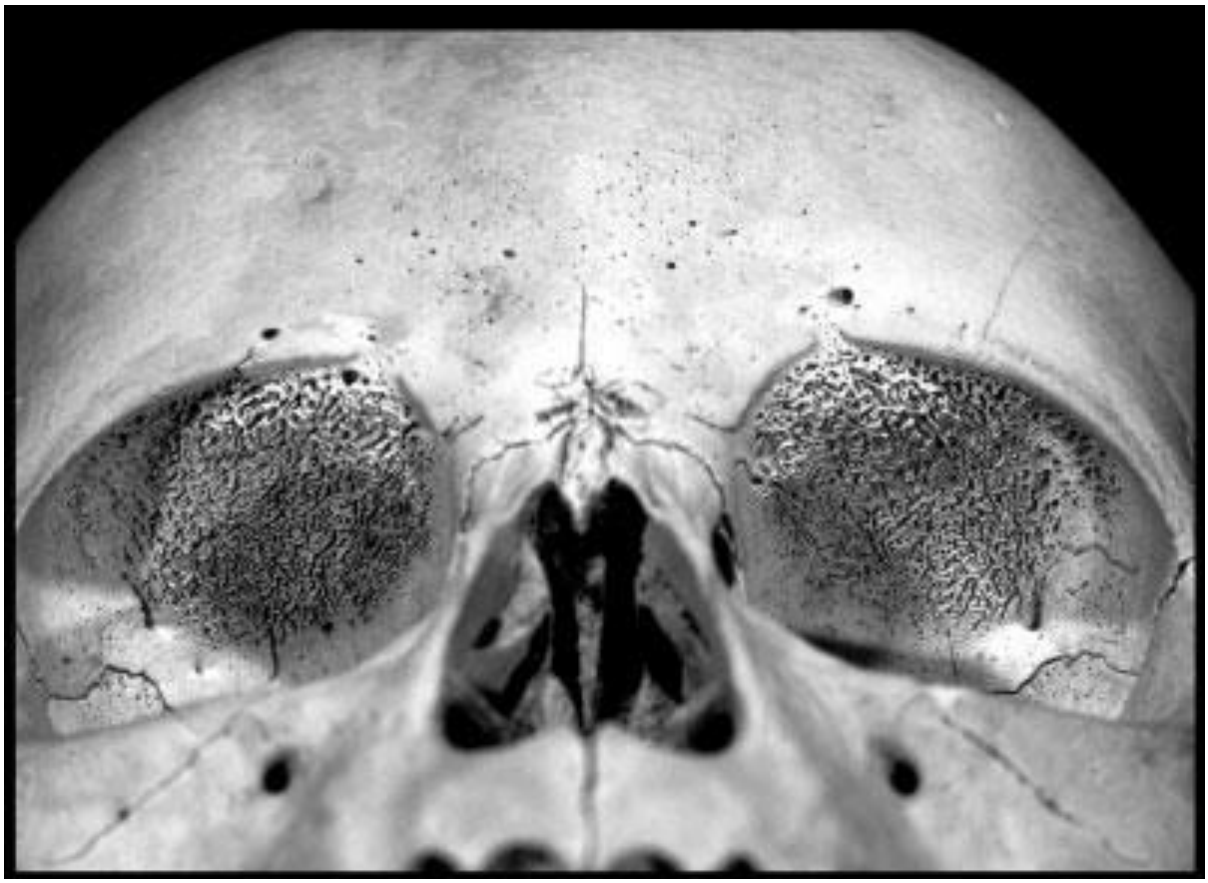
Source: Curate *et al*. (2014) adapted from Genant *et al*. (1993)

Figure 2.12: Genant's classification method for vertebral compression.

2.4.3.3 Porotic hyperostosis/cribra orbitalia

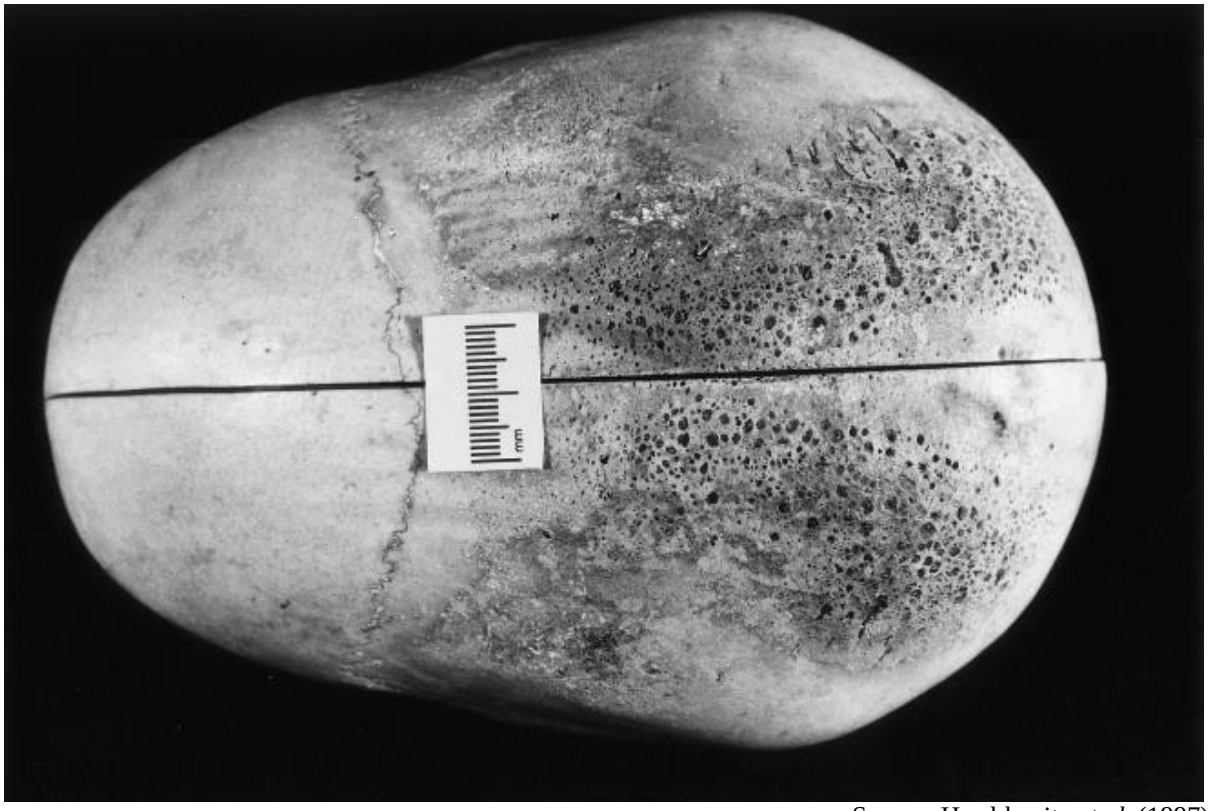
Porotic hyperostosis is characterized by areas of porosity on the external cranial vault and roof of the orbits (Facchini *et al*., 2004; Walker *et al*., 2009). Specific names can be given depending on the different areas affected namely CO (Figure 2.13) which affects the roof of the orbits, and cribra cranii (Figure 2.14) which affects the external surface of the cranial vault, with the occipital and parietal bones most commonly involved (Facchini *et al*., 2004).

They are believed to be related, with CO occurring first followed by the cranial vault if metabolic stress continues (Stuart-Macadam, 1987; Facchini *et al*., 2004; Wapler *et al*., 2004). Anaemic stress can cause an increase in erythrocyte production leading to hypertrophy and hyperplasia of the hemopoietic bone marrow and diploe (Mensforth *et al*., 1978).



Source: Walker *et al*. (2009)

Figure 2.13: Cribra orbitalia



Source: Hershkovitz *et al*. (1997)

Figure 2.14: Porotic hyperostosis (cribra cranii) of the parietal bones

Different criteria for grading PH and CO have been used and are summarized by Jacobi & Danforth (2002). The criteria developed by Nathan & Hass (1966) consists of three types of PH: 1) porotic type which consists of small pores, 2) cribrotic type which has larger openings that is still separated, and 3) trabecular type in which the openings are joined to form trabeculae (Fairgrieve & Molto, 2000). The criteria outlined by Buikstra & Ubelaker (1994), which was adapted from Stuart-Macadam (1985), consists of four severity levels: 1) fine scattered foramina, 2) isolated small and large foramina, 3) foramina with some having joined to form trabeculae with no thickening visible, and 4) foramina are joined and trabecular structures form outgrowths from the normal bone surface. Lesions can also be graded according to their state of healing as either reactive or healed lesions as described by Mensforth *et al*. (1978). In a study done on inter-observer scoring using the standard criteria from Buikstra & Ubelaker (1994), the authors concluded that the criteria could be improved significantly if more detailed descriptions and photographic examples are used (Jacobi & Danforth, 2002).

Different causes have been ascribed to the occurrence of both PH and CO which will be discussed in the following paragraphs (Angel, 1966; Stuart-Macadam, 1992; Hershkovitz *et*

al., 1997; Holland & O'Brien, 1997; Fairgrieve & Molto, 2000; Salvadei *et al.*, 2001; Facchini *et al.*, 2004; Walker *et al.*, 2009). The iron deficiency theory is the most commonly accepted theory (Walker *et al.*, 2009). Iron deficiency can be due to low iron intake in the diet, parasitic infections and other infectious diseases, malabsorption of iron in the intestinal tract, and inhibition of the bio-availability of iron (Fairgrieve & Molto, 2000). An anaemic response of the host to an infectious disease may be beneficial to the host as hypoferremia (mild iron deficiency) also deprives the pathogens from iron (Stuart-Macadam, 1992; Holland & O'Brien, 1997).

Another cause of iron deficiency is weanling diarrhoea which occurs due to infections when children ingest contaminated water and food after they stopped feeding on sterile breast milk (Facchini *et al.*, 2004). Children have a strong physiological iron requirement as they are still in a growing and developing stage (Facchini *et al.*, 2004). Several studies show that more severe and active lesions are found in subadults with healing increasing and severity decreasing with age, supporting the iron deficiency theory (Fairgrave & Molto, 2000; Salvadei *et al.*, 2001; Kozak & Krenz-Niedbala, 2002; Piontek & Kozlowski, 2002; Facchini *et al.*, 2004; Obertová & Thurzo, 2004; Keenleyside & Panayotova, 2006). Walker *et al.* (2009) argues that iron-deficiency anaemia cannot be the cause of haemopoietic marrow hypertrophy as it will decrease red blood cell production. Haemolytic and megaloblastic anaemia, however, will cause an increase in haemopoietic marrow as the body will try to compensate for the premature destruction of red blood cells (Walker *et al.*, 2009).

Hereditary haemolytic diseases such as thalassemia and sickle cell anaemia have been found to cause PH (Angel, 1966; Hershkovitz *et al.*, 1997). Although the lesions from genetic and acquired anaemia cause a similar response on the cranial vault, the genetic anaemia will also result in changes of the facial and extra-cranial bones (Aufderheide & Rodríguez-Martin, 1998). The distribution of genetic anaemia can be correlated with the geographical distribution of endemic malaria (Keenleyside & Panayotova, 2006).

A multifactorial approach to epidemiological studies of CO and PH has been suggested (Fairgrieve & Molto, 2000; Salvadei *et al.*, 2001). Several different factors can influence the presentation of this pathology with each environment having certain factors that predominate (Fairgrieve & Molto, 2000). Other deficiencies that should be considered together with iron include vitamin B9 (folic acid) and vitamin C deficiency (Fairgrieve & Molto, 2000). A deficiency of any one of these may influence the physiological status of the other two

(Fairgrieve & Molto, 2000). Nutritional megaloblastic anaemia is caused by a deficiency in vitamins B9 and B12 (cobalamin) and will cause hypertrophy of haemopoietic marrow (Walker *et al*., 2009). This type of deficiency can be found in strict vegetarians and can be found together with deficiency in iron and other animal derived nutrients (Walker *et al*., 2009). Wapler *et al*. (2004) found porosities in the orbital roof to be caused by factors not related to diploic hypertrophy. Through histological examination, the authors determined that only 43.5% of CO cases studied showed signs of anaemia (Wapler *et al*., 2004). The cause of CO in the other individuals was attributed to inflammation in the orbit, post-mortem damage and other undetermined factors (Wapler *et al*., 2004).

2.4.3.4 Enamel hypoplasia

When tooth enamel formation is disrupted due to metabolic insult, defects can occur in the tooth enamel structure (White *et al*., 2012). This defect is known EH (White *et al*., 2012). It is observed as horizontal grooves of thinner enamel running circumferentially around the tooth crown (Figure 2.15) (Aufderheide and Rodríguez-Martin, 1998). EH can be interpreted as markers of nutritional stress in a population (Huss-Ashmore *et al*., 1982).

Source: Watts (2012)

Figure 2.15: Linear Enamel Hypoplasia

2.4.3.5 Harris lines

The term HL refers to transverse lines of radiodensity observed in long bones. HL are most commonly observed in the long bones of the lower limbs in young adults (Mays, 1985). It presents bilaterally symmetrically with the tibia being the most commonly affected bone (Hughes *et al*., 1996; Ameen *et al*., 2005). HL results from a slowing down of cell division in cartilage cells in the growth plates during a metabolic insult, while mineralisation still continues (Aufderheide & Rodríguez-Martin, 1998). HL can therefore be used as an indicator of nutritional and general stress in the growth stage of an individual (Huss-Ashmore *et al*., 1982).

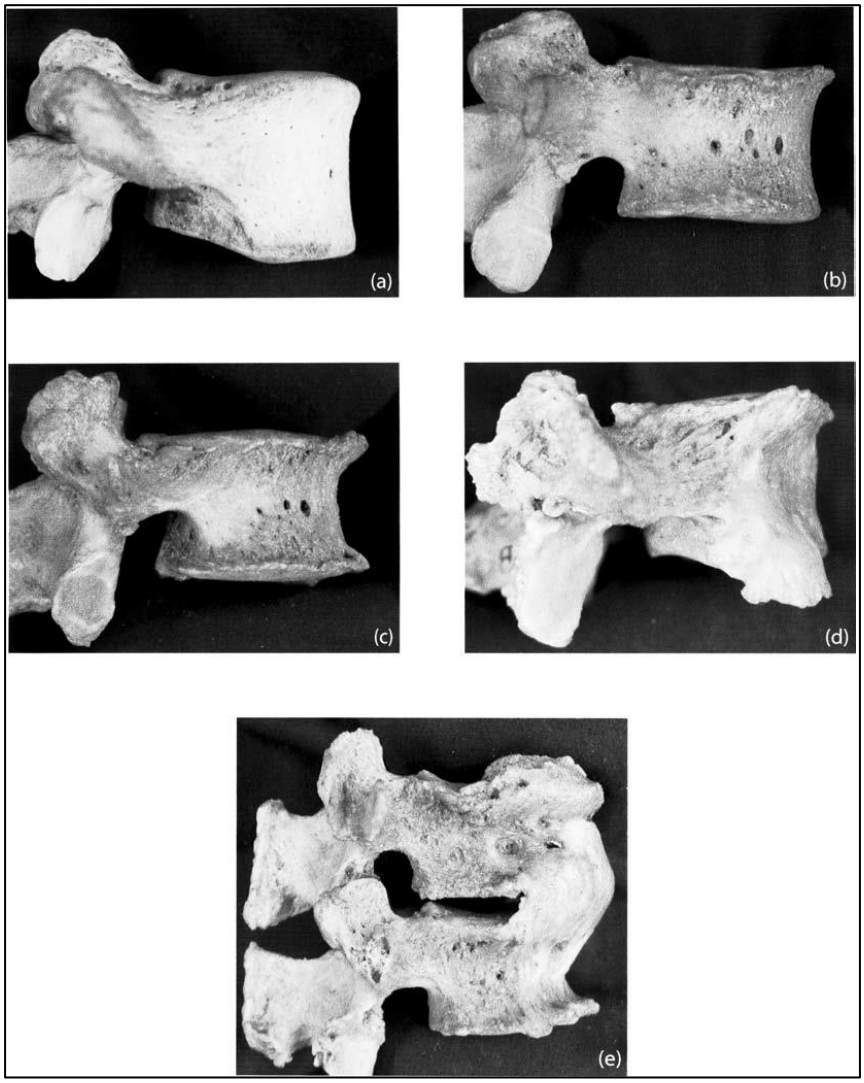
2.4.4 Degenerative bone diseases

Degenerative bone diseases refer to any disease or injury that influences various joints and therefore, articulation in the body. These can include inflammatory diseases, and non-inflammatory disorders. Degenerative diseases can be organized into lesions of abnormal bone formation (e.g. osteophytes) or bone-eroding lesions (e.g. eburnation) (Ortner, 2003; White *et al*., 2012). The most commonly known degenerative disease is degenerative joint disease (DJD), also known as osteoarthritis, and will be discussed in detail below. Other degenerative diseases that will be discussed include diffuse idiopathic skeletal hyperostosis (DISH), ankylosing spondylitis (AS), and rheumatoid arthritis (RA).

2.4.4.1 Degenerative Joint Disease

Degenerative joint disease can also be referred to as osteoarthritis or osteophytosis. On dry bones, this is one of the most common and easily diagnosed diseases (Waldron, 1997; Weiss & Jurmain, 2007). It is a non-inflammatory pathological condition resulting from direct contact between bony surfaces in joints due to the loss of articular cartilage. It can occur as an idiopathic condition or as a result of factors including physical strain, metabolic disorders, infectious agents, genetics, and motion of a joint (Kellgren & Lawrence, 1958; Jurmain, 1977; Knüsel *et al*., 1997; Aufderheide & Rodríguez-Martin, 1998; Derevenski, 2000; Meulenbelt *et al*., 2006; Brown *et al*., 2008). DJD occurs most commonly in large, weight bearing joints. Features that are characteristic of DJD include the loss of joint cartilage, bone formation at the margins of the bone (osteophytes), small cysts with surrounding sclerosis, eburnation, a fibrotic thickened capsule, and Schmorl's nodes (Aufderheide & Rodríguez-Martin, 1998; Weiss & Jurmain, 2007). Radiologically it can be observed as narrowing of the joint space and visible osteophytes (Aufderheide & Rodríguez-Martin, 1998).

The vertebral column is an important area of study for DJD as humans commonly suffer from vertebral osteophytosis and osteoarthritis (Brown *et al*., 2008). Osteophytes on the margins of the vertebra can be a useful indicator of age as the severity of osteophytes increase with age (Snodgrass, 2004). The severity of osteophytosis can be scored according to a five-stage classification system established by Stewart (1958), outlined by Snodgrass (2004), with stages ranging from 0 (indicates no osteophytes) to 4 (indicates maximum lipping) (Figure 2.16).



Source: Snodgrass (2004)

Figure 2.16: Classification stages of osteophyte development.
This image illustrates the stages of osteophyte development. (a**)** Stage 0: no osteophyte formation; (b) Stage 1: Only minor osteophyte formation with vertebral rim beginning to form; (c) Stage 2: More extensive rim formation and larger osteophytes; (d) Stage 3: Large osteophytes which may extend to the centre of the vertebral body or extending to the neighbouring vertebra; and (e) Stage 4: Most severe stage with osteophytes bridged to the adjacent vertebra making contact.

Some studies have suggested that DJD on peripheral sites (e.g. weight bearing joints) can be a good indicator of specific habitual activities such as heavy weight bearing work (Gerszten *et al*., 2001). Eburnation, which is considered an indicator of severe osteoarthritis, is mostly observed in major weight bearing joints supporting the involvement of habitual activities (Weiss & Jurmain, 2007). Most authors, however, agree that the development of DJD is highly age dependent and cannot primarily be attributed to activity and occupation (Lovell, 1994; Knüsel *et al*., 1997; Weiss & Jurmain, 2007; Brown *et al*., 2008).

Schmorl's nodes are the term used to describe small circular indentations in the vertebral bodies observed macroscopically or as small circular radiolucent areas radiologically (Fahey *et al*., 1998). It is caused by protrusion of a herniated intervertebral disk into the vertebral body adjacent to it (Fahey *et al*., 1998). It is not clear why these nodes develop but different theories have been suggested. These include mechanical load, trauma, genetic and developmental defects, pathological infections, and most importantly, degeneration (Fahey *et al*., 1998; Wagner *et al*., 2000; Peng *et al*., 2003; Williams *et al*., 2007). Schmorl's nodes can occur on the superior and inferior aspects of the vertebral bodies and at any vertebral level; however, the lower thoracic vertebrae are affected the most (Fahey *et al*., 1998; Williams *et al*., 2007; Faccia & Williams, 2008). Although mechanical load increases from T1 to L5, the ability of the lumbar vertebrae to resist load is better than that of the thoracic vertebrae due to a larger surface area and less movement (Dar *et al*., 2010).

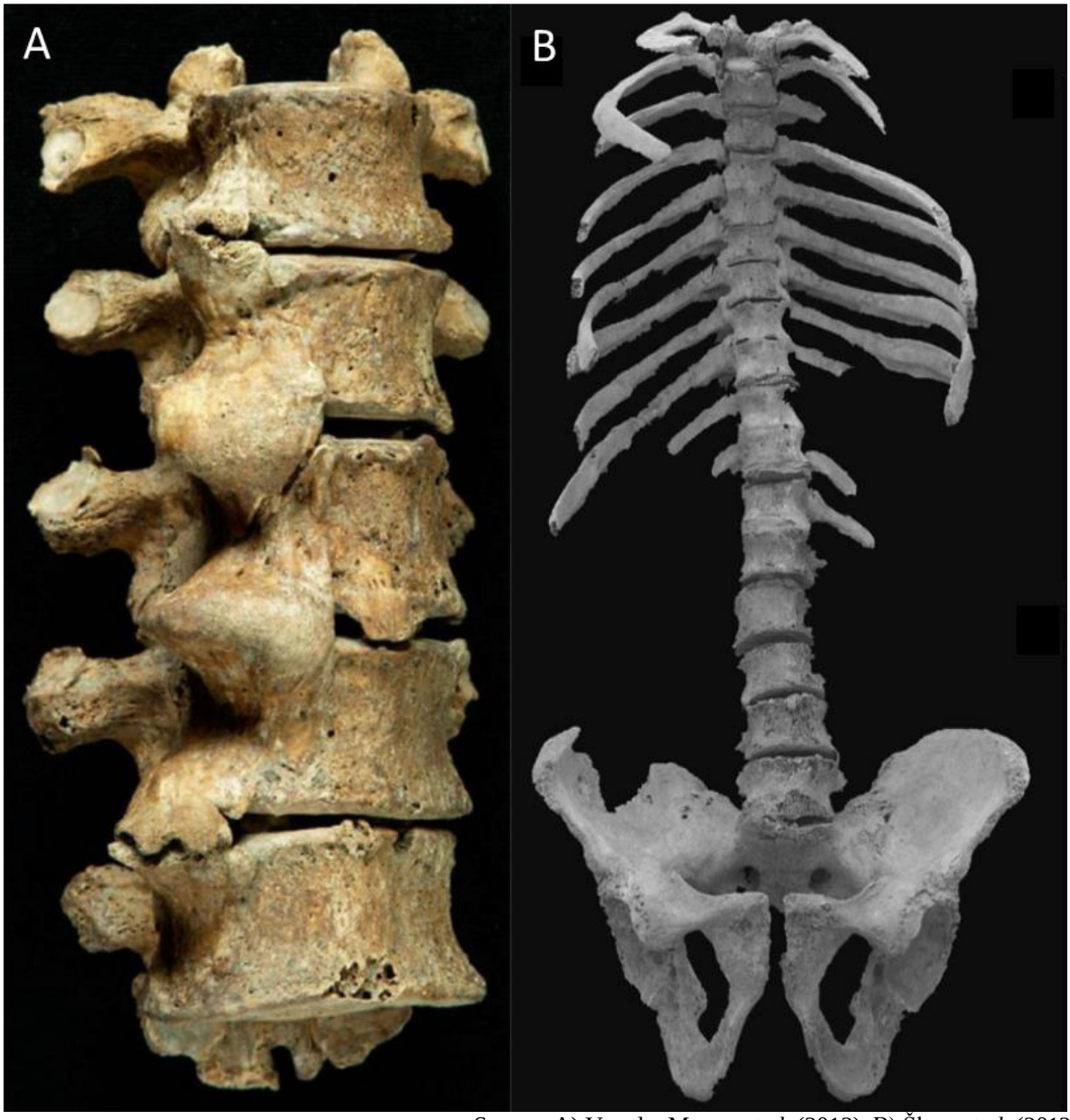
2.4.4.2 Diffuse idiopathic skeletal hyperostosis

Diffuse idiopathic skeletal hyperostosis, also known as Forestier's disease or ankylosing hyperostosis, is a degenerative disorder mostly involving the axial skeleton. It is characterized by calcification of ligaments and soft tissue such as the anterior longitudinal ligament of the vertebral column (Figure 2.17A) (Olivieri *et al*., 2009). The specific cause is unknown and it is mostly observed in older (>50 years of age) male individuals (Cammisa *et al*., 1998; Resnick *et al*., 1978). Three criteria can be used to diagnose DISH: (1) the occurrence of flowing ossification and calcification of the anterior longitudinal ligament on the anterolateral aspect of the vertebral bodies ("candle wax" appearance) for at least four segments; (2) the preservation of the height of the intervertebral disc space in the affected area and a lack of significant degenerative changes of the affected vertebrae; and (3) the lack of sacroiliac joint erosion, bony ankyloses of apophyseal joints, or sclerosis of sacroiliac joints (Resnick *et al*., 1978). Ossification usually occurs on the right side of the thoracic

vertebrae (Kim *et al*., 2012). Characteristics of DISH not involving the vertebral column includes enthesophytes (abnormal bony projections where ligaments and tendons attach to bone) on the ischial tuberosity and iliac wing, calcification and ossification of the iliolumbar ligaments, hyperostosis of the distal clavicle, olecranon and calcaneal spurs, thickening of metacarpals and phalanges of the hand, as well as periarticular osteophytes (Hannallah *et al*., 2007).

2.4.4.3 Ankylosing spondylitis

Ankylosing spondylitis is a chronic inflammatory disorder influencing the synovial joints of the axial skeleton. The aetiology of AS is not well understood. It occurs mostly in young individuals (<30 years of age) with men being more affected than women (Braun & Sieper, 2007). Characteristics of AS include structural changes of the vertebral column such as ossified assymetrical smooth sheets of bone (bamboo spine appearance), bilateral sacrailiitis, osteoporosis, enthesopathic changes on the peripheral skeleton, and increased fracture rates (Braun & Sieper, 2007; Jordana *et al*., 2009) (Figure 2.17B).



Source: A) Van der Merwe *et al*. (2012). B) Šlaus *et al*. (2012)

Figure 2.17: Diffuse idiopathic skeletal hyperostosis and Ankylosing Spondylitis
A) Flowing ossification of the anterior longitudinal ligament on the right anterolateral aspect of the lower thoracic vertebrae. B) Anterior view of fused thoracic vertebrae (T3–T7) and ribs as well as bilateral sacroiliitis.

Differentiating between AS and DISH is sometimes difficult as both are complex diseases involving primarily the axial skeleton, are characterized by ankyloses and bony proliferation, as well as the appendicular skeleton (e.g. the iliac crest, greater trochanter and patella) undergoing enthesopathic changes (Jordana *et al*., 2009). Bilateral sacroiliitis (sacroiliac ankylosis) is a hallmark characteristic of AS which can be used for differential diagnosis (Jordana *et al*., 2009).

2.4.4.4 Rheumatoid arthritis

Rheumatoid arthritis is a chronic inflammatory disorder affecting smaller joints in the body. Although the exact aetiology of this disease is unknown, it is associated with an autoimmune response (Kilgore, 1989). Diagnostic criteria for RA set by Leden *et al*. (2008), as described by Kim *et al*. (2011), include multiple joints affected symmetrically, primarily erosive joint changes and no signs of sacroiliitis or other spondyloarthropathies. Other changes previously considered to be significant to RA include narrowing of joint spaces, hands and feet involvement, and radiological findings (Kilgore, 1989; Rothschild & Woods, 1990; Blondiaux *et al*., 1997; Kim *et al*., 2011). Radiological characteristics that have been observed include marginal and central erosions at joints, subcortical porosities and thinning of the bone cortex (Kilgore, 1989; Blondiaux *et al*., 1997).

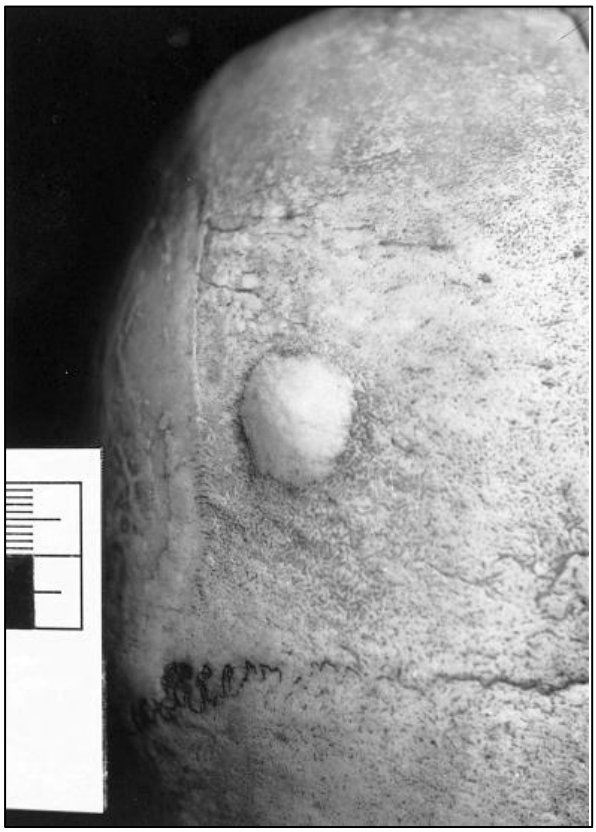
2.4.5 Neoplastic conditions

The term neoplasm is used to define localized areas of growth where cellular proliferation is uncontrolled (Aufderheide & Rodríguez-Martin, 1998; Marks & Hamilton, 2007; White *et al*., 2012). Benign tumours are well differentiated small tissue growths that are unable to destroy the tissue around it or migrate to other parts of the body (Aufderheide & Rodríguez-Martin, 1998; Ortner, 2003; Marks & Hamilton, 2007; White *et al*., 2012). Malignant growths consist of poorly differentiated tissue that has the potential to destroy surrounding cells and migrate to other parts of the body through blood or lymphatic vessels (metastases) (Aufderheide & Rodríguez-Martin, 1998; Ortner, 2003; Marks & Hamilton, 2007; White *et al*., 2012). This genre of neoplasms is more commonly known as cancer (Aufderheide & Rodríguez-Martin, 1998; Marks & Hamilton, 2007; White *et al*., 2012).

Tumours can be classified according to the tissue of origin (White *et al*., 2012). Primary bone tumours originate directly from bone tissue and are observed mostly in young individuals with actively growing bone (Ortner, 2003; White *et al*., 2012). Skeletal tumours arising from other tissue through metastases can be termed metastatic tumours and is more prevalent in older individuals (Ortner, 2003). Identifying a specific type of tumour from the skeletal remains alone is a difficult and, at times, impossible task (Ortner, 2003; Marks & Hamilton, 2007). This is particularly true for metastatic tumours which often presents on bone similarly to and irrespective of the primary tumour site (Marks & Hamilton, 2007). Neoplastic conditions that will be discussed in more detail include button osteoma (BO), enostosis, enchondroma, chondrosarcoma, osteosarcoma and skeletal metastases.

2.4.5.1 Osteoma

A button osteoma is a small circular benign tumour observed mostly on the external surface of the skull or facial bones (Figure 2.18) (Aufderheide & Rodríguez-Martin, 1998). In most cases this tumour is asymptomatic and varies from 1-6 cm in diameter (Cerase & Priolo, 1998). It has been suggested that the tumour can be the result of inflammation, trauma, monostotic fibrous dyplasia, and meningiomas (Perou, 1964 as cited by Eshed *et al.*, 2002). It is also known to be associated with Gardner's syndrome (Cerase & Priolo, 1998). The tumour can either be composed of spongy or compact bone and has a slow growth-rate (De Chalain & Tan, 2003). Radiologically a BO will be observed as a well-defined, radiodense, sclerotic nodule on the external surface of bone (Cerase & Priolo, 1998). It can occur on its own or in groups. Small, circular bone nodules lying close to a large BO can be termed "satellite osteomas" and more than one nodule of the same size are in contact with each other, they are termed "nested" osteomas (Eshed *et al.*, 2002). The term "disseminated" osteoma is used when a large number of lesions observed are spread across the cranial vault (Eshed *et al.*, 2002).

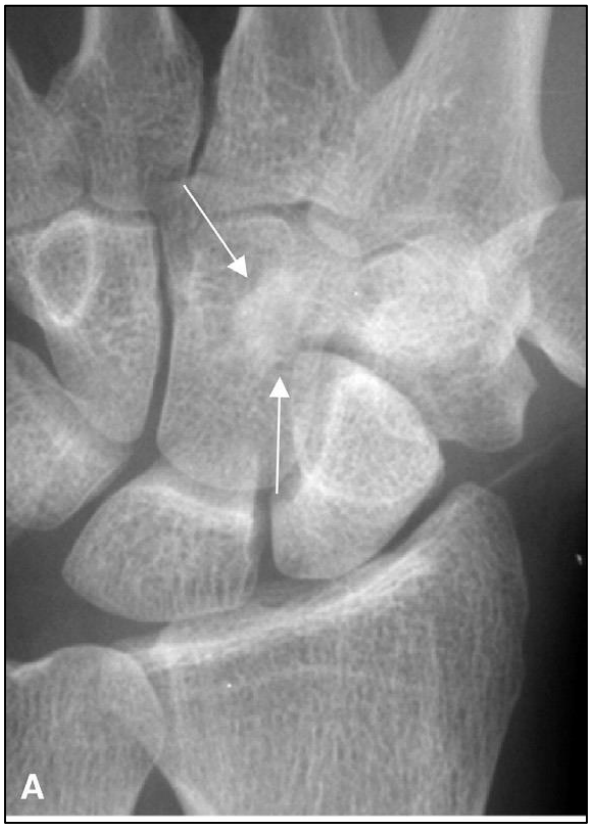


Source: Eshed *et al.* (2002)

Figure 2.18: Button osteoma on cranial vault

2.4.5.2 Enostoses (Bony Island)

Enostoses, also known as bony islands, are relatively common small (1-20 mm) benign lesions (Gould *et al*., 2007). It can occur in any age group and are usually identified incidentally as it is asymptomatic (Cerase & Priolo, 1998). Although it mostly occurs in the vertebral column, ribs, and pelvis, it can be observed in any bone throughout the body (Cerase & Priolo, 1998). Radiologically it is observed as a round or oval sclerotic lesion of increased radiodensity inside cancellous bone (Figure 2.19). It may have spiculated margins as it blends with the cancellous bone surrounding it (Gould *et al*., 2007).



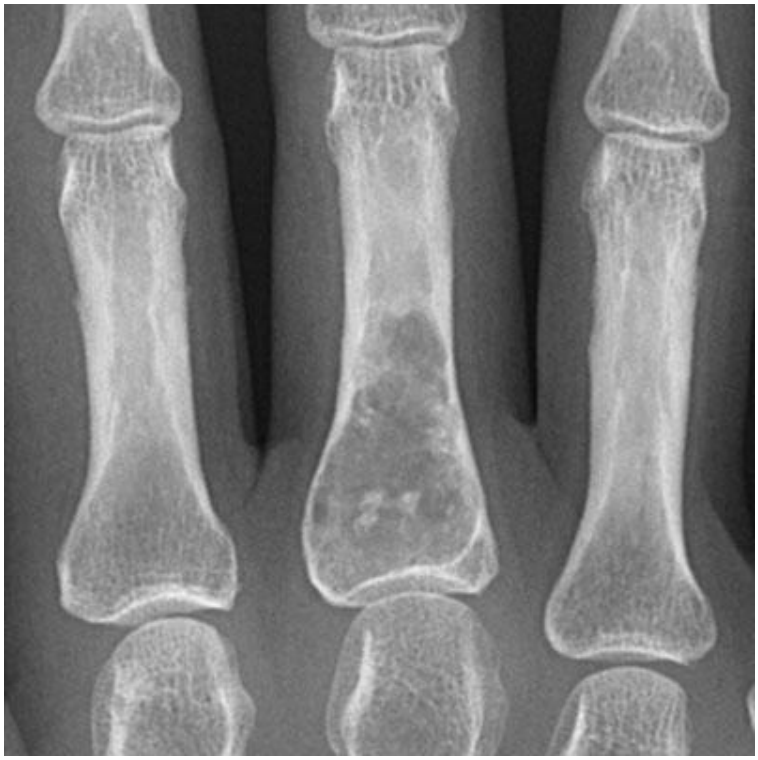
Source: Gould *et al*. (2007)

Figure 2.19: Enostosis (Bony Island)
Anteroposterior radiograph of the wrist. Arrows indicate enostosis (sclerotic lesion) of the capitate bone with a spiculated margin.

2.4.5.3 Enchondroma

Enchondromas are cartilaginous tumours frequently affecting the hands and long bones (Figure 2.20) (Ortner, 2003). According to Shimizu *et al*. (1997), enchondroma is one of the

most common primary benign tumours. It usually develops in individuals younger than 40 years of age; however, it can occur at any age (Kendell *et al*., 2004). In most cases enchondromas are asymptomatic and is only discovered when pathological fractures occur or as an incidental finding (Geirnaerdt *et al*., 1997). Distinguishing between enchondromas and grade 1 chondrosarcoma can be difficult due to overlapping characteristics (Geirnaerdt *et al*., 1997; Kendell *et al*., 2004). Characteristics that may be similar include the location of the neoplasm, minor cortical scalloping, definition of the margin, and the appearance of mineralized matrix (Kendell *et al*., 2004). According to Geirnaerdt *et al*. (1997), enchondromas are more likely to occur in more peripheral bones (e.g. the hands) and are usually small in size but in some cases large enchondromas can be found in the long bones.



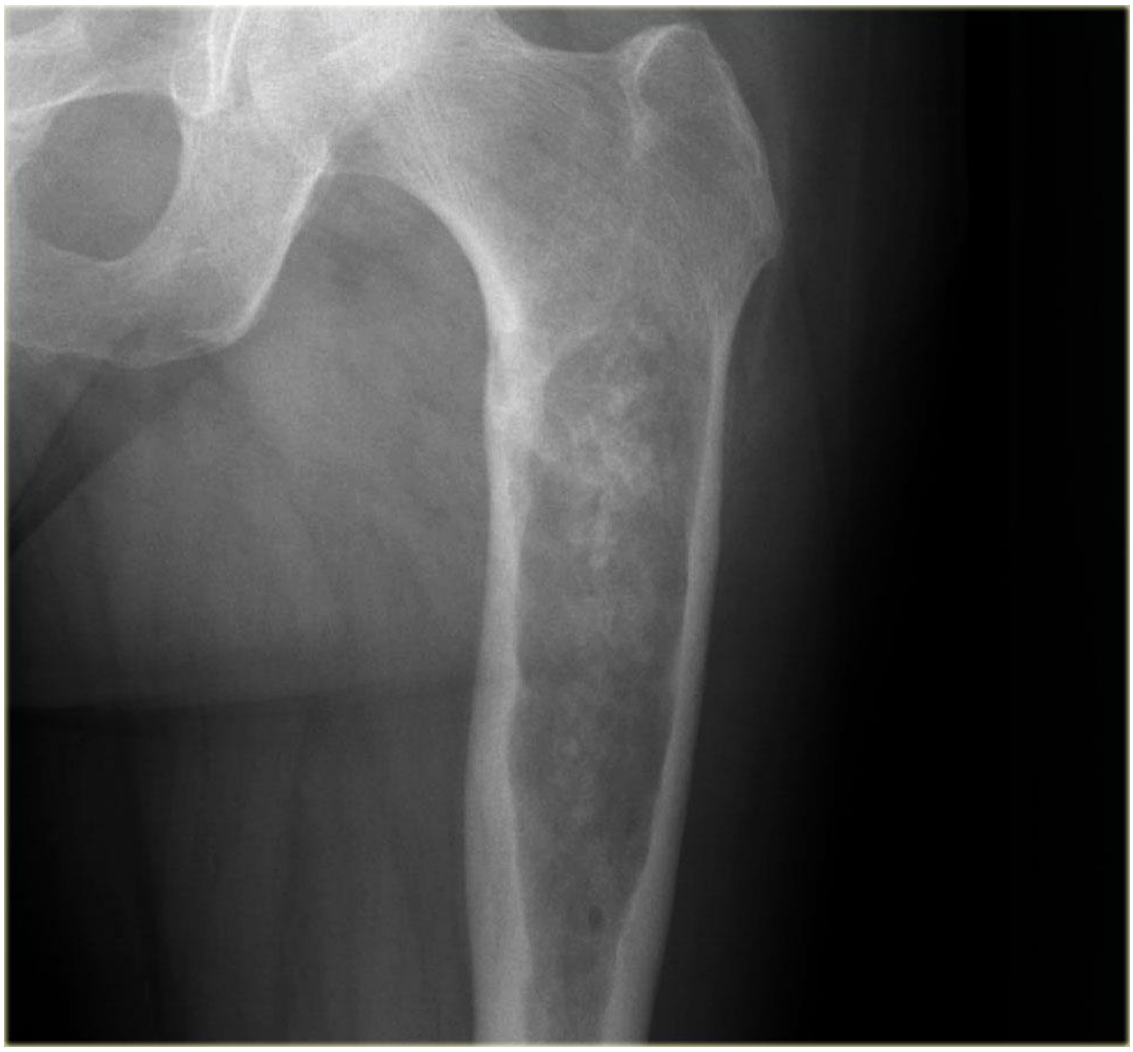
Source: Chew (2015)

Figure 2.20: Enchondroma of the proximal phalanx
Anteroposterior radiograph of a hand showing an enchondroma with lobular morphology of the proximal end of the proximal phalanx of the third digit.

2.4.5.4 Chondrosarcoma

Chondrosarcoma have been reported to occur in between 8.0%-17.0% of all primary bone tumours and is one of the most prevalent malignant tumours (Pring *et al*., 2001).

Characteristics indicative of chondrosarcoma include a larger size (>4cm) relative to benign neoplasms, endosteal scalloping, lobulated contours, cortical remodelling and thickening, and general expansion of bone (Figure 2.21) (Wang *et al*., 2001; Kendell *et al*., 2004). Chondrosarcoma can develop as a malignant tumour from the beginning or can develop secondarily from an enchondroma (Garrison *et al*., 1982; Björnsson *et al*., 1998). Common sites for chondrosarcoma development include the pelvis, humerus and femur while the tibia, fibula, scapula, ribs, and skull may also be affected in some cases (Henderson & Dahlin, 1963; Pritchard *et al*., 1980; Garrison *et al*., 1982; Buirski *et al*., 1986; Healey & Lane, 1986; Nakashima *et al*., 1986; Müller *et al*., 2004).

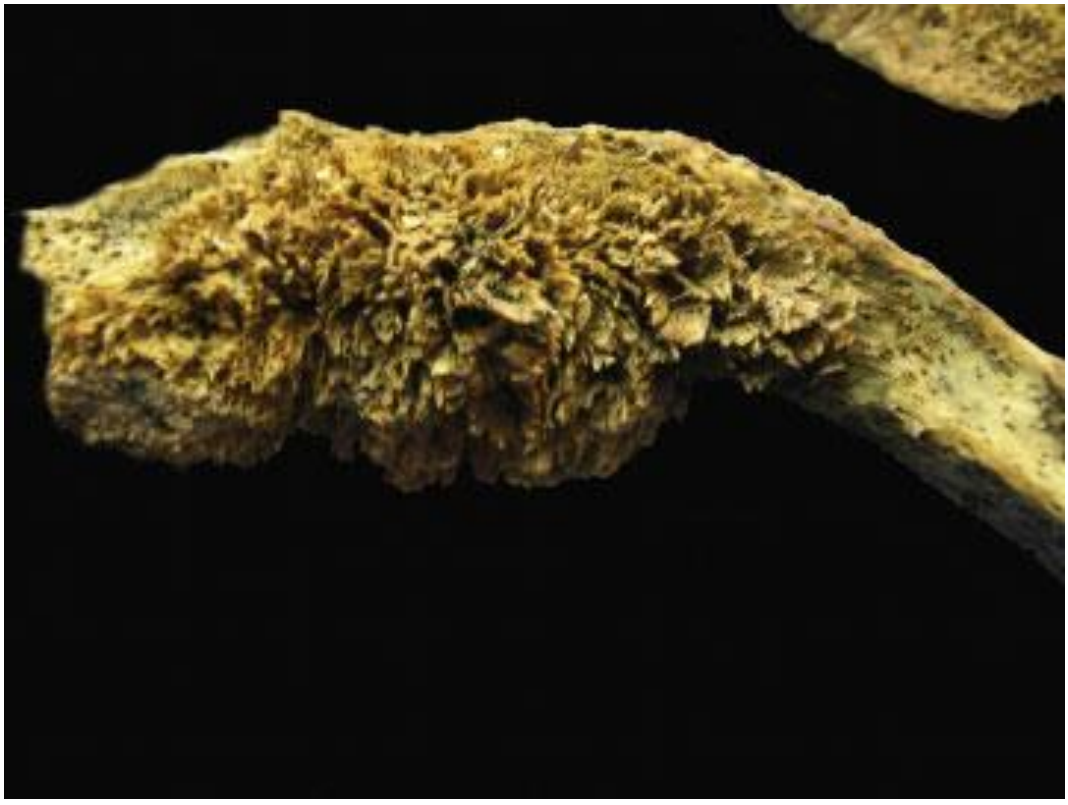


Source: Van der Woude & Smithuis (2016)

Figure 2.21: Chondrosarcoma
Anteroposterior radiograph of the femur. Cortical thickening and expansion can be observed.

2.4.5.5 Osteosarcoma

An osteosarcoma (Figure 2.22) is a malignant tumour observed mostly in the extremities of long bones where tumour cells form osteoid tissue and immature bone directly (Aufderheide & Rodríguez-Martin, 1998). It can also, in certain cases, arise from soft tissue (Picci, 2007). According to Picci (2007), osteosarcoma is the second most common primary malignant neoplasm of the skeleton. It can present as an uncontrolled bone growth with jagged edges (Ortner *et al*., 2012). A characteristic radiological trait of osteosarcoma is Codman's triangle, a subperiosteal triangular area of radiolucency (Aufderheide & Rodríguez-Martin, 1998).



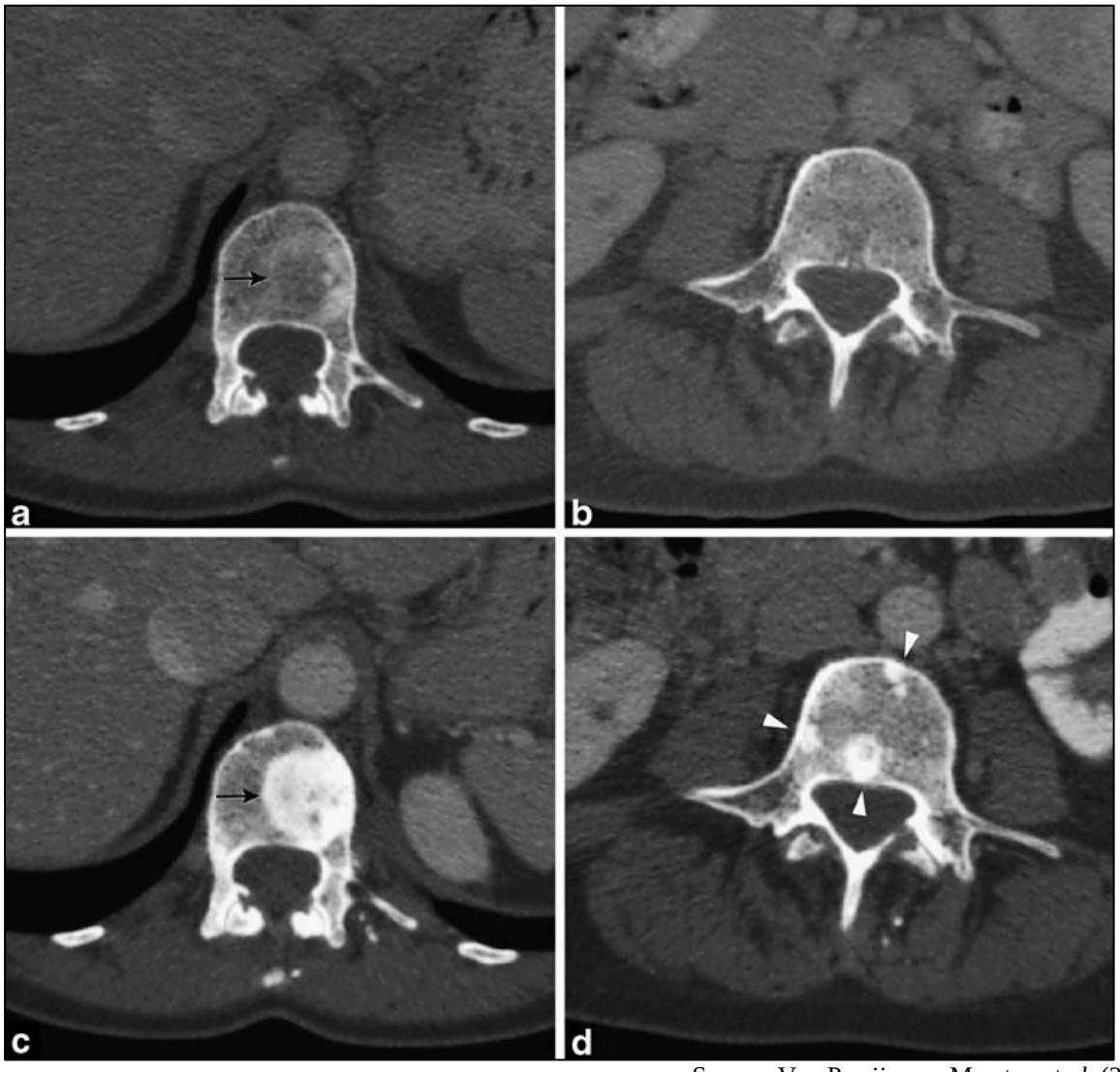
Source: Ortner *et al.* (2012)

Figure 2.22: Osteosarcoma
Digital image of the visceral surface of a left rib 7 showing a sunburst type lesion of osteosarcoma.

2.4.5.6 Secondary skeletal metastases

According to Coleman (2006), the skeleton is the most frequently affected site for metastases from carcinomas. Carcinomas which show the most skeletal metastases at the time of death (±70.0%) include breast and prostate carcinoma. Other carcinomas that also commonly metastasise to the skeleton (30.0%-40.0%) include bronchus, kidney, and thyroid carcinoma.

Carcinomas with the lowest frequency of metastases to the skeleton are those that occur in the gastrointestinal tract (Coleman, 2006). Metastatic lesions in the bone can either be lytic, sclerotic or a combination of these. Lesions usually start as a lytic lesion however, after chemotherapy osteoblasts can proliferate which allow for the formation of sclerotic lesions (Figure 2.23) (Van Persijn van Meerten *et al*., 2010).



Source: Van Persijn van Meerten *et al*. (2010)

Figure 2.23: Skeletal metastases from breast carcinoma
CT images of the vertebral column (50 year old female) with skeletal metastases from breast carcinoma.

a) Thoracic vertebra with lytic metastatic lesion indicated by arrow.
b) Lumbar vertebra without any sign of metastases.
c) Thoracic vertebra after chemotherapy in which the lytic lesion changed into an osteoblastic lesion indicated by the arrow.
d) Lumbar vertebra after chemotherapy in which small sclerotic lesions are observed where small lytic lesions most likely were present but not observed previously.

Haematogenous routes are largely responsible for the distribution of metastases throughout the skeleton. Previous studies suggest that the axial skeleton is the most common site for skeletal metastases as it is rich in red bone marrow (Kim *et al*., 1987; Mundy, 1997; Rybak & Rosenthal, 2001; Coleman, 2006). Batson's vertebral-venous plexus also contributes to the haematogenous route that allows for metastases to the axial skeleton (Rosenthal, 1997; Rybak & Rosenthal, 2001). The ribs and proximal long bones are also well vascularised sites (Mundy, 1997). Other routes by which carcinomas can reach the skeleton include lymphatic extension and direct extension from adjacent soft tissue (Adbul-Karim *et al*., 1990).

2.4.6 Miscellaneous conditions

Diseases which cannot easily be classified into any of the other categories are referred to as miscellaneous conditions. These diseases may have a complex nature and a poorly understood aetiology and pathogenesis (Ortner, 2003). Only one disease included in this category will be discussed, namely Paget's disease.

2.4.6.1 Paget's disease

Paget's disease is characterized by disruption of the mechanisms for normal bone turnover causing excessive remodelling (Delmas & Meunier, 1997; Ortner, 2003; Cundy & Reid, 2011). An increase in bone resorption will take place followed by an increase in bone formation (Aufderheide & Rodríguez-Martin, 1998; Ortner, 2003). A disorganized arrangement of woven and lamellar bone and an overall increase in bone size will result from the abnormal remodelling (Delmas & Meunier, 1997; Rogers *et al*., 2002; Ortner, 2003). Radiologically two phases of Paget's disease can be observed. The lytic phase appears first and presents as a localized region of radiolucency visible on a radiograph due to increased resorption (Aufderheide & Rodríguez-Martin, 1998). The sclerotic phase is observed as an increased radio-dense area due to new bone formation (Aufderheide & Rodríguez-Martin, 1998). Between these two phases a mixed appearance of sclerotic and lytic bone lesions can be observed (Delmas & Meunier, 1997; Aufderheide & Rodríguez-Martin, 1998; Cundy & Reid, 2011). Radiological criteria for the diagnosis of Paget's disease, as described by Eekhoff *et al*. (2004), includes an increase in the size of bones, areas of increased radiodensity, disorganized architecture of new bone, enhanced pattern of trabeculae, cortical thickening, and iliopectineal thickening in the pelvis. Histologically a mosaic pattern can be observed which is pathognomonic to Paget's disease (Aufderheide & Rodríguez-Martin, 1998; Rogers *et al*., 2002; Ortner, 2003; Roodman & Windle, 2005).

Paget's disease occurs more in older individuals (>60 years) and is more prevalent in males than in females (Cooper *et al*., 1999; Altman *et al*., 2000; Ortner, 2003; Cundy & Reid, 2011). The skull is commonly affected; however, the facial bones are usually not involved as severely (Aufderheide & Rodríguez-Martin, 1998). Other bones affected by Paget's disease include the pelvis, femur, tibia, clavicle, sternum, lumbar vertebral column, sacrum and ribs (Aufderheide & Rodríguez-Martin, 1998; Ortner, 2003)

Chapter 3 AIM & OBJECTIVES

3.1 PROBLEM STATEMENT

From reviewing the literature, it is clear that many different factors can influence the presentation and prevalence of different diseases and it can be difficult to determine the exact causes of certain responses in the skeleton. With some skeletal lesions (e.g. CO or PH) there are different theories as to what causes it and with some lesion (e.g. osteophytes) there are many known factors that can on its own or in combination with others, cause a response on the skeleton. Examining diseases from different population groups with different lifestyles could improve the understanding of the factors influencing diseases. Previous literature shows that the Kirsten Skeletal Collection is representative of the three main population groups in the Western Cape (black, mixed, white) with the mixed population group being unique. To the author's best knowledge, no in depth research has been done using a combination of three different methods (macroscopic, microscopic, and full body x-rays) to evaluate the general presentation of diseases in a skeletal collection representative of a low socio-economic population of the Western Cape.

3.2 AIM

The aim of this research is to describe and evaluate the presentation of diseases and metabolic disorders in the Kirsten Skeletal Collection at Stellenbosch University.

3.3 OBJECTIVES

The objectives for the current study are:

- To examine, describe and record the presentation of disease and metabolic disorders using the macroscopic morphological appearance of pathology as it manifests in the skeleton;
- To use histological and microscopic techniques to study the skeletal material where disease and metabolic disorders are observed to determine the extent to which bony components are involved and establish a more accurate diagnosis;
- To use radiological analysis of the skeletal material to identify disease and metabolic disorders not visible through macroscopic morphological analysis of the skeletal material; and,
- To combine the results of all three methods above and use statistical methods to get a detailed and accurate description of the presentation and distribution of disease and

metabolic disorders among different sexes, age groups, and population groups in the skeletal material from the Kirsten Skeletal Collection and compare it to other studies.

Chapter 4 MATERIALS AND METHODS

4.1 SKELETAL MATERIALS

Information regarding the demographics of the Kirsten Skeletal Collection was discussed in the literature review (see section 2.1). A total of 300 individuals in the Kirsten Skeletal Collection, at Stellenbosch University, were studied (Appendix A). All skeletons were received into the collection between the years 1967 and 2000. Skeletons were chosen according to completeness. The complete skeletons were included first, followed by skeletons with only one bone missing, continuing this sequence till 300 skeletons were included. Damaged bones was not regarded as a missing bone while selecting the skeletons, however, they were excluded from statistical analysis if the damage was too severe to observe disease. The distribution of age, sex and population groups of the skeletons studied is indicated in Table 4.1. Table 4.2 indicates the age and sex distribution within each population group. The age of the skeletons ranged from 15 to 82 years with the mean age of the population studied being 48.5 years. The mean age at death for each sex and population group is indicated in Table 4.3. According to the National Health Act (Act 61 of 2003) (Republic of South Africa, 2004), human tissue received by an academic institution may be used for research purposes. Ethical clearance for the study was granted by the ethics committee at Stellenbosch University on 26 June 2013 with protocol number S13/05/100.

Table 4.1: Distribution of skeletons among age, sex, and population groups

	Group	Number of skeletons
Age:	<31	31
	31-45	100
	46-60	110
	>60	59
Sex	Male	202
	Female	98
Population	Black	47
	Mixed	209
	White	43
	Indian	1

Table 4.2: Age and sex distribution of skeletons within each population group

		Number of skeletons		
	Group	Black	Mixed	White
Age:	<31	6	25	0
	31-45	16	78	5
	46-60	19	76	15
	>60	6	30	23
Sex	M	39	138	24
	F	8	71	19

Table 4.3: Mean age at death (years)

	Black	Mixed	White	Total
Males	48.5	48.9	57.2	49.8
Females	37.9	42.8	63.1	46.3
Combined	46.7	46.8	59.8	48.5

A list of all consumables, equipment, software packages and research facilities used in the present study are given in Appendix B.

4.2 METHODS

4.2.1 Macroscopic analysis

Macroscopic analysis was done under light and low magnification using a magnifying lamp (Magnification: 3x. 5x, 8x). All skeletal elements present were examined for features corresponding with diseases or congenital malformations. A table (Appendix C) was used to mark a disease or feature as present or absent in each skeleton. A grading score (discussed separately for each feature in section 4.2.2) was also indicated in the table for features that could be graded. The age, sex, and population origin of each skeleton were indicated in the table.

For each skeleton examined, a booklet was constructed to include detailed information on that skeleton (Appendix D). Each booklet included general information about the skeleton, a complete skeletal inventory, and diagrams of the teeth, skull, vertebral column, ribs and the anterior and posterior aspect of the entire skeleton. Also included was a table in which diseases were indicated for each skeletal element.

4.2.2 Diagnosis and grading of diseases or features of diseases

Different skeletal changes or markings were observed for the different diseases. This section discusses the different markings or changes on skeletal material that was used to identify different diseases or features of diseases and how some features were graded according to type or severity. In cases where pathology was difficult to diagnose, second or third opinions were gained from other physical anthropological researchers.

4.2.2.1 Lumbosacral transitional vertebrae

Lumbosacral transitional vertebrae were observed as either sacralisation or lumbarisation. It was classified as sacralisation if the fifth lumbar vertebra (L5) incompletely or completely became part of the sacrum and lumbarisation if the first sacral segment (S1) incompletely fused or separated from the sacrum. Lumbosacral transitional vertebrae were further

classified according to the classification system described by Konin & Waltz (2010) adapted from Castellvi *et al*. (1984) (see Figure 2.7). The presence as well as the type of lumbosacral transitional vertebrae was documented for each skeleton with the lower lumbar vertebrae and sacrum present.

4.2.2.2 Spina Bifida

Spina bifida was observed as an opening at the midline of the posterior neural arch of a vertebra where it failed to fuse (Groza *et al*., 2012). Each vertebra with spina bifida was documented. Spina bifida was only marked as present on the sacrum if the posterior neural arches of S1, S2 and S3 or more than one of these were open (Boone *et al*., 1985; Fidas *et al*., 1987; Schweitzer *et al*., 1993). An open posterior neural arch of S4 and S5 was observed as normal variation.

4.2.2.3 Scoliosis and kyphosis

Vertebral columns were viewed from anterior in order to observe any lateral curvature of the vertebral column. Kyphosis was observed by viewing the vertebral column from the lateral side in order to identify a spinal curvature greater than natural kyphosis observed in the thoracic spine (see section 2.4.1.4). The presence/absence of scoliosis and kyphosis were documented for each vertebral column.

4.2.2.4 Spondylolysis

Spondylolysis was diagnosed if a cleft existed in the vertebral arch at the *pars interarticularis*, unilaterally or bilaterally (Mays, 2006). In bilateral spondylolysis, the affected vertebra was divided into two segments articulating with each other.

4.2.2.5. Periostitis

Each bone with periostitis was documented and the affected region indicated on a diagram. The severity of periostitis was graded according to scoring adapted from Friedling (2007):

0 = no periostitis
1 = mild periostitis (porosity and striation of bone surface)
2 = severe periostitis (multiple layers of new bone and proliferation of the periosteal surface)

4.2.2.6 Visceral rib lesions

Visceral rib lesions formed part of the data for periostitis but was examined in more detail. The affected area of the rib was illustrated on a diagram of left and right ribs. In order to determine the part of the thoracic cavity most affected by rib lesions, ribs were divided into three groups, apical ribs (ribs 1-3), middle ribs (ribs 4-8), and basal ribs (ribs 9-12) for both the left and right side. To determine the area on the rib which was most commonly affected, each rib was divided into three regions, vertebral region (posterior third of rib), middle region (middle third of rib), and sternal region (anterior third of rib).

4.2.2.7 Pott's disease

If two or more of the characteristics described by Mays *et al*. (2001b) (see section 2.4.2.2) were present on a vertebrae, it was diagnosed as possible Pott's disease. Vertebrae with possible Pott's disease were documented.

4.2.2.8 Osteomalacia

If two or more features of osteomalacia described by Brickley *et al*. (2005) (see section 2.4.3.1) occurred in a skeleton, a histological section was made from the proximal femur and examined under a polarizing light microscope. Lodox® Scans were also examined to identify possible micro-fractures (Looser's zones) on the scapulae or os coxae. If microscopic characteristics of osteomalacia, as described by Brickley *et al*. (2007), or Looser's zones were present together with macroscopic features, a diagnosis of possible osteomalacia was made..

4.2.2.9 Porotic hyperostosis/cribra orbitalia

Porotic hyperostosis was observed as porosity on the external cranial vault and CO as porosity in the orbital roof (Facchini *et al*., 2004; Walker *et al*., 2009). Porotic hyperostosis and CO were indicated on diagrams of the skull. A grading system outlined by Buikstra and Ubelaker (1994), which was adapted from Stuart-Macadam (1985), was used to grade PH and CO. The grades were as follows:

1 = scattered fine foramina
2 = isolated small and large foramina
3 = some linked foramina forming trabecular structure with no thickening visible
4 = linked foramina forming trabecular structure with outgrowth from the normal bone surface.

Porotic hyperostosis on the cranium was graded separately for each bone for both left and right sides. Cribra orbitalia was graded separately for each orbit.

4.2.2.10 Enamel hypoplasia

Teeth inspected for EH included the incisors and canines. Enamel hypoplasia was marked as present if at least one defect in the tooth enamel (presenting as a horizontal groove) was visible (Aufderheide & Rodríguez-Martin, 1998). The defect was indicated on a diagram of the teeth. In the present study population, a large number of skeletons lacked the necessary teeth needed for examination and was, therefore, excluded from analysis of EH.

4.2.2.11 Harris lines

Harris lines were examined radiologically on the tibiae, fibulae, femora, radii, ulnae, and humerii. A diagnosis of HL was only made of it occurred bilaterally and symmetrically.

4.2.2.12 Vertebral compression

Vertebral compression was graded according to Genant's semi-quantitative scoring method (Genant *et al*., 1993) as described by Curate *et al*. (2014) (see Figure 2.12).

The scoring was as follows (Curate *et al*., 2014):

0 = no reduction
1 = mild reduction (20-35% decrease in vertebral height)
2 = moderate reduction (25-40% decrease in vertebral height)
3 = severe reduction (>40% decrease in vertebral height)

Each vertebra was graded separately. For statistical analysis, vertebrae were divided into groups of three (in order to reduce the number of comparisons needed) with each group graded according to the most compressed vertebra in that group.

4.2.2.13 Vertebral osteophytes

Vertebral osteophytes were graded using a 5-stage method as described by Snodgrass (2004) (see Figure 2.16). The stages of osteophyte development are as follows:

0 = no osteophytes
1 = minor osteophytes with vertebral rim starting to form

2 = larger osteophytes with more extensive rim
3 = large osteophytes extending to the centre of the vertebral body or to the neighbouring vertebrae
4 = Osteophytes bridge to make contact with the adjacent vertebra

Each vertebra was graded separately. For statistical analysis vertebrae were divided into groups of three (in order to reduce the number of comparisons needed) with each group graded according to the vertebra with the most severe osteophytes in that group.

4.2.2.14 Peripheral osteophytes and eburnation

Peripheral DJD was graded using a scoring system described by Friedling (2007) to grade osteophytes and eburnation. The grading was as follows:

0 = no osteophytes
1 = slight lipping
2 = marked lipping
3 = eburnation

Each bone was graded separately and the distribution of osteophytes illustrated on a diagram of the skeleton.

4.2.2.15 Schmorl's nodes

Schmorl's nodes (see section 2.4.4.1) were identified for each vertebra separately. For statistical analysis vertebrae were divided into groups of three (in order to reduce the number of comparisons needed) with the number of vertebrae with Schmorl's nodes in a group indicated for each group.

4.2.2.16 Diffuse Idiopathic Skeletal Hyperostosis

Criteria described by Resnick *et al*. (1978) were used to identify DISH (see section 2.4.4.2). If two or more of the criteria were met, it was diagnosed as possible DISH and the vertebrae affected were indicated on a diagram of the vertebral column.

4.2.2.17 Ankylosing spondylitis

Criteria used for the identification of AS included smooth asymmetrical ossification along the vertebral column (bamboo appearance/bamboo spine), bilateral sacroiliitis, osteoporosis, and

enthesopathic changes on the peripheral skeleton (Braun & Sieper, 2007; Jordana *et al*., 2009). If two or more of these characteristics were present, it was considered as possible AS.

4.2.2.18 Rheumatoid arthritis

Diagnostic criteria of RA described in section 2.4.4.4 were used. If these features were present bilaterally, it was diagnosed as possible RA.

4.2.2.19 Reiter's syndrome (reactive arthritis)

Reiter's syndrome is characterized by asymmetrical patches of ligament ossification along the vertebral column. Asymmetrical sacroiliitis (even if bilateral) and degenerative changes in a large joint (e.g. knee) unilaterally was considered as suggestive of Reiter's syndrome (Fox *et al*., 1979; Winchester *et al*., 1987). If two or more of these characteristics were present, a diagnosis of possible Reiter's syndrome was made.

4.2.2.20 Primary benign neoplasms

Primary benign neoplasms are small well-defined tumours in bone. Most of the diagnosis of primary benign neoplasms was made radiologically with the help of a musculoskeletal radiologist, Dr Wagener. Characteristics used for diagnosis of different primary benign neoplasm (BO, enostoses, enchondroma) are described in sections 2.4.5.1-2.4.5.3. Bones affected by the neoplasms were noted and illustrated on a diagram.

4.2.2.21 Primary malignant neoplasms

Primary malignant neoplasms are proliferative bone tumours without well-defined borders. Characteristics used for diagnosis of different primary malignant neoplasms (osteosarcomas, chondrosarcomas) are described in sections 2.4.5.4-2.4.5.5. The bones affected by the neoplasms were noted and illustrated on a diagram.

4.2.2.22 Skeletal metastases

Feature of secondary skeletal metastases are described in section 2.4.5.6. If these features were observed in skeletons with a documented COD of carcinoma, it was diagnosed as possible skeletal metastases. All bones with lesions were indicated on a diagram of the skeleton.

4.2.2.23 Paget's disease

Macroscopic, radiological, and histological characteristics of Paget's disease are described in section 2.4.6.1. If macroscopic or radiological characteristics were present on a bone, a dry bone histological section was made of that bone. If histological examination illustrated characteristics of Paget's disease as well, a diagnosis of Paget's disease was made and the affected bones documented.

4.2.3 Histology

Histology was done for skeletons where signs of possible osteomalacia or Paget's disease were present in order to improve differential diagnosis and describe the effects of these diseases on the bone. The bones of the Kirsten Skeletal Collection are mostly non-fragile dry bone and therefore no embedding was needed when preparing the sample. The manual preparation of undecalcified bone for histology was developed by Frost (1958) and was refined by Maat *et al*. (2001).

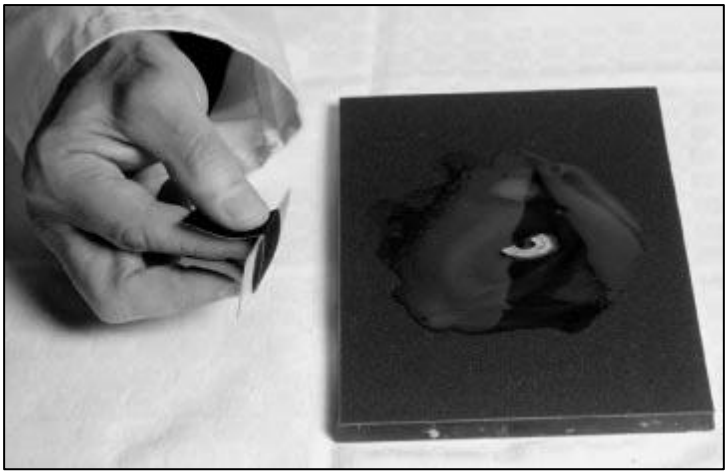
The technique was used as follows (Adapted from Maat *et al*., 2001):

1. A sheet of waterproof abrasive paper (Grit p220) was cut into halves and placed on a glass slab greased with petroleum jelly with the abrasive side facing up. This served as a grinding platform.

2. A piece of masking tape was placed over the area on the bone where the section was to be taken in order to minimize damage to the bone. The bones were cut with a hand hacksaw by means of two parallel cuts, ± 2-3 mm thick slice, and removed with a small chisel.

3. The central area of the abrasive paper was moistened with tap water. The section was grinded on both sides by hand with a rotating motion until it was smooth.

4. Using Frost's device (glass slide folded in a slip of abrasive paper), grinding continued by applying light to medium pressure onto the section during the rotating motion (Figure 4.1). Grinding with Frost's device was started in the central area of the sheet of abrasive paper, where it is less rough due to step 3, working gradually to the periphery.



Source: Maat *et al.* (2001)

Figure 4.1: Frost's gripping device
The image illustrates the use of Frost's gripping device to which the bone will stick during a rotation motion.

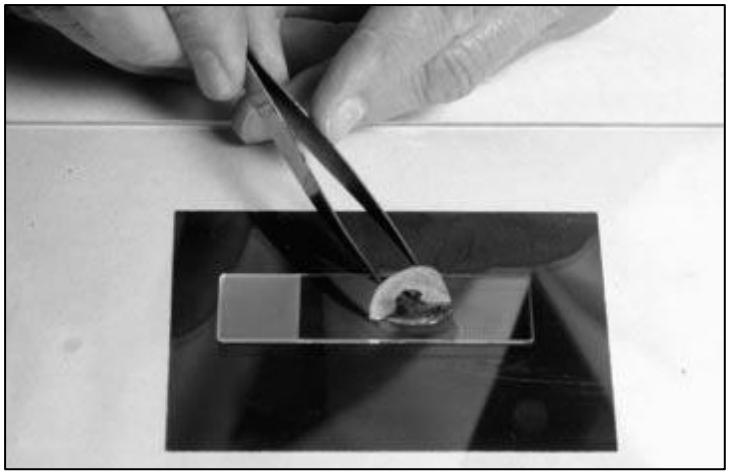
5. The section was grinded on both sides until it became flexible. Grinding was then continued using a medium coarse abrasive paper (Grit p800) until the section becomes opaque.

6. Tap water and less coarse abrasive paper (P1200A) was used to polish the section by grinding the section with the index and middle finger without applying pressure until it was transparent.

7. The section was kept wet to prevent it from curling and cleaned by submerging it in distilled water.

8. The cleaned section was lifted out of the water using a soft brush and placed onto a piece of filter paper in a Petri dish to dry.

9. A clean microscope slide was placed on a clean surface. Mounting medium was placed on the centre of the slide, and the dry section placed on it with a pair of pointed tweezers (Figure 4.2). More mounting medium was then immediately added. A cover slip was and placed over the immersed section.



Source: Maat *et al.* (2001)

Figure 4.2: Placing the finished section on a slide.
The section is positioned using tweezers.

For possible osteomalacia cases dry bone cross sections were taken from the medial proximal femur shaft. For possible Paget's disease the sections were taken from the affected skeletal element. All crania were previously separated in the transverse plane for the removal of the brain. Sections for histology were taken perpendicular to the existing transverse cut. Sections taken for the os coxae were cut perpendicular to the inferior border of the greater sciatic notch. Histological sections were examined by the author with the help of a histologist (Ms Mandi Alblas) for lesions and changes particular to each of the diseases under a light microscope with phase and POL contrast. Microphotographs were taken for each section.

4.2.4 Radiology

Skeletal material was transported to the Western Cape Forensic Pathology Service medico-legal mortuary at Tygerberg Hospital, Cape Town where the Lodox® Statscan® imaging system is situated. Software used to create DICOM® format images and enhance image processing, were DVS® version 2.8, and lucid™. The software used to observe and access DICOM® files was ImageJ® 1.46r. Skeletons were placed in anatomical position on the table surface and a full body x-ray completed. The Lodox® Statscan® imaging system is more cost-effective and less hazardous than conventional x-rays and can do a full body scan in 13 seconds, which made it a good system to use for the purpose of this project. Lodox® Statscan® images were analysed with the help of Prof Pitcher and a musculoskeletal radiologist, Dr Wagener from the Division of Radiodiagnosis (Department of Medical Imaging and Clinical Oncology, Faculty of Medicine and Health Sciences, Stellenbosch University). The features used to identify pathology and neoplasms are established

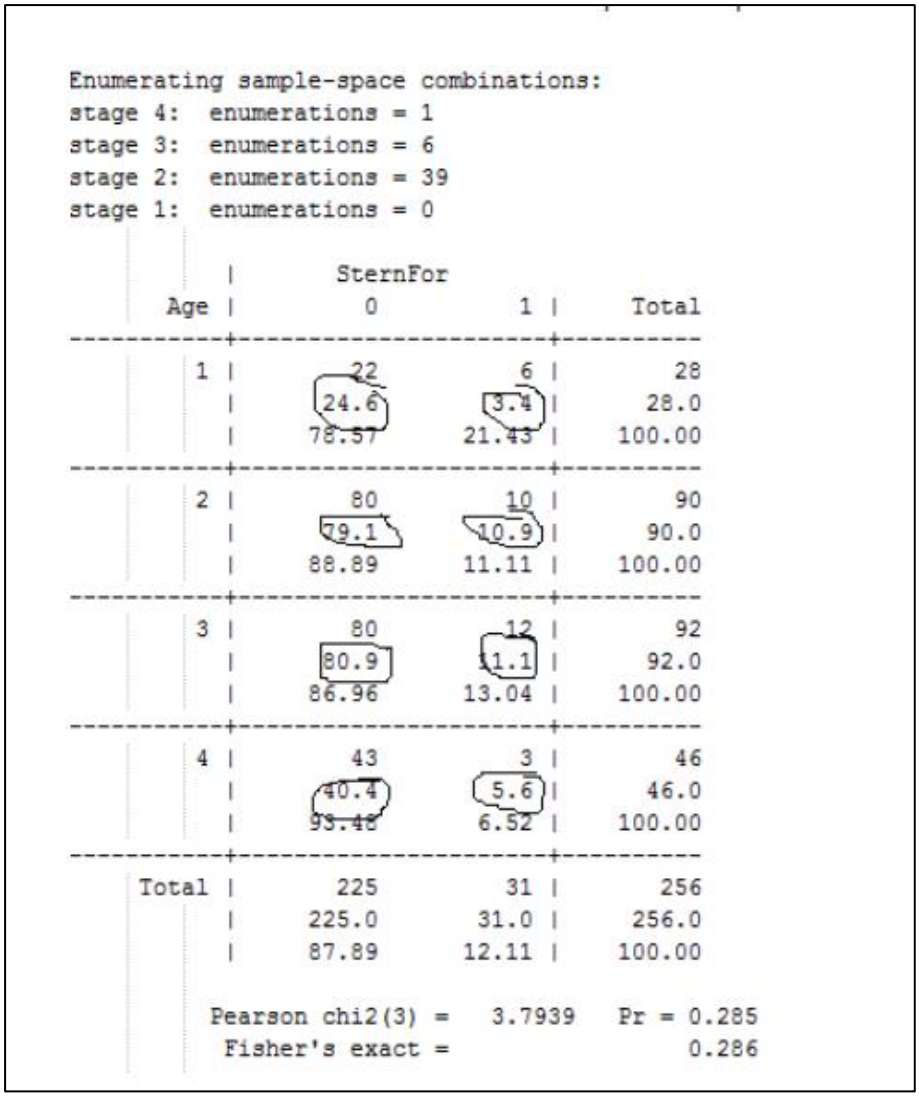
characteristics unchanged by presence or absence of soft tissue. Radiological diagnoses were also correlated with macroscopic and histological findings to ensure accurate diagnosis.

4.2.5 Data analysis

Some diseases have been shown to differ between sexes, population groups, or age groups. Therefore, the present study included comparisons for sex, population and age groups to determine if statistical differences exist between groups for each disease. The present study sample had a male (n=202) to female (n=98) ratio of approximately 2:1. Four population groups were documented in the study sample, black (n=47), mixed (n=209), white (n=43) and Indian (n=1). As only one skeleton was classified as Indian, this skeleton was excluded for comparison between population groups. Skeletons were divided into four different age groups; <31 (n=31), 31-45 (n=100), 46-60 (n=110) and >60 (n=59). The age intervals were chosen to extend across a period of 15 years each with a minimum of 30 skeletons per group. For certain diseases, different bones were compared with each other. These bones differed for each disease and will be described in more detail.

Statistical analysis was performed by a statistician from the biostatistics unit, Faculty of Medicine and Health Sciences, Stellenbosch University. Data were analysed using STATA® statistical software version 13.0 SE (StataCorp®, College Station, TX). Chi-squared tests for independence and Fisher's exact test was used to explore associations between categorical variables. Statistical significance for association between variables was assessed using 5 percent level of significance (i.e. $p<0.05$).

Two p-values were obtained for each comparison: one for the Chi-squared test and one for the Fisher's exact test. For each table if less than 20.0% of expected frequencies were less than 5, then p-value from the chi-squared test was used and if not, then the Fisher's exact p-value was used. Figure 4.3 illustrates the expected frequencies in an example table. In this example only 12.5% of the expected frequencies are less than five and therefore the p-value of the chi squared test would be used. If the relevant p-value was $p<0.05$, then the association was considered statistically significant.



```
Enumerating sample-space combinations:
stage 4:  enumerations = 1
stage 3:  enumerations = 6
stage 2:  enumerations = 39
stage 1:  enumerations = 0

           |       SternFor
       Age |         0          1 |     Total
-----------+----------------------+----------
         1 |        22          6 |        28
           |      24.6        3.4 |      28.0
           |     78.57      21.43 |    100.00
-----------+----------------------+----------
         2 |        80         10 |        90
           |      79.1       10.9 |      90.0
           |     88.89      11.11 |    100.00
-----------+----------------------+----------
         3 |        80         12 |        92
           |      80.9       11.1 |      92.0
           |     86.96      13.04 |    100.00
-----------+----------------------+----------
         4 |        43          3 |        46
           |      40.4        5.6 |      46.0
           |     93.48       6.52 |    100.00
-----------+----------------------+----------
     Total |       225         31 |       256
           |     225.0       31.0 |     256.0
           |     87.89      12.11 |    100.00

      Pearson chi2(3) =   3.7939   Pr = 0.285
       Fisher's exact =                 0.286
```

Figure 4.3: Statistical results table
Circles indicate the expected frequencies.

Statistical analysis was performed on nine separate Excel® data sheets. These are described in the following sections.

4.2.5.1 Ungraded Skeletal groups

The disease columns in this Excel® sheet included sacralisation, lumbarisation, spina bifida, scoliosis, kyphosis, spondylolysis, periostitis, VRL, PH, CO, EH, HL, osteoporosis, vertebral osteophytes, peripheral osteophytes, Schmorl's nodes, DISH, benign neoplasms, primary malignant neoplasms, and secondary skeletal metastases. All disease columns consisted of the numbers 0 and 1 (0 = disease absent, 1 = disease present). The percentage of skeletons with the disease was determined for each disease column. Data points that were missing were excluded from the calculation.

In the “age” column, age groups 1, 2, 3 and 4 (1 = <31 years, 2 = 31-45 years, 3 = 46-60 years, 4 = >60 years) was compared with each other for each disease column in order to determine how much a disease occurred for the different age groups and if there was a statistical significant difference between the groups. If the age of a skeleton was unavailable, that skeleton was excluded from the comparison.

In the “sex” column, sex groups 1 and 2 (1 = Male, 2 = Female) was compared with each other for each disease column in order to determine how much a disease occurred for the different sex groups and if there was statistical significant difference between the groups. If the sex of a skeleton was unavailable, that skeleton was excluded from the comparison.

For the “population group” column, population groups 1, 2 and 3 (1 = black, 2 = mixed, 3 = white) was compared with each other for each disease column in order to determine how much a disease occurred for the different ancestry groups and if there was statistical significant difference between the groups. If the population group of a skeleton was unavailable, that skeleton was excluded from the comparison.

4.2.5.2 Graded Skeleton Groups

The disease columns in this Excel® sheet included sacralisation, lumbarisation, spina bifida, CO left orbit, and CO right orbit. Each disease column consisted of numbers 0, 1, 2, 3, and 4 which indicated the different types/severity of the disease. The percentage of each type/severity was determined for each disease column. For example: for CO left orbit, 70.0% had grade 0, 15.0% had grade 1, 10.0% had grade 2, 3.0% had grade 3, and 4.0% had grade 4 CO.

For the “age” column, age groups 1, 2, 3 and 4 (1 = <31 years, 2 = 31-45 years, 3 = 46-60 years, 4 = >60 years) was compared with each other for each disease column in order to determine if the type/severity of the disease differed between age groups and if there was a statistical significant difference between groups.

In the “sex” column, sex groups 1 and 2 (1 = Male, 2 = Female) was compared with each other for each disease column in order to determine if the type/severity of the disease differed between sex groups and if there was a statistical significant difference between groups.

For the “population group” column, population groups 1, 2 and 3 (1 = black, 2 = mixed, 3 = white) was compared with each other for each disease column in order to determine if the

type/severity of the disease differed between ancestry groups and if there was a statistical significant difference between groups.

4.2.5.3 Spina Bifida

Only skeletons with spina bifida were included in this comparison. Each skeleton had 9 different bones listed in the “bones” column. A column “Presence” contained the numbers 0 and 1 (0 = disease absent, 1 = disease present).

Bones 1, 2, 3, 4, 5, 6, 7, 8, and 9 (1 = atlas, 2 = C7, 3 = T1, 4 = T2, 5 = T11, 6 = T12, 7 = L1, 8 = sacrum, 9 = other) was compared with each other for the column “Presence” in order to determine how much each bone was affected by the disease and if there is a statistical significance between the bone groups.

4.2.5.4 Periostitis

Only skeletons with periostitis were included in this comparison. Each skeleton had 16 different bones listed in the “bones” column. A column “Presence” contained the numbers 0 and 1 (0 = disease absent, 1 = disease present). A second column “Grading” contained numbers 0, 1, and 2. (0 = disease absent, 1 = disease mild, 2 = disease severe).

Bones 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, and 16 (1 = cranium, 2 = facial, 3 = mandible, 4 = ribs L, 5 = Ribs R, 6 = Clavicles, 7 = Scapula, 8 = Humerus, 9 = Radius, 10 = Ulna, 11 = Os Coxae, 12 = Femur, 13 = Tibia, 14 = Fibula, 15 = Hands, 16 = Feet) were compared with each other for the column “Presence” in order to determine how much each bone was affected by the disease and if there was a statistical significance between bone groups. For example: 60.0% of the tibiae were affected while only 1.0% of hands were affected.

Bones 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, and 16 (1 = cranium, 2 = facial, 3 = mandible, 4 = ribs L, 5 = Ribs R, 6 = Clavicles, 7 = Scapula, 8 = Humerus, 9 = Radius, 10 = Ulna, 11 = Os Coxae, 12 = Femur, 13 = Tibia, 14 = Fibula, 15 = Hands, 16 = Feet) was compared with each other for the column “Grading” in order to determine the severity by which the different bones were affected by the disease and if there was a statistical significance between bone groups. For example: The tibia was the most severely affected bone.

4.2.5.5 Osteoporosis

Only skeletons with vertebral compression were included in this comparison. Each skeleton had 8 different bone groups listed in the "bones" column. The column "Number of Vertebra" contained the numbers 0, 1, 2, and 3 (0 = none, 1 = 1 vertebra affected, 2 = 2 vertebrae affected, 3 = 3 vertebrae affected). The column "Grading" contained numbers 0, 1, 2, and 3 (0 = disease absent, 1 = disease mild, 2 = disease medium, 3 = disease severe).

Bone groups 1, 2, 3, 4, 5, 6, 7 and 8 (1 = C1-C3, 2 = C4-C6, 3 = C7-T2, 4 = T3-T5 , 5 = T6-T8 , 6 = T9-T11, 7 = T12-L2, 8 = L3-L5) were compared with each other for the column "Number of Vertebra" in order to determine how many vertebrae in each bone group were affected by the disease and if there was a statistical significance between bone groups. For example: group 6 had the most vertebrae affected by the disease.

Bone groups 1, 2, 3, 4, 5, 6, 7 and 8 (1 = C1-C3, 2 = C4-C6, 3 = C7-T2, 4 = T3-T5 , 5 = T6-T8 , 6 = T9-T11, 7 = T12-L2, 8 = L3-L5) were compared with each other for the column "Grading" in order to determine the severity by which the different bone groups were affected by this disease and if there was a statistical significance between bone groups. For example: Group 6 had the most severe osteoporosis.

4.2.5.6 Vertebral Osteophytes

Only skeletons with vertebral osteophytes were included in this comparison. Each skeleton had 9 different bone groups listed in the "bones" column. The column "Number of Vertebra" contained the numbers 0, 1, 2, and 3 (0 = None, 1 = 1 vertebra affected, 2 = 2 vertebrae affected, 3 = 3 vertebrae affected). The column "Grading" contained numbers 0, 1, 2, 3, and 4 (0 = disease absent, 1 = disease mild, 2 = disease medium, 3 = disease severe, 4 = vertebra fused).

Bone groups 1, 2, 3, 4, 5, 6, 7, 8 and 9 (1 = C1-C3, 2 = C4-C6, 3 = C7-T2, 4 = T3-T5 , 5 = T6-T8 , 6 = T9-T11, 7 = T12-L2, 8 = L3-L5, 9 = Sacrum) were compared with each other for the column "Number of Vertebra" in order to determine how many vertebrae in each bone group were affected by this disease and if there was a statistical significance between bone groups. For example: group 6 had the most vertebrae affected by the disease.

Bone groups 1, 2, 3, 4, 5, 6, 7, 8 and 9 (1 = C1-C3, 2 = C4-C6, 3 = C7-T2, 4 = T3-T5 , 5 = T6-T8 , 6 = T9-T11, 7 = T12-L2, 8 = L3-L5, 9 = Sacrum) were compared with each other for

the column “Grading” in order to determine the severity by which the different bone groups were affected by this disease and if there was a statistical significance between bone groups. For example: Group 6 had the most severe osteoporosis.

4.2.5.7 Peripheral Osteophytes

Only skeletons with peripheral osteophytes were included in this comparison. Each skeleton had 13 different bones listed in the “bones” column. The column “Presence” contained the numbers 0 and 1 (0 = disease absent, 1 = disease present). The column “Grading” contained numbers 0, 1, 2, and 3 (0 = disease absent, 1 = disease mild, 2 = disease severe, 3 = eburnation).

Bones 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 (1 = ribs, 2 = Clavicles, 3 = Scapula, 4 = Humerus, 5 = Radius, 6 = Ulna, 7 = Os Coxae, 8 = Femur, 9 = Patella, 10 = Tibia, 11 = Fibula, 12 = Hands, 13 = Feet) were compared with each other for the column “Presence” in order to determine how much each bone were affected by this disease and if there was a statistical significance between bone groups. For example: 60.0% of the tibiae were affected while only 1.0% of the hands were affected.

Bones 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 (1 = ribs, 2 = Clavicles, 3 = Scapula, 4 = Humerus, 5 = Radius, 6 = Ulna, 7 = Os Coxae, 8 = Femur, 9 = Patella, 10 = Tibia, 11 = Fibula, 12 = Hands, 13 = Feet) were compared with each other for the column “Grading” in order to determine the severity by which the different bones were affected by this disease and if there was a statistical significance between bone groups. For example: The tibia was the most severely affected bone.

4.2.5.8 Schmorl’s nodes

Only skeletons with Schmorl’s nodes were included in this comparison. Each skeleton had 8 different bone groups listed in the “bones” column. The column “Number of Vertebra” contained the numbers 0, 1, 2, and 3 (0 = none, 1 = 1 vertebra affected, 2 = 2 vertebrae affected, 3 = 3 vertebrae affected).

Bone groups 1, 2, 3, 4, 5, 6, 7 and 8 (1 = C1-C3, 2 = C4-C6, 3 = C7-T2, 4 = T3-T5 , 5 = T6-T8 , 6 = T9-T11, 7 = T12-L2, 8 = L3-L5) were compared with each other for the column “Number of Vertebra” in order to determine how many vertebrae in each bone group were

affected by this disease and if there was a statistical significance between bone groups. For example: group 6 had the most vertebrae affected by the disease.

4.2.5.9 Harris lines

Only skeletons with HL were included in this comparison. Each skeleton had 6 different bones listed in the “bones” column. The column “Presence” contained the numbers 0 and 1 (0 = disease absent, 1 = disease present).

Bones 1, 2, 3, 4, 5, and 6 (1 = Humerus, 2 = Radius, 3 = Ulna, 4 = Femur, 5 = Tibia, 6 = Fibula) were compared with each other for the column “Presence” in order to determine how much each bone were affected by this disease and if there was a statistical significance between bone groups. For example: 60.0% of the tibiae were affected while only 1.0% of the hands were affected.

Chapter 5 RESULTS

Using macroscopic, radiologic and microscopic examination, changes in the skeletal architecture brought on by diseases listed in Table 5.1, were observed.

Table 5.1: List of traits and diseases observed

Disease types	Diseases or traits of diseases
Congenital and acquired malformations:	Sacralisation
	Lumbarisation
	Spina bifida
	Scoliosis
	Kyphosis
	Spondylolysis
Infectious diseases:	Periostitis
	Visceral rib lesions
Metabolic disorders:	Osteomalacia
	Cribra orbitalia/Porotic hyperostosis
	Enamel hypoplasia
	Harris lines
	Osteoporosis
Degenerative bone diseases:	Vertebral and peripheral osteophytes
	Schmorl's nodes
	DISH
	Rheumatoid arthritis
Neoplasms:	Primary benign neoplasm
	Primary malignant neoplasm
	Metastases
Miscellaneous conditions:	Paget's disease

5.1 CONGENITAL AND AQUIRED MALFORMATIONS

Congenital and acquired malformations occurred in 45.7% (n=137) of the skeletons examined. Of these, 28.5% (n=39) showed more than one congenital or acquired malformation. Observed malformations included lumbosacral transitional vertebrae, spina bifida, scoliosis, kyphosis, and spondylolysis. Table 5.2 summarizes the percentages of skeletons affected with each malformation in the different age, sex, and population groups.

Table 5.2. Percentage of skeletons with malformation for each sex, population, and age group

		Sex		Population group			Age			
Malformations	**All**	**M**	**F**	**Black**	**Mixed**	**White**	**<31**	**31-45**	**46-60**	**>60**
Sacralisation	12.0	13.3	10.4	17.4	10.8	12.2	9.7	13.7	13.6	8.8
Lumbarisation	7.3	4.7*	12.6*	6.7	7.9	5.0	12.9	5.3	5.9	9.1
Spina bifida	14.0	12.9	16.5	4.3*	13.4*	28.6*	12.9	13.4	13.0	17.2
Scoliosis	4.7	5.0	4.1	8.5	3.4	7.1	3.2	2.1	6.5	5.2
Kyphosis	17.0	16.3	17.5	10.6*	15.8*	26.2*	6.5	14.4	16.7	27.6
Spondylolysis	2.7	3.0	1.0	2.1	2.9	2.4	0.0	2.1	1.9	5.2

Statistically significant differences ($p<0.05$) between sex, population or age groups are indicated by *.

Possible congenital malformations not listed in Table 5.2 but were observed include fused vertebrae (n=8), accessory thoracic vertebrae and ribs (n=3), cervical ribs (n=2), and a butterfly vertebra T12 (n=1). Of the 8 skeletons with fused vertebrae (some of which may not be congenital malformations but rather the result of trauma or other pathological conditions), two showed posterior fusion of C2-3 (AN 291, AN 637), one anterior fusion of C5-6 (AN 815), one a fusion of T5-6 (AN 417), one a fusion of T9-T10 (AN 568), one a fusion of the left transverse processes of C2-4 (AN 805), one a fusion of C2-3 and C6-7 (AN 554), and one with a fusion of C2-7 (AN 691). The last case can be diagnosed as Klippel-Feil syndrome in which the neck is shortened and cervical movement restricted due to fused cervical vertebrae (Figure 5.1). This skeleton also showed spina bifida of C1 where the posterior neural arch failed to fuse. Skeletons AN 805 and AN 554 might also suffer Klippel-Feil syndrome as a differential diagnosis however, other factors (e.g. trauma) may also be responsible for fusion of the vertebrae.

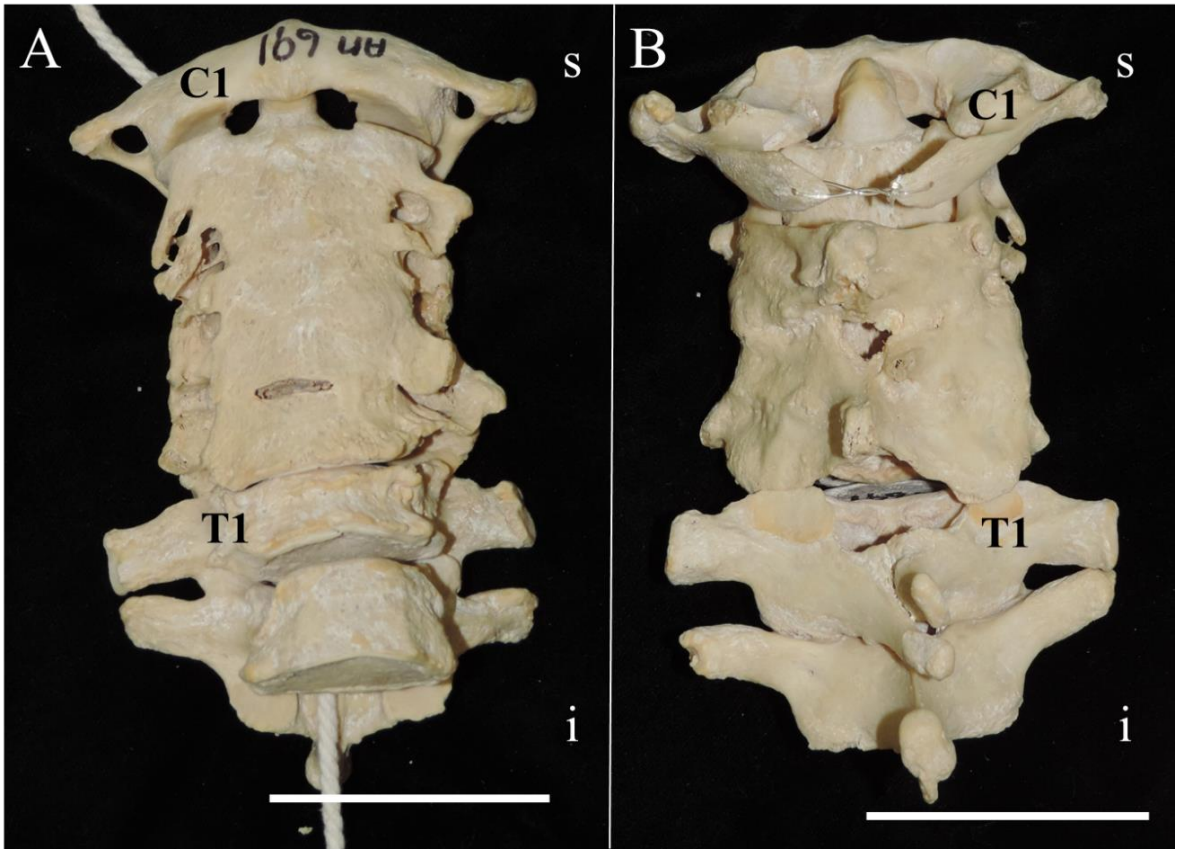


Figure 5.1: Klippel-Feil Syndrome
Digital image of the cervical vertebrae of AN 691. s=superior. i=inferior. C1=atlas. T1=first thoracic vertebra. Scale bar=5cm.
A) Anterior aspect of cervical vertebrae.
B) Posterior aspect of cervical vertebrae.

The accessory thoracic vertebrae of skeletons AN 313 and AN 710 extended the thoracic vertebral column to include 13 vertebrae with 13 pairs of ribs. Cervical ribs were observed bilaterally on C7 of skeleton AN 247, and on the left only on C7 of skeleton AN 640. In the one case of a butterfly vertebra, the vertebral body of T12 of skeleton AN 202 had a sagittal cleft giving it a funnel shape laterally (Figure 5.2).

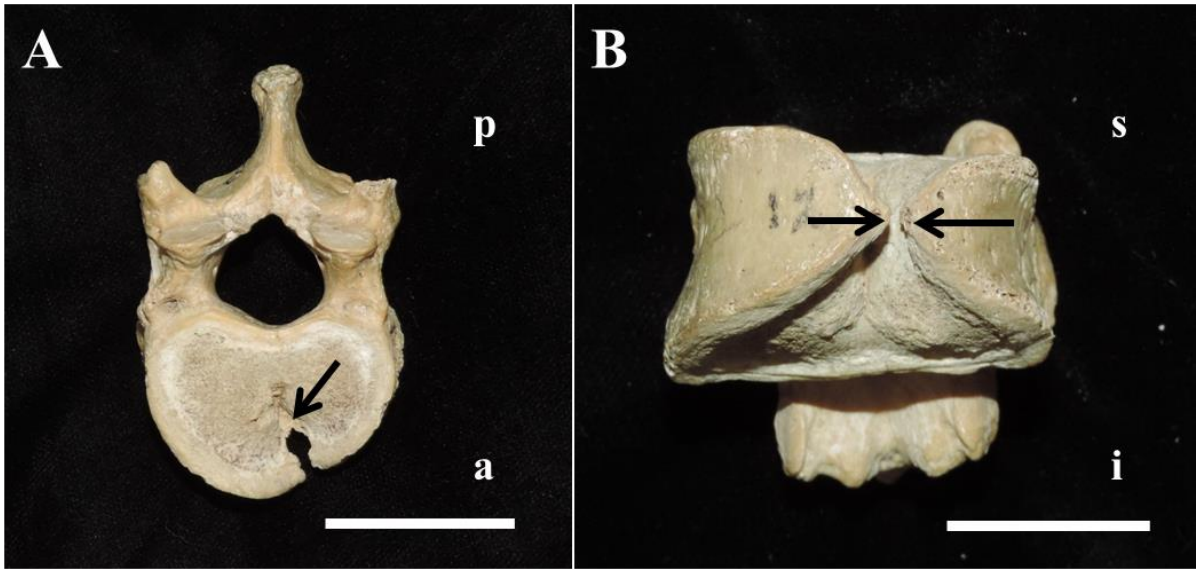


Figure 5.2: Butterfly vertebra
Digital image of the thoracic vertebra T12 of skeleton AN 202. The arrows indicate the sagittal cleft in the vertebral body. Scale bar=2cm.
A) Superior aspect of vertebra T12. a=anterior. p=posterior.
B) Anterior aspect of vertebra T12. s=superior. i=inferior.

Two cases showed unilateral cranial caudal border shifting where the left and right halves of vertebrae differ in features. One case (AN 637) presented with a first thoracic vertebra of which the left side had cervical features such as a transverse foramen and a lack of a first rib while the right half had normal thoracic features. The first and second ribs on the right side were fused. The other case (AN 398) had a L1 vertebra of which the left side had features of a thoracic vertebra with a costal facet while the right side had normal lumbar features (Figure 5.3). A sixth lumbar vertebra was present of which the right side fused with the sacrum while the left side showed normal lumbar features (sacralisation type IIIa).

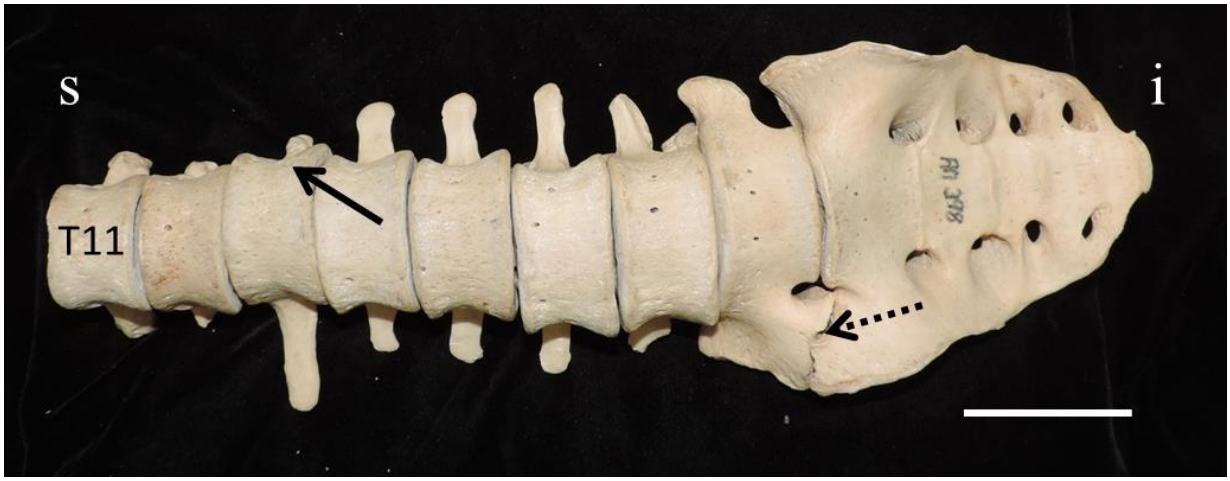


Figure 5.3: Unilateral cranial caudal border shifting
Digital image of the anterior aspect of the lower vertebral column of skeleton AN 398. A unilateral cranial caudal border shifting can be observed. The arrow indicates the L1 vertebra with the characteristics of a thoracic vertebra on the left side. The dotted arrow indicates sacralisation on the right side. T11=thoracic vertebra 11. s-superior. i-inferior. Scale bar=5cm.

5.1.1 Lumbosacral transitional vertebrae

Lumbosacral transitional vertebra occurred in 19.3% (n=56) of skeletons with sacralisation (Figure 5.4) observed in 12.0% (n=35) and lumbarisation in 7.3% (n=21) of skeletons (Table 5.2). Females showed statistically significantly more lumbarisation than males (p=0.014) (Table 5.2). Different types of lumbosacral transitional vertebra occurred in the skeletal population for this study (see Figure 2.7). The percentages of Type I, II, III, and IV sacralisation and lumbarisation are indicated in Table 5.3. Type III was the most commonly observed for both sacralisation and lumbarisation and is observed as a complete fusion, unilateral or bilateral, between the transitional vertebra and sacrum.

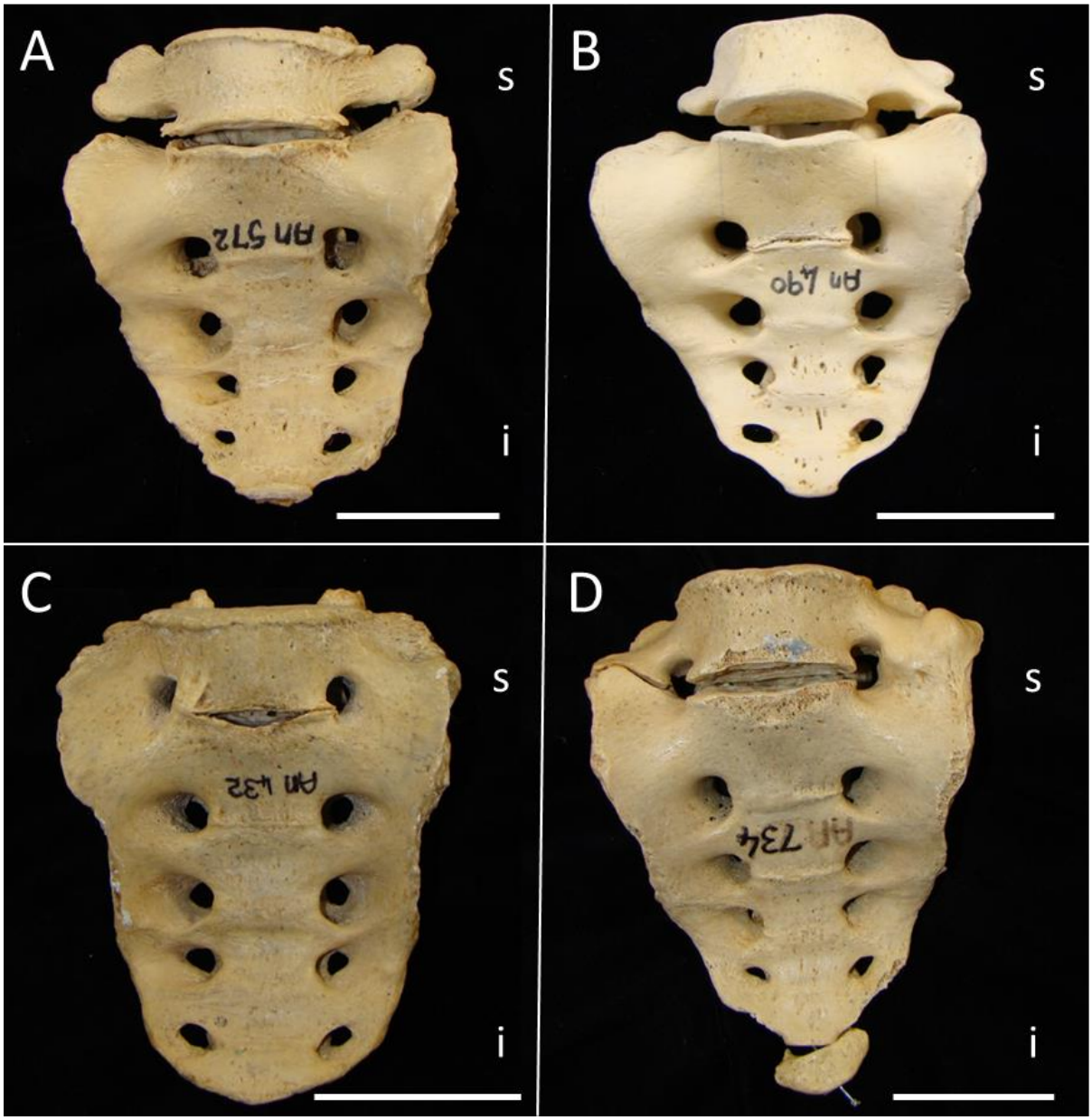


Figure 5.4: Types of sacralisation
Digital images of the anterior aspect of the sacrum indicating the different TypeI-IV sacralisation. s=superior. i=inferior. Scale bar=5cm.

A) Type I sacralisation of skeleton AN 572 with bilateral dysplastic transverse processes.
B) Type II sacralisation of skeleton AN 490 with a unilateral diarthrodial joint between the transverse process and sacrum.
C) Type III sacralisation of skeleton AN 432 with bilateral fusion of the transverse processes to the sacrum.
D) Type IV sacralisation of skeleton AN 734 with a unilateral diarthrodial joint and contralateral fused transverse process.

Table 5.3: Percentage of the different types of sacralisation and lumbarisation

	Type I	Type II	Type III	Type IV
Sacralisation	17.1	22.9	51.4	8.6
Lumbarisation	4.8	28.6	61.9	4.8

5.1.2 Spina bifida

Spina bifida was observed in 14.0% (n=42) of the skeletons and occurred statistically significantly more in the white population group than the black or mixed groups (p=0.008) (Table 5.2). Vertebrae most commonly affected in skeletons with spina bifida were the atlas posteriorly (Figure 5.5A) in 39.0% and sacrum in 58.5% (Figure 5.5B). Spina bifida occurred statistically significantly more (p<0.001) in these two vertebrae than any other. No spina bifida was observed in vertebrae C2-6, T3-10, and L2-5. Figure 5.6 illustrates the percentage of skeletons with spina bifida in different vertebrae.

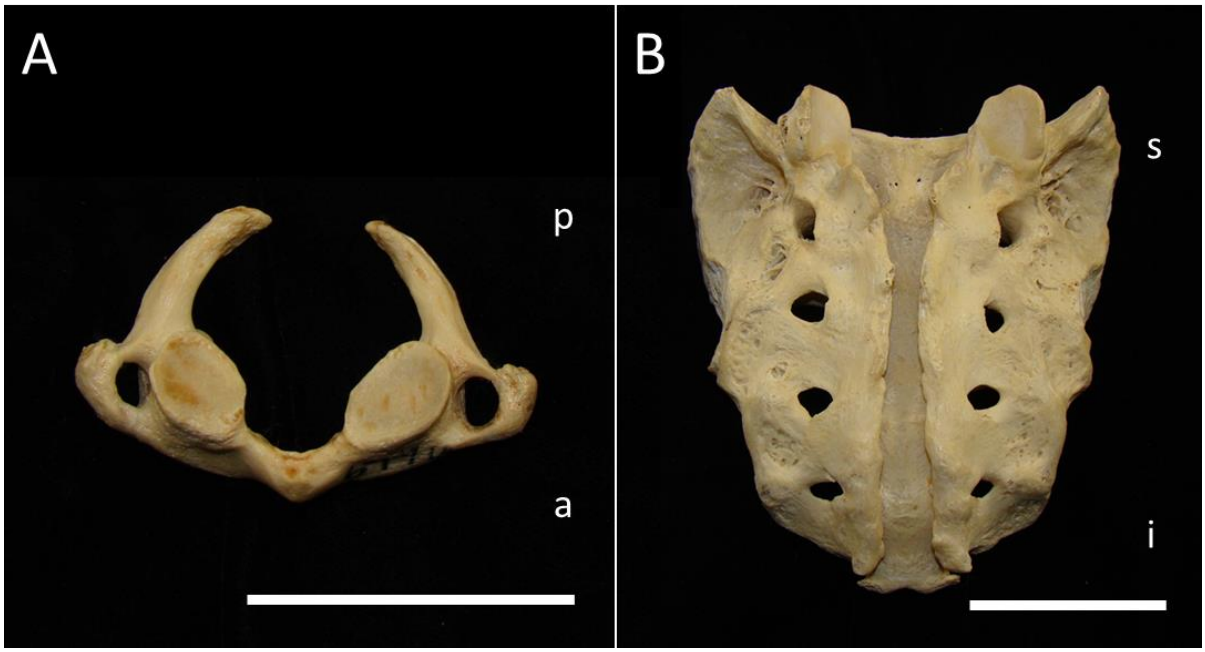


Figure 5.5: Spina bifida
Incomplete closure of posterior neural arches. Scale bar=5cm.

A) Digital image of spina bifida of the atlas of skeleton AN 469 (superior view). p=posterior. a=anterior
B) Digital image of spina bifida of the complete sacrum of skeleton AN 460 (posterior view). s=superior. i=inferior

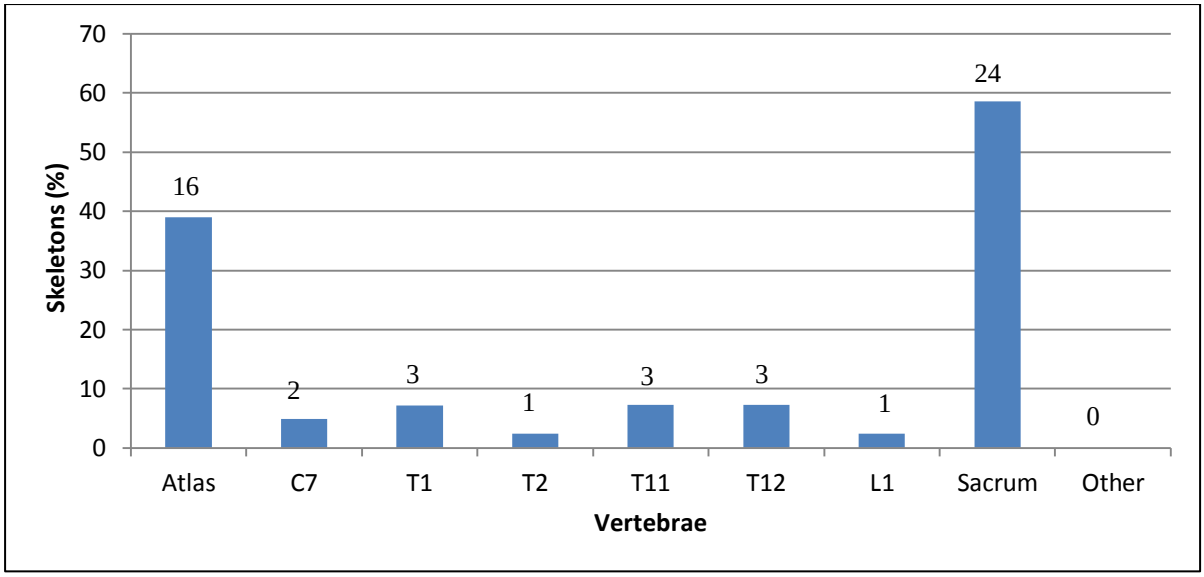


Figure 5.6: Skeletons with spina bifida for each vertebra
The graph illustrates the percentage of skeletons with spina bifida on each vertebra. The numbers above bars indicate the number of skeletons.

5.1.3 Scoliosis/Kyphosis

Scoliosis occurred in 4.7% (n=14) of all skeletons (Figure 5.7) (Table 5.2). Kyphosis occurred in 17.0% (n=51) of all skeletons (Figure 5.8) (Table 5.2). The number of skeletons showing kyphosis increased with age although no statistical significance was observed between age groups (p=0.057) (Table 5.2). Kyphosis occurred statistically significantly more (p=0.046) in the white population group than the black population group.

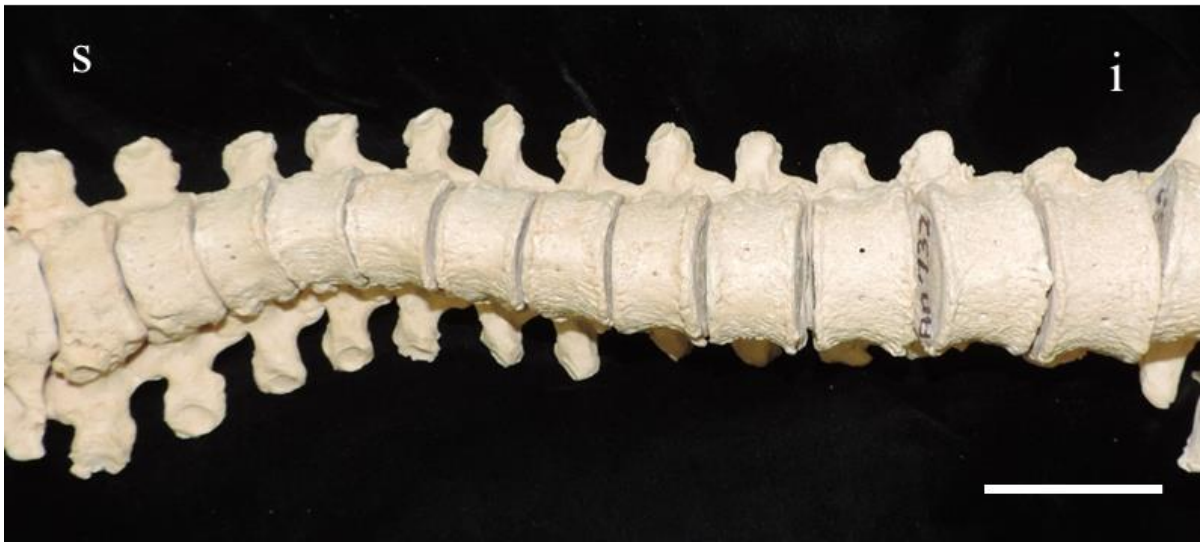


Figure 5.7: Scoliosis
Digital image of the anterior aspect of the vertebral column of skeleton AN 732. An abnormal curvature can be observed in the thoracic region. s=superior. i=inferior. Scale bar=5cm.

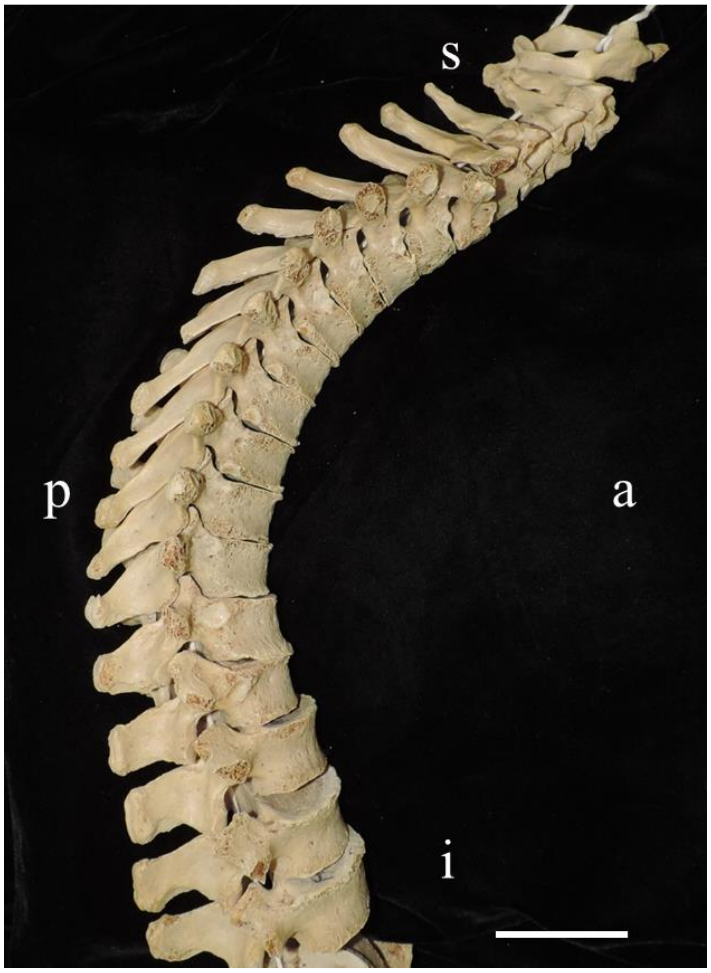


Figure 5.8: Kyphosis
Digital image of the lateral aspect of the vertebral column of skeleton AN 555. An increased curvature can be observed in the thoracic vertebral column. s=superior. i=inferior. p=posterior. a=anterior. Scale bar=5cm

5.1.4 Spondylolysis

Spondylolysis (Figure 5.9) occurred in 2.7% (n=8) of skeletons (Table 5.2). All cases of spondylolysis were observed in the lower lumbar vertebrae with six cases presenting on L5 and two on L4. The age group >60 years had the highest percentage of spondylolysis, however it was not statistically significant (p=0.552) compared to the other age groups (Table 5.2). All cases represented with a bilateral separation of the neural arch resulting in vertebrae divided into two separate parts.

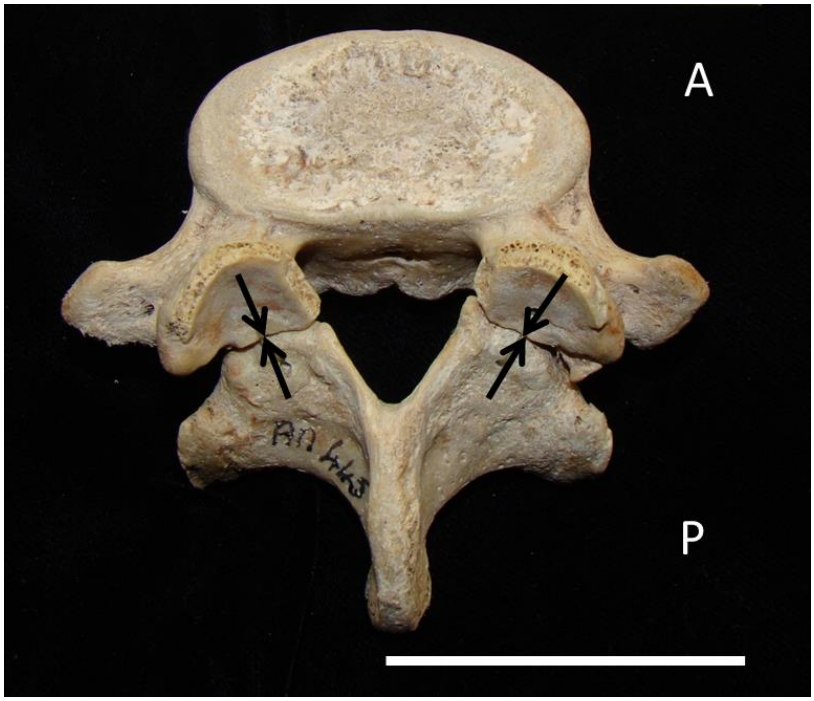


Figure 5.9: Spondylolysis
Digital image of the postero-superior aspect of the neural arch of vertebra L5 of skeleton AN 445. The arrows indicate unfused segments on the vertebral arch. A=anterior. P=posterior. Scale bar=5cm.

5.2 INFECTIOUS DISEASES

Infectious diseases affecting the skeleton presented mostly as a periosteal reaction on skeletal elements. Table 5.4 gives the percentage of skeletons with visible periostitis and VRL (subdivision of periostitis) for each sex, population, and age group. A possible diagnosis of Pott's disease was observed in one skeleton (AN 780, 32-year-old female) on lumbar vertebra L1 (Figure 5.10). A destructive lesion or abscess is visible on the vertebral body and a decrease in the intervertebral disk space was observed. A radiolucent area of the abscess was visible on the Lodox® scan.

Table 5.4: Percentage of skeletons with periostitis and VRL for each sex, population, and age group

		Sex		Population group			Age			
Infectious diseases	**All**	**M**	**F**	**Black**	**Mixed**	**White**	**<31**	**31-45**	**46-60**	**>60**
Periostitis	60.7	58.9	62.9	44.7*	70.3*	26.2*	54.8*	70.1*	61.1*	44.8*
Visceral rib lesions	29.3	31.2	25.8	31.9*	34.0*	4.8*	32.3*	42.3*	25.0*	13.8*

Statistical significant differences ($p<0.05$) between sex, population or age groups are indicated by *.

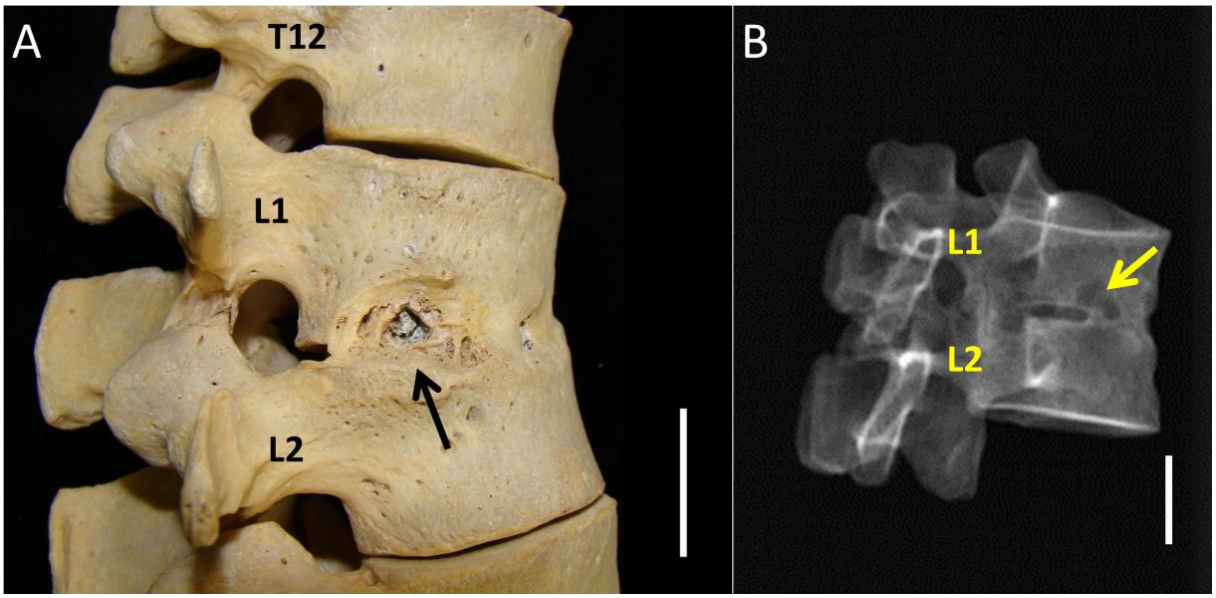


Figure 5.10: Pott's disease
T12=Thoracic vertebra 12. L1=Lumbar vertebra 1. L2=Lumbar vertebra 2. Scale bar=2cm.

A) Digital image of the lateral aspect of the vertebral column from T12 to L3 of skeleton AN 780. Arrow indicates possible Pott's disease on vertebra L1 and L2.
B) Lateral radiograph (Lodox® scan) of vertebra L1 and L2 of skeleton AN 780. Arrow indicates radiolucent area on vertebrae L1.

5.2.1 Periostitis

Periostitis was observed as new parallel layers of bone formation on bone surfaces, irregular surfaces on bone including bony spicules, or a porous appearance of the bone surface due to woven bone formation. Of the 60.7% (n=182) of skeletons showing signs of periostitis, the mixed population group had a statistically significantly ($p<0.001$) higher percentage (70.3%) than the black (44.7%) and white (26.2%) population groups (Table 5.4). A statistical significance ($p=0.018$) was also observed between the age groups with age group 31-45 years affected the most (70.1%) (Table 5.4). Figure 5.11 shows the percentage by which the different skeletal elements were affected. Skeletal elements with the highest percentage of periostitis were the tibia and fibula which was statistically significant ($p<0.001$). A high percentage of periostitis was also observed on the left and right ribs and femur. The clavicle was the least affected skeletal element (2.0%). Bilateral distribution of periostitis on the tibiae and fibulae was observed in 34.3% (n=103) of the skeletons (Figure 5.12). Systemic periosteal reaction in combination with an infectious disease of the lung indicated as the COD and/or VRL, was observed in 16.7% (n=50) cases. Of these cases, five skeletons showed signs of periosteal nodules on the inferior aspect of the fibulae (Figure 5.13).

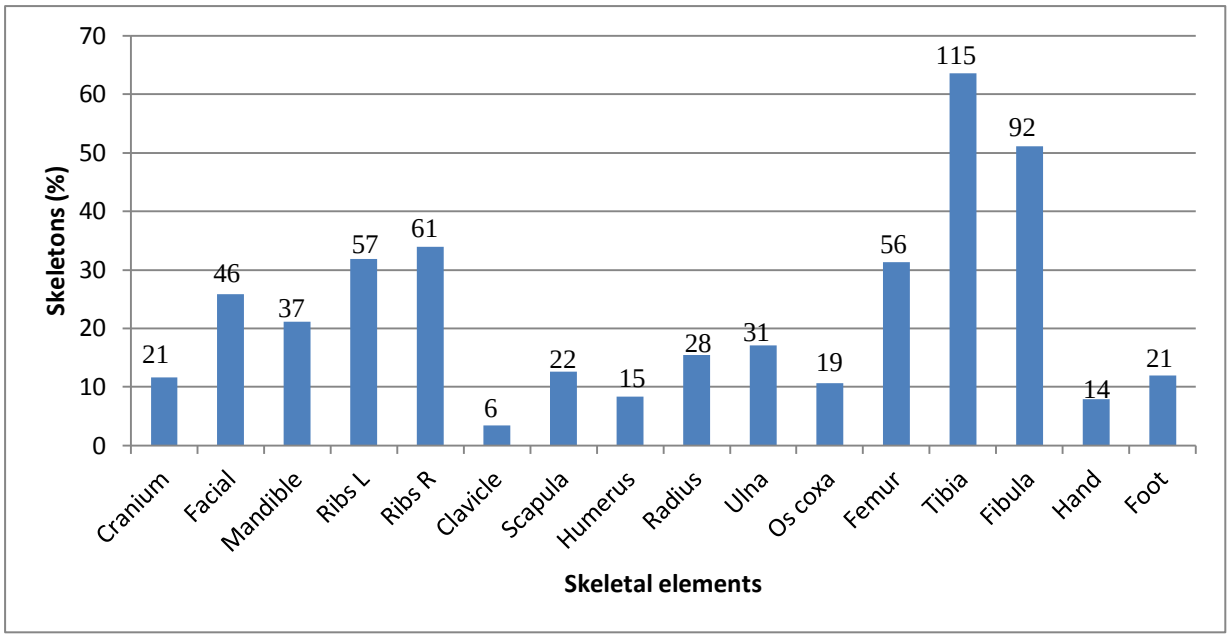


Figure 5.11: Skeletons with periostitis for each skeletal element
The graph illustrates the incidence of periostitis for skeletal elements. The tibia and fibula had significantly more (p=<0.05) periostitis than the other skeletal elements. The numbers above bars indicate the number of skeletons.

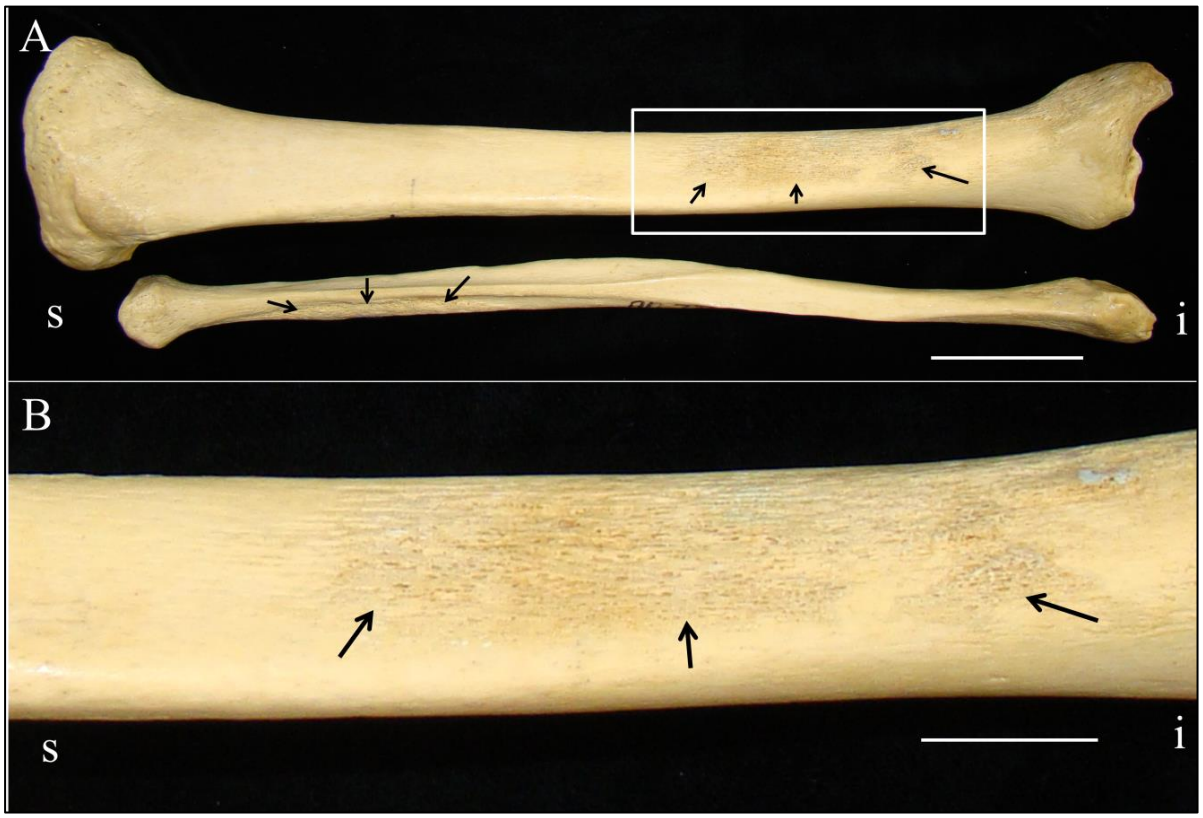


Figure 5.12: Periostitis on tibia and fibula
Digital image of the anterior aspect of the right tibia and fibula of skeleton AN 734. Arrows indicate areas with a periosteal reaction. s=superior. i=inferior.
A) Digital image of the whole tibia and fibula. Scale bar=5cm.
B) Enlarged image of area indicated by white box on (A). Scale bar=2cm.

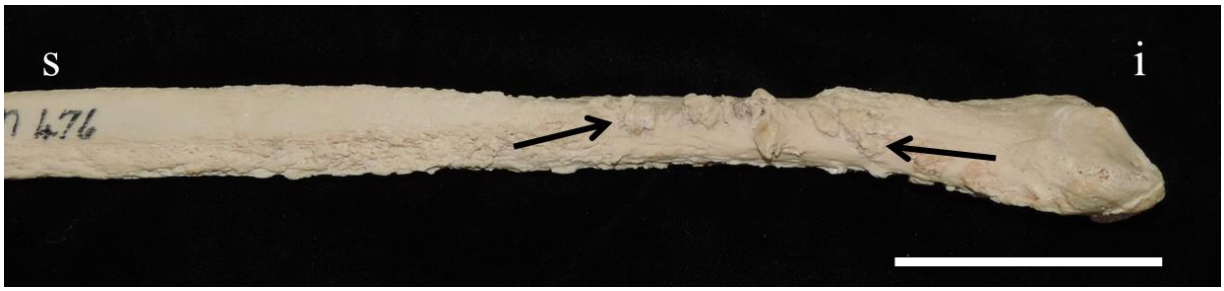


Figure 5.13: Periosteal nodules
Digital image of the posterior aspect of the left fibula of skeleton AN 476. Arrows indicate nodules formed by a periosteal reaction. s=superior. i=inferior. Scale bar=5cm.

5.2.2 Visceral rib lesions

Visceral rib lesions (Figure 5.14) were present in 29.3% (n=88) of skeletons (Table 5.4). It occurred statistically significantly more ($p<0.001$) in the black (31.9%) and mixed (34.0%) population groups than the white (4.8%) group (Table 5.4). A statistical significance ($p=0.001$) was also observed between the age groups with age group 31-45 years affected the most (42.3%) (Table 5.4). Table 5.5 gives the percentage of affected skeletons with VRL in the different rib groups. It also gives the percentages of affected skeletons with TB or pneumonia as a COD with VRL on each group of ribs.

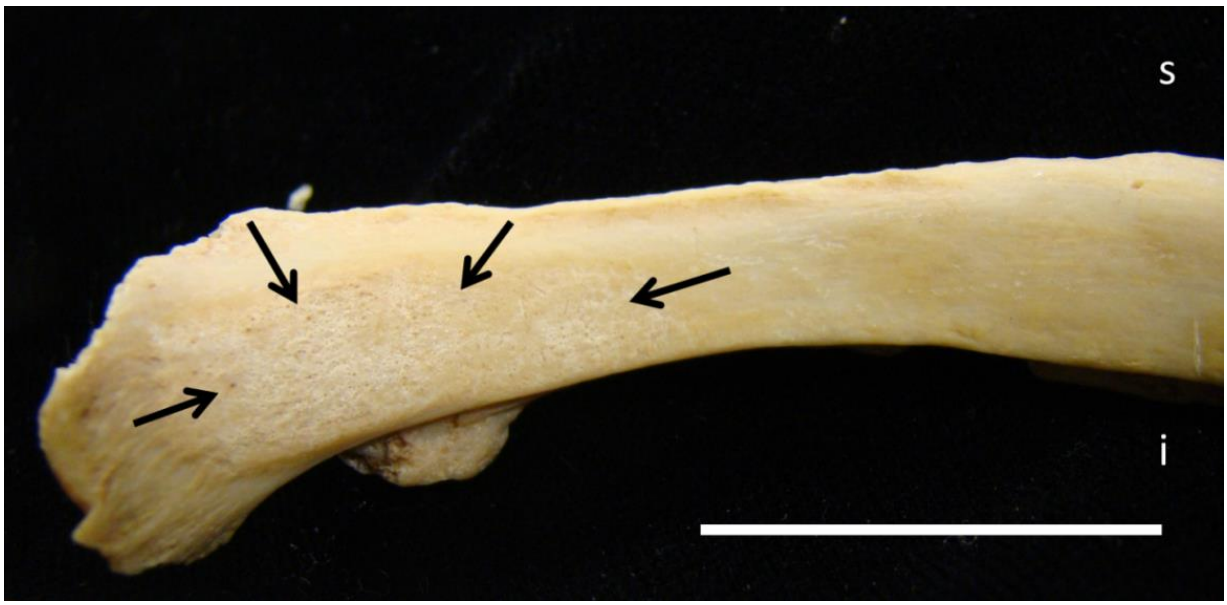


Figure 5.14: Visceral rib lesion
Digital image of the visceral aspect of the vertebral end of a left rib of skeleton AN 567. Arrows indicate an area with a periosteal reaction. s=superior. i=inferior. Scale bar=2cm.

Table 5.5: Percentage of skeletons with VRL on the different rib groups

Rib groups	All	TB	Pneumonia
L 1-3	17.7	25.0	36.4
L 4-8	59.0	50.0	54.6
L 9-12	54.0	33.3	18.2
R 1-3	39.0	38.9	45.4
R 4-8	65.4	82.4	72.7
R 9-12	60.9	66.7	54.6

L=left. R=right.

In 31 skeletons with a documented COD of TB, 58.1% (n=18) showed VRL. In 23 skeletons with a documented COD of pneumonia, 47.8% (n=11) showed VRL. Other diseases indicated as the COD that could have caused VRL included lung abscesses, bronchus carcinoma, lung carcinoma, and pulmonary embolism. In general, the most commonly affected ribs were 4-8 on both left and right sides (Table 5.5). Ribs were affected more on the right side than on the left for both TB and pneumonia cases (Table 5.5). When ribs of known TB and pneumonia cases were observed, ribs on the left were slightly more affected in skeletons with pneumonia than in skeletons with TB, and ribs on the right were slightly more affected in skeletons with TB than in skeletons with pneumonia (Table 5.5). No statistical analysis was performed between TB and Pneumonia cases. Table 5.6 gives the percentage of ribs with VRL on the different rib regions. It also gives the percentages of affected ribs with VRL on the different rib region for skeletons with TB or pneumonia as a COD. Rib regions included the vertebral (posterior third), middle (middle third), and sternal (anterior third) areas of the ribs.

Table 5.6: Percentage of ribs with VRL on the different rib regions

Rib regions	All	TB	Pneumonia
Only vertebral	56.6	58.8	53.6
Only middle	6.8	9.8	0.0
Only sternal	15.8	9.8	3.6
Vertebral/middle	7.2	9.8	14.3
Vertebral/sternal	5.1	7.8	10.7
Middle/sternal	5.1	0.0	3.6
Entire rib	11.9	3.9	14.3

L=left. R=right.

Of all the ribs with VRL, most had lesions on the vertebral region only (Table 5.6). When comparing skeletons with known TB or pneumonia as a COD, most lesions occurred on the vertebral region only with TB showing a slightly higher percentage (58.8%). Cases with TB illustrated more rib lesions for only single regions (only vertebral, only middle, only sternal), while cases with pneumonia showed more lesions on multiple regions (vertebral/middle,

vertebral/sternal, middle/sternal) (Table 5.6). The entire rib was affected in only 3.6% of ribs in cases with known TB while the entire rib was affected in 14.3% of ribs in cases with known pneumonia. These values illustrate a more localized distribution on ribs for cases with TB than pneumonia.

5.3 METABOLIC DISORDERS

Metabolic disorders observed frequently in the skeletal sample studied include PH, CO, EH, HL and osteoporosis. Of all the skeletons studied, 72.0% showed at least one of the above mentioned metabolic disorders. Table 5.7 indicates the percentage of skeletons with metabolic disorders for each sex, population and age group.

Table 5.7: Percentage of skeletons with metabolic disorders for each sex, population, and age group

		Sex		Population group			Age			
Metabolic disorders	**All**	**M**	**F**	**Black**	**Mixed**	**White**	**<31**	**31-45**	**46-60**	**>60**
Porotic hyperostosis	10.7	12.4	7.2	14.9	11.5	2.4	38.7*	12.5*	5.5*	3.5*
Cribra orbitalia	35.6	40.1*	25.8*	34.8	37.2	25.0	51.6	34.4	29.5	35.1
Enamel hypoplasia	43.8	43.0	45.3	35.1	47.4	28.6	62.1*	50.0*	34.5*	28.0*
Harris lines	24.3	23.8	25.8	31.9	23.9	16.7	38.7	23.7	22.2	22.4
Osteoporosis	41.3	42.6	38.1	29.8*	38.8*	64.3*	19.4*	28.9*	45.4*	63.8*

Statistically significant differences ($p<0.05$) between sex, population or age groups are indicated by *.

Five cases of possible osteomalacia were observed under a polarising light microscope (Figure 5.15). Some defect cement lines were visible in the dry bone histology sections taken from the proximal left femur of skeletons with suspected osteomalacia. Only minor macroscopic changes (e.g. prominent supraorbital ridge, curved sacrum, flaring of humerus inferiorly) were visible on the skeletons and could not be used to form a diagnosis. No Looser zones were observed on the Lodox® scans. All these illustrate the presence of only a mild form of osteomalacia. One case of possible secondary hyperparathyroidism was observed radiologically (Figure 5.16). Permeative regions on the Lodox® scan indicate increased osteoclast activity. Possible brown tumours were also observed on the scapulae which can result from excessive osteoclast activity.

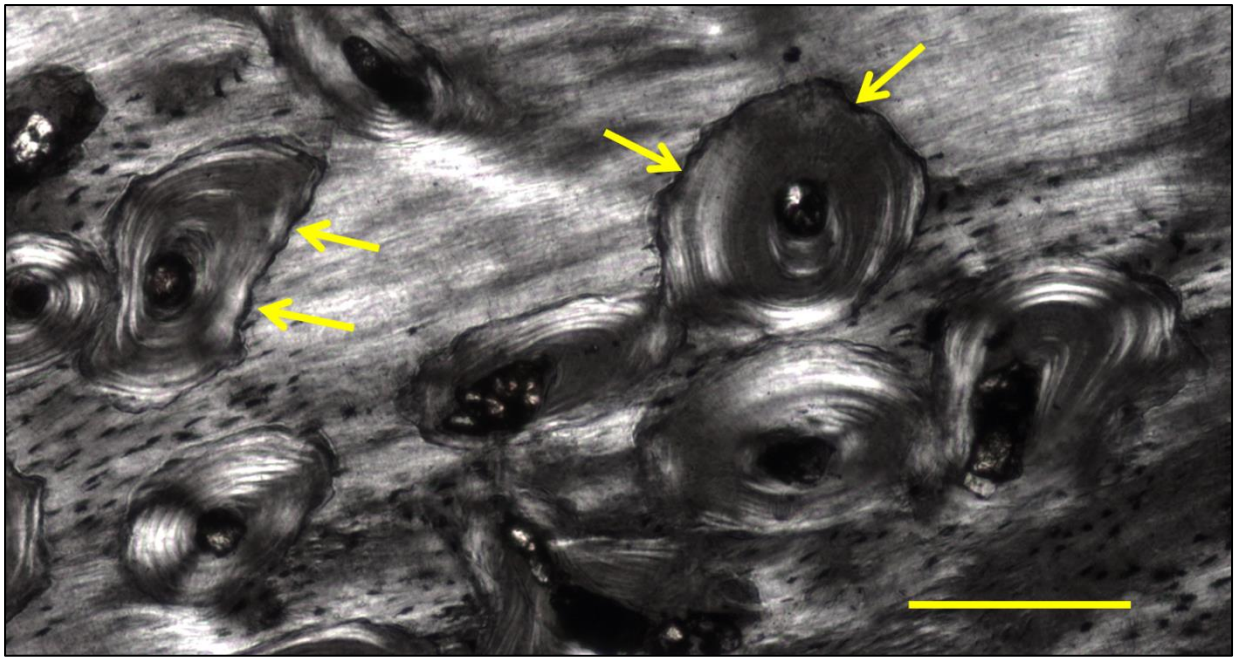


Figure 5.15: Dry bone histology of osteomalacia
Microphotograph of a cross section of the proximal left femur shaft of AN 224. Image taken with a Nikon® light microscope with DCI contrast at 80X magnification. Arrows indicate defective cement lines around osteons. Scale=200µm.

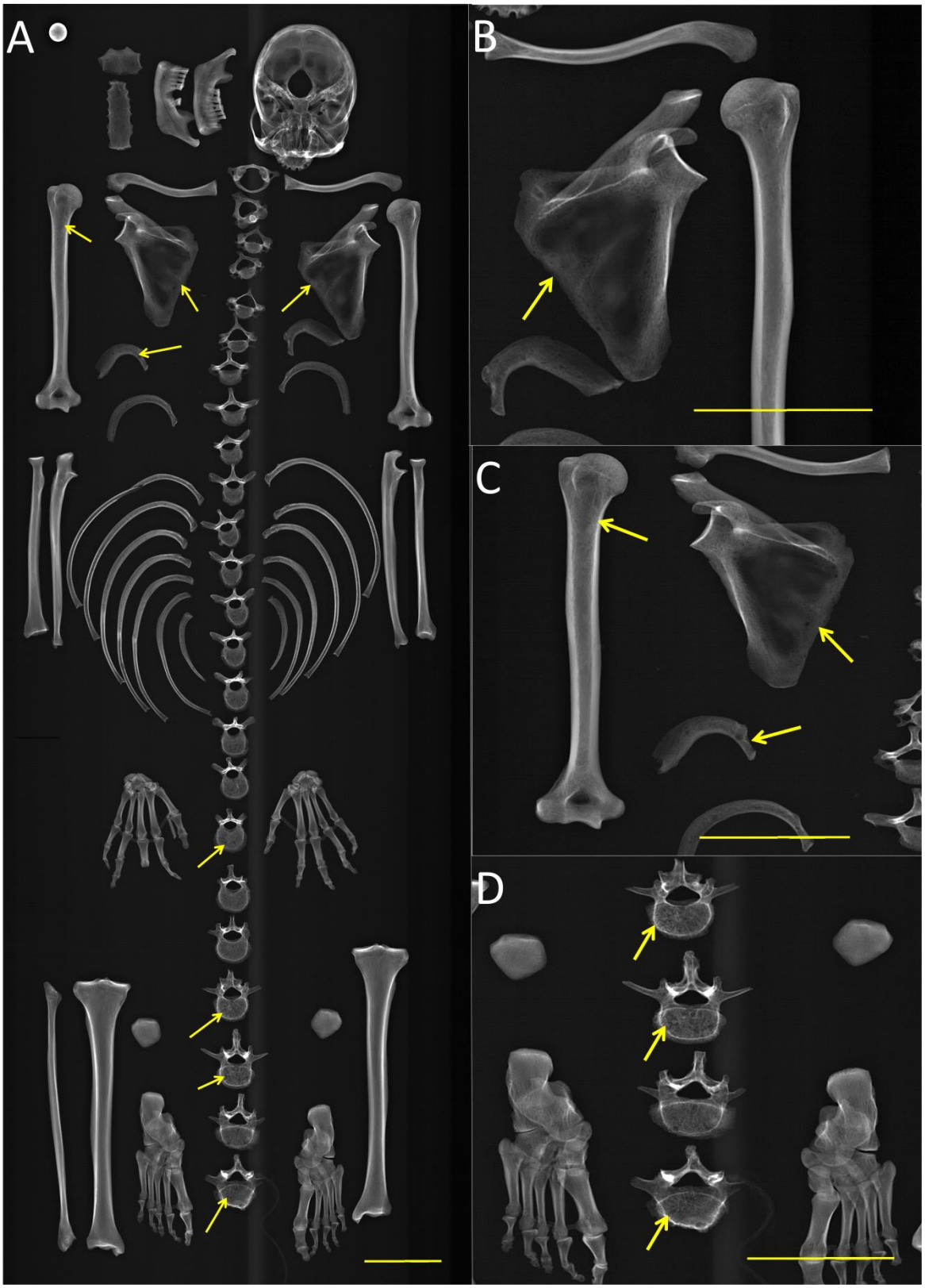


Figure 5.16: Possible secondary hyperparathyroidism
Lodox® scan of skeleton AN542 showing signs of secondary hyperparathyroidism. The arrows indicate permeative areas observed throughout the skeleton caused by osteoclast activities. Scale bar =10cm.

A) Full body Lodox® scan showing distribution of lesions
B) Enlarged image of lesions on the left scapula
C) Enlarged image of lesions on the right scapulat, humerus and rib 1
D) Enlarged image of lesions on the 2nd, 3rd, and 5th lumbar vertebrae.

5.3.1 Porotic hyperostosis/Cribra orbitalia

Porotic hyperostosis occurred in 10.7% (n=32) and CO in 35.6% (n=105) of skeletons (Table 5.7). Cribra orbitalia occurred statistically significantly more (p=0.016) in males (40.1%) than in females (25.8%) (Table 5.7). A statistical significance (p<0.001) for PH was observed between age groups with the age group <31 years (38.7%) affected the most (Table 5.7). All cases of PH had a grading of 1. Gradings 1, 2, 3, and 4 were observed in CO cases (Figure 5.17). Figure 5.18 illustrates the grading percentages of CO found in the left and right orbits. Most of the skeletons illustrated grade 1 CO. In skeletons with PH, 75.0% (n=24) showed signs of CO while 22.9% of skeletons with CO showed signs of PH.

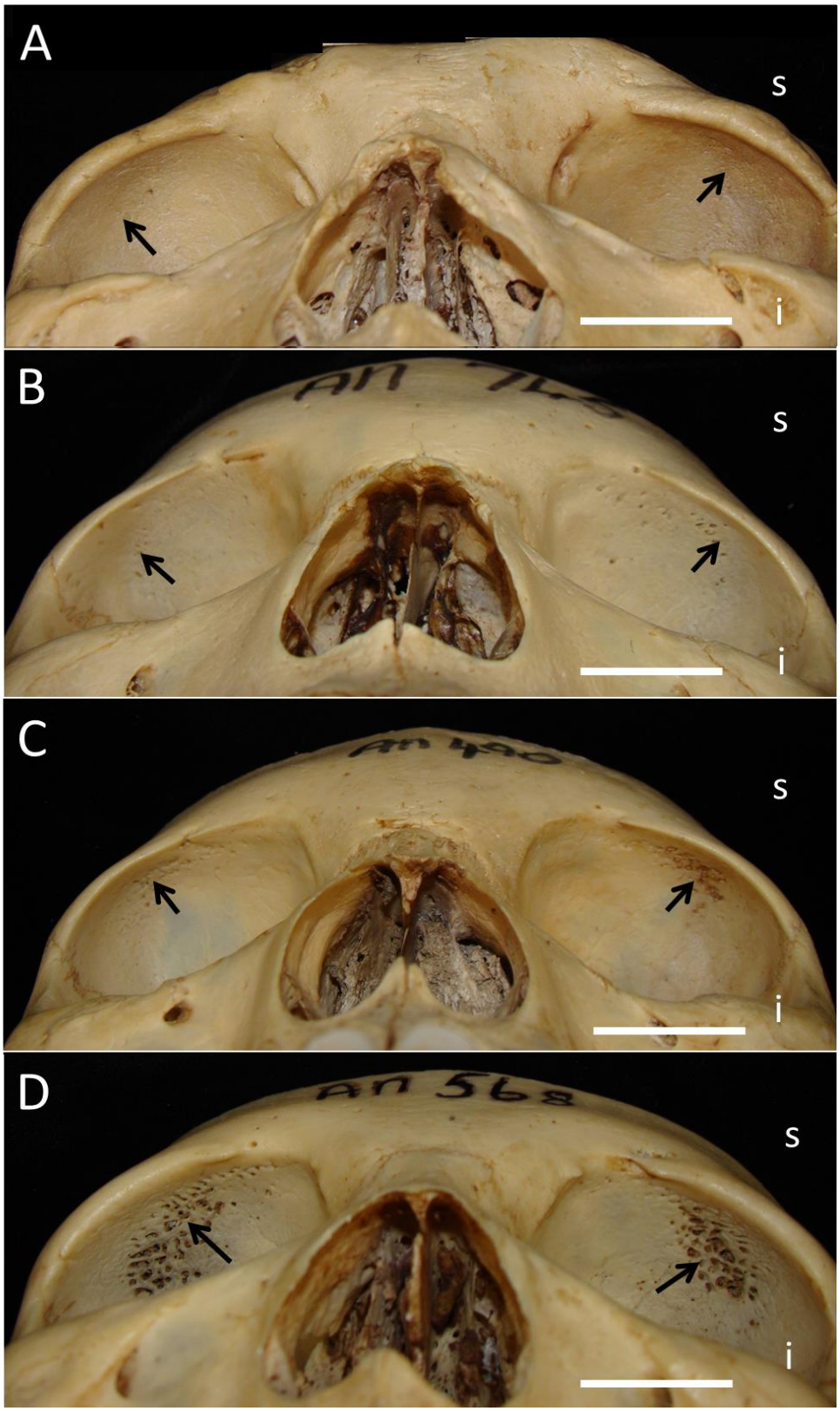


Figure 5.17: Cribra orbitalia
Digital images of the inferior aspect of the left and right orbital roofs illustrating the degrees of CO observed. Arrows indicate CO lesions. s=superior. i=inferior. Scale bar=2cm.

A) Scattered fine foramina of grade 1 CO of skeleton AN 447.
B) Large and small isolated foramina of grade 2 CO of skeleton AN 745.
C) Linked foramina of grade 3 CO of skeleton AN 490.
D) Large linked foramina with trabecular outgrowths of grade 4 CO of skeleton AN 568.

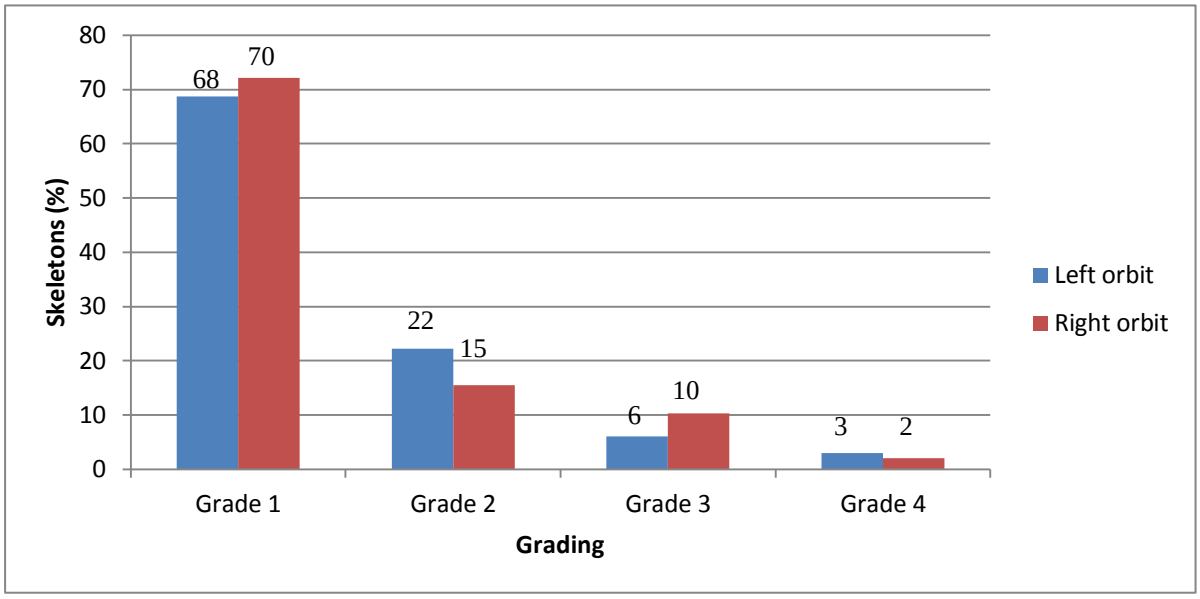


Figure 5.18: Percentage of skeletons with each grading of CO
The graph illustrates the percentage of skeletons with each grading of CO for the left and right orbits. The numbers above bars indicate the number of skeletons.

5.3.2 Enamel hypoplasia

Enamel hypoplasia was observed in 43.8% (n=81) of skeletons (Table 5.7). A statistical significance (p=0.022) was observed between age groups with the age group <31 years affected the most (62.1%) (Table 5.7). Due to the lack of teeth in the present population, this may not be an accurate representation of the number of EH cases in the skeletal population. Of the skeletons with EH, 43.2% showed signs of CO as well.

5.3.3 Harris lines

Harris lines (Figure 5.19) were observed in 24.3% of skeletons with age group <31 years (38.7%) affected the most (Table 5.7). In age groups 31-45 (23.7%), 46-60 (22.2%) and >60 years (22.4%) similar percentages of the skeletal material were effected (Table 5.7). The black population group was affected the most (31.9%) followed by the mixed (23.9%) and white (16.7%) groups (Table 5.7). Males and females showed a similar prevalence for HL with 23.8% and 25.8% of skeletons affected respectively (Table 5.7). No statistical significance was observed between sex, age, and population groups (p=0.705, p=0.277, p=0.120, respectively). Figure 5.20 illustrates the percentage by which each long bone was affected with the tibia showing a statistically significantly higher (p<0.001) percentage of HL than the other long bones in the skeleton. Harris lines were observed on the tibiae in almost

all the cases with only 7 cases with other long bones affected (e.g. fibula, femur) but not the tibia.

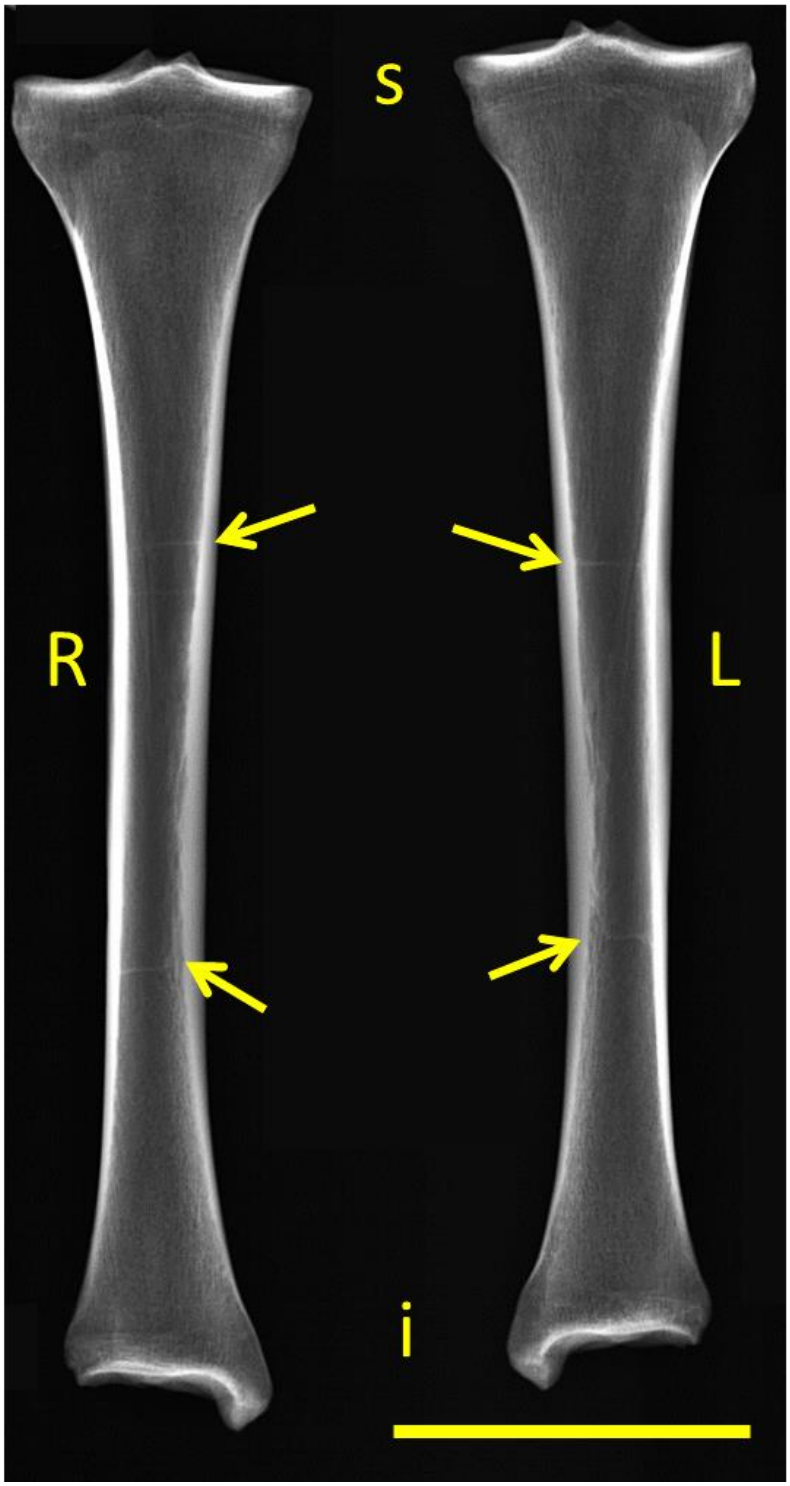


Figure 5.19: Harris lines
An anterior-posterior radiograph (Lodox® scan) of the tibiae of skeleton AN 471. The arrows indicate HL. R=right. L=left. s=superior. i=inferior. Scale bar=10cm.

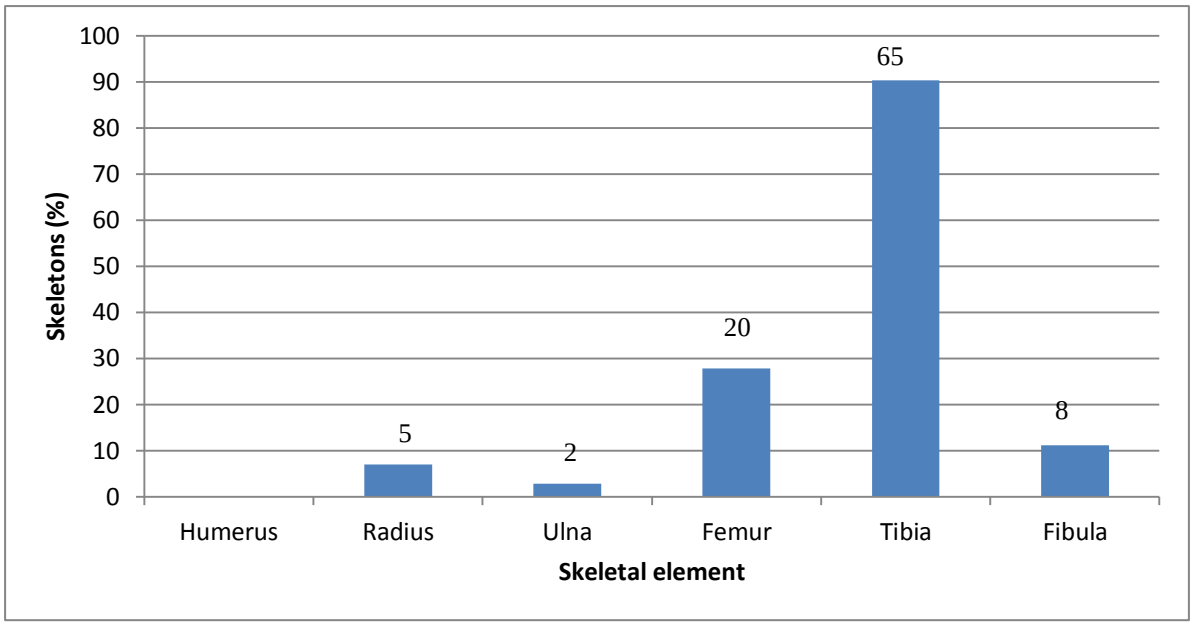


Figure 5.20: Skeletons with HL for each skeletal element
The graph illustrates the percentage of skeletons with HL for the skeletal elements listed. The numbers above bars indicate the number of skeletons.

5.3.4 Vertebral compression

Some degree of vertebral compression was observed in 41.3% of skeletons (Table 5.7). A statistically significant difference ($p<0.001$) was observed between age groups for vertebral compression (Table 5.7). The age group >60 years showed the highest prevalence of vertebral compression (63.8%) (Table 5.7). The number of vertebrae affected for each vertebral group is illustrated in Figure 5.21 and differed significantly ($p<0.001$). The vertebrae most affected were T6-T8 in 67.3% of skeletons showing vertebral compression for that group. Figure 5.22 illustrates the percentage of skeletons with different degrees of compression for each vertebral group. Most vertebrae had a grade 1 degree of compression. The most severe compression was observed on vertebrae T6-8 with grade 3 compression observed in 4.5% of skeletons with vertebral compression for that group.

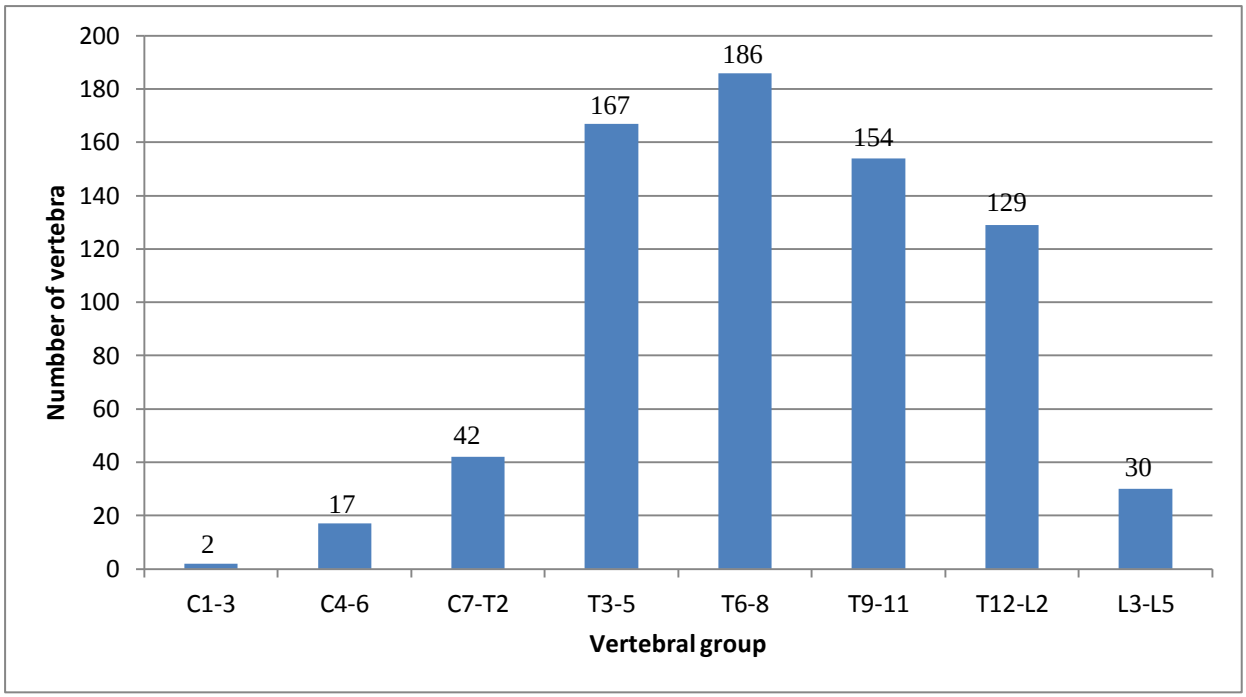


Figure 5.21: Number of vertebra with vertebral compression for each vertebral group
The graph illustrates the number of vertebrae with some degree of compression for each vertebral group. The numbers above bars indicate the number of vertebrae.

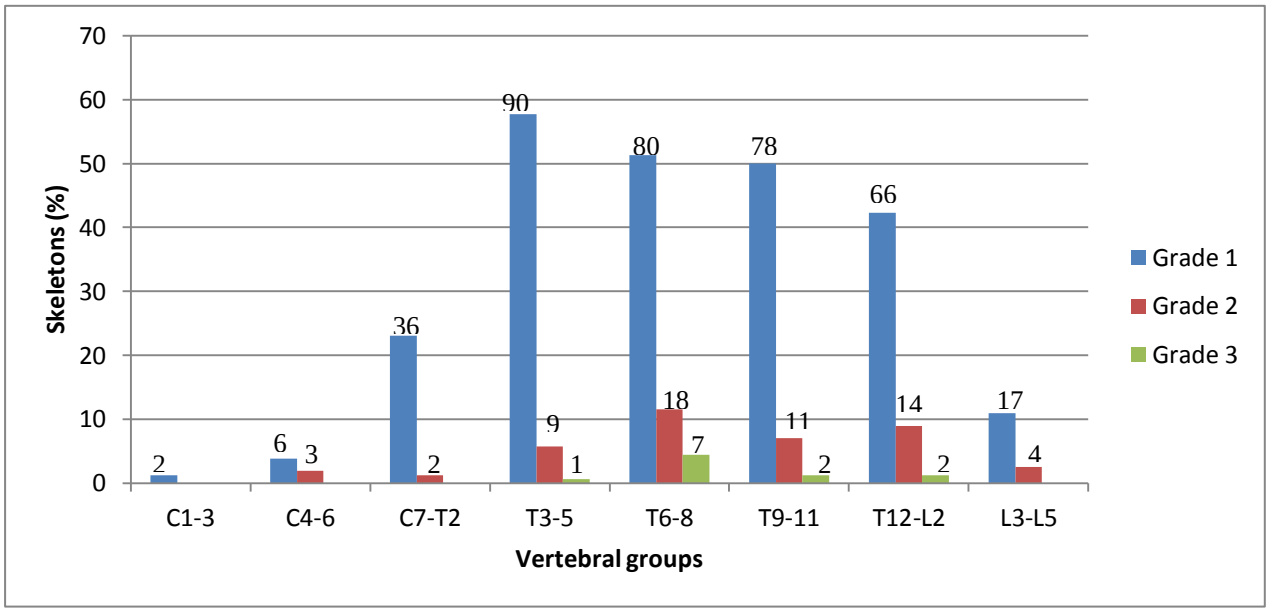


Figure 5.22: Degree of vertebral compression for each vertebral group
The graph illustrates the percentage of skeletons for each grading of vertebral compression for each vertebral group. The numbers above bars indicate the number of skeletons.

5.4 DEGENERATIVE BONE DISEASES

Bone markings that relates to degenerative diseases that were observed in the present study include vertebral osteophytes, peripheral osteophytes, Schmorl's nodes and DISH. Table 5.8

gives the percentage of skeletons with the above-mentioned bone markings for each sex, age, and population group. A statistical significance was observed between age groups for vertebral osteophytes ($p<0.001$), peripheral osteophytes ($p<0.001$), Schmorl's nodes ($p=0.014$) and DISH ($p=0.001$), with the age group >60 years showing the highest percentage for all these traits (100.0%, 81.0%, 19.0%, 15.5% respectively) (Table 5.8).

Table 5.8: Percentage of skeletons with bone markings of degenerative diseases for each sex, population, and age group

		Sex		Population group			Age			
Bone markings	**All**	**M**	**F**	**Black**	**Mixed**	**White**	**<31**	**31-45**	**46-60**	**>60**
Osteophytes vertebral	81.0	83.7	75.3	66.0*	80.9*	97.6*	19.4*	72.2*	95.4*	100.0*
Osteophytes peripheral	43.0	47.5*	33.0*	40.4	40.2	57.1	3.2*	18.6*	54.6*	81.0*
Schmorl's nodes	9.3	9.4	9.3	4.3	10.5	9.5	12.9*	4.1*	7.4*	19.0*
DISH	5.7	5.9	5.2	4.3	5.3	9.5	0.0*	1.0*	6.5*	15.5*

Statistically significant differences ($p<0.05$) between sex, population or age groups are indicated by *.

One skeleton (AN 503) showed signs of Reiter's syndrome (reactive arthritis) with asymmetrical patches of ligamentous ossification along the vertebral column, unilateral arthritis of the left knee with eburnation, and bilateral sacroiliitis (Figure 5.23). Possible RA was observed in one skeleton (AN 833). In this case severe osteophytes were observed on the cervical vertebrae and wrist, elbow, and ankle joints. Geodes (small circular radiolucent areas) near the wrists, elbows, L5 and left ankle joint could clearly be observed on the Lodox® scan (Figure 5.24).

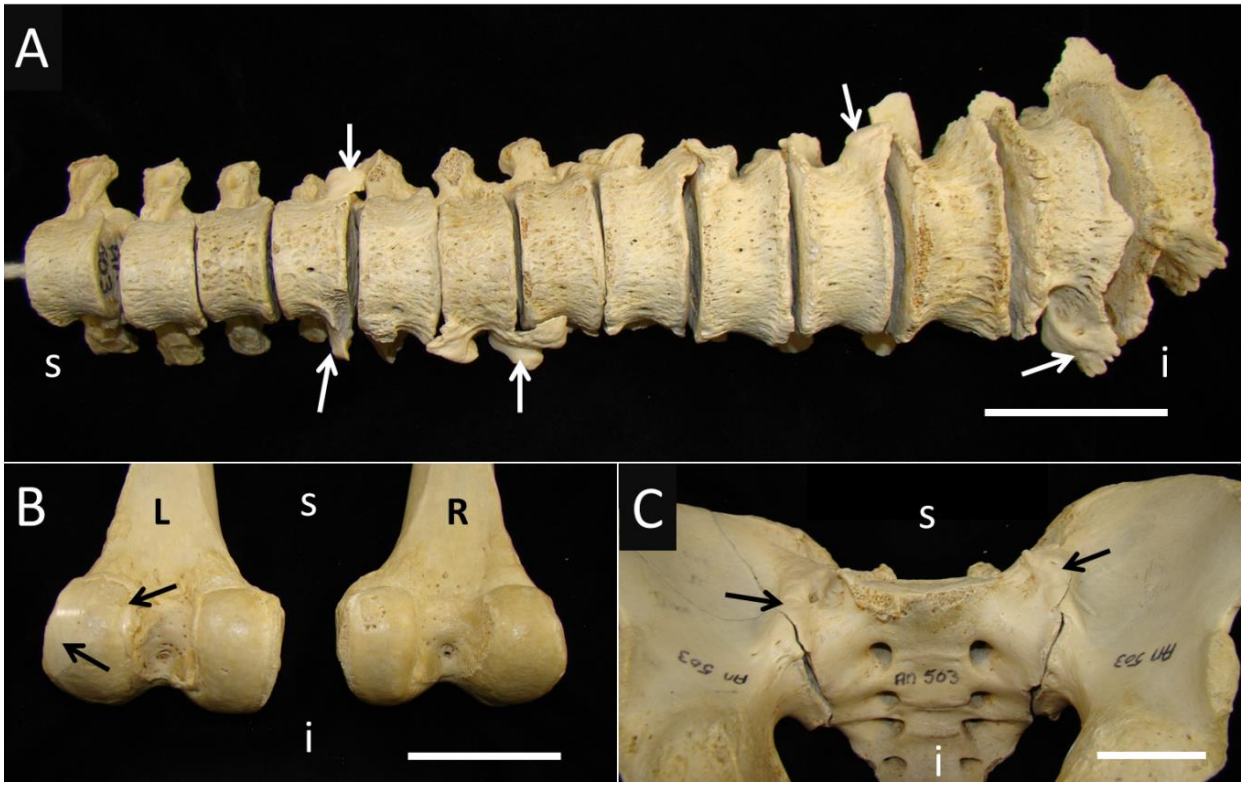


Figure 5.23: Reiter's syndrome
Characteristics of Reiter's syndrome on skeleton AN 503. s=superior. i=inferior. Scale bar=5cm.

A) Digital image of the anterior aspect of the vertebral column from T5-L5. Arrows indicate non-symmetrical patches of ossification along the vertebral column.
B) Digital image of the posterior aspect of the left and right distal femora. Arrows indicate unilateral osteophytes and eburnation. L=left. R=right
C) Anterior digital image of the os coxae and sacrum. Arrows indicate bilateral fusion between the sacrum and iliac bones.

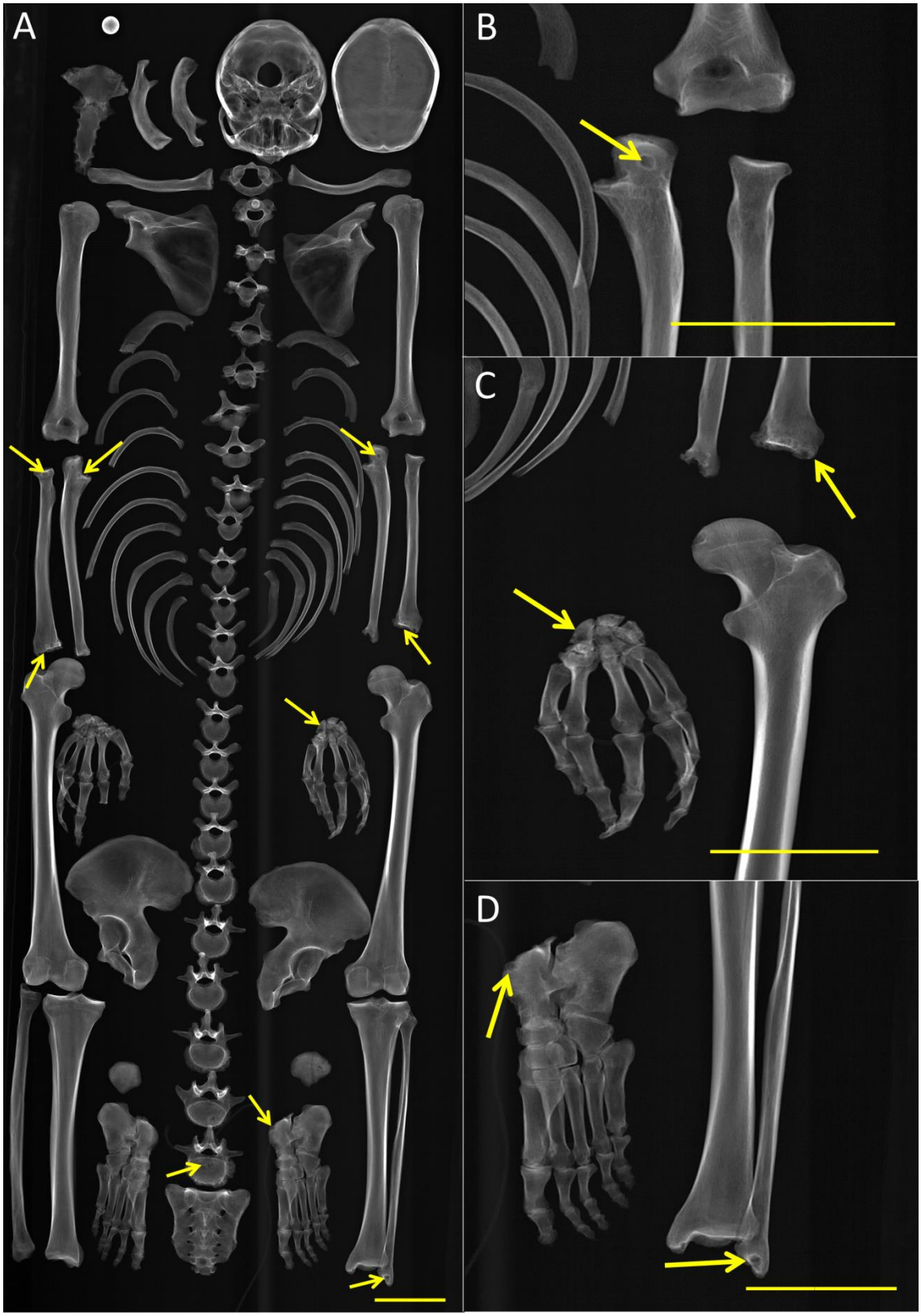


Figure 5.24: Rheumatoid arthritis
Lodox® scan of skeleton AN 833 with possible RA. Arrows indicate geodes commonly observed near joints in individuals with RA. Scale bar=10cm.

A) Full body Lodox® scan
B) Enlargement of the left elbow joint
C) Enlargement of the left wrist
D) Enlargement of the left anckle joint

5.4.1 Vertebral Osteophytes

Marginal osteophytes on at least one vertebral body were observed in 81.0% (n=243) of skeletons with 100.0% of the age group >60 years affected (Table 5.8). These marginal bone changes can result from irritation between vertebrae due to degeneration of the joint. Figure 5.25 illustrates the number of vertebrae with osteophytes for each vertebral group and a statistically significant difference was observed between groups ($p<0.001$). The vertebrae most commonly affected were L3-L5. Figure 5.26 illustrates the percentage of skeletons with each degree of vertebral osteophytes (see Figure 2.16), for each vertebral group.

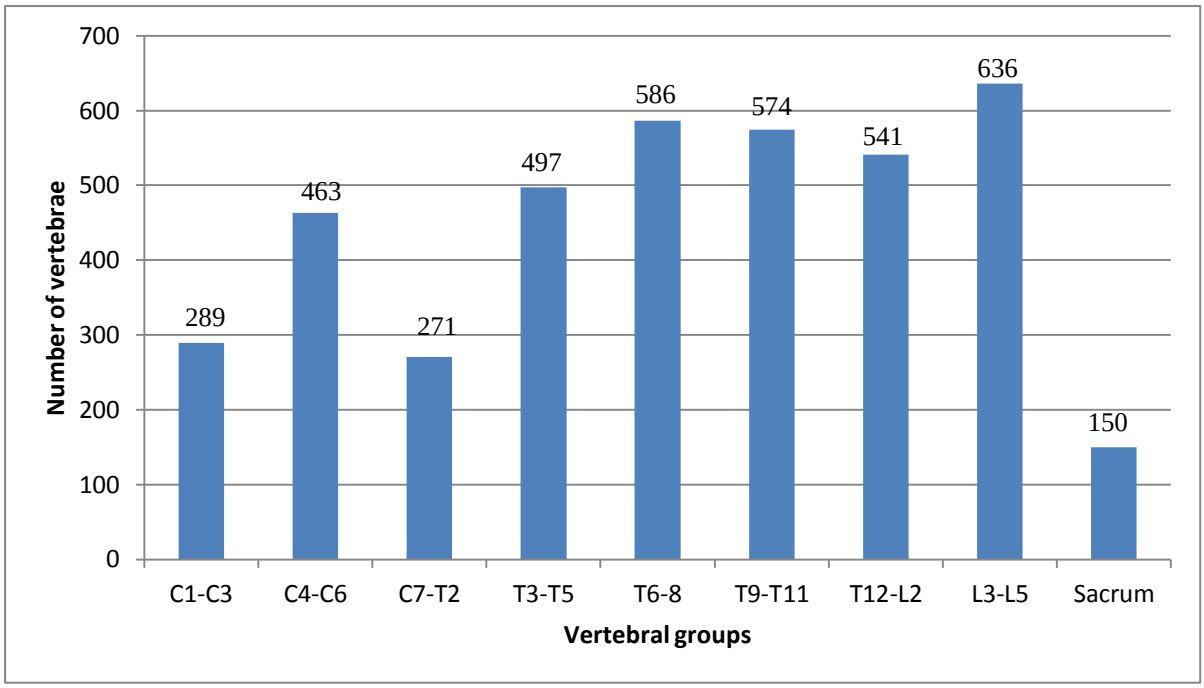


Figure 5.25: Number of vertebrae with osteophytes for each vertebral group
The graph illustrates the number of vertebrae with some degree of osteophytes in each vertebral group. The numbers above the bars indicate the number of vertebrae.

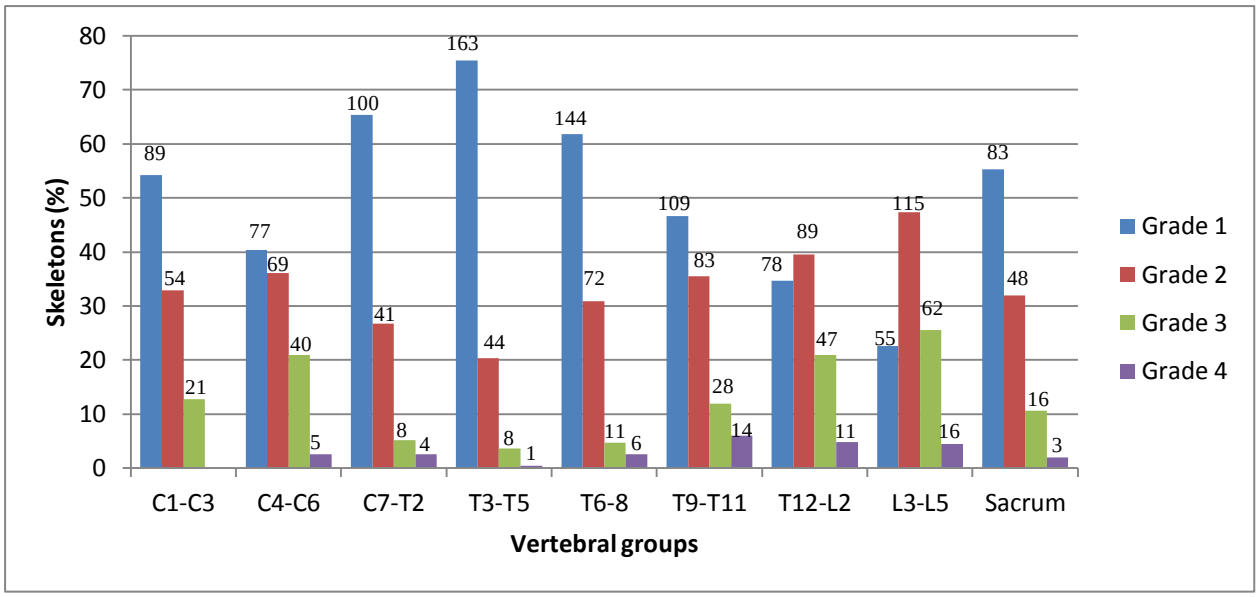


Figure 5.26: Degrees of osteophytes for each vertebral group
The graph illustrates the percentage of skeletons with each grading of vertebral osteophytes for each vertebral group. The numbers above the bars indicate the number of skeletons.

5.4.2 Peripheral Osteophytes and eburnation

Peripheral osteophytes were observed on the margins of synovial joint surfaces throughout the body (e.g. glenoid cavity of the scapula). Eburnation was observed in combination with osteophytes where degeneration of joint surfaces resulted in bone on bone articulation (e.g. knee joint). If eburnation was present, a severity grading of 3 was given for degeneration of that joint. Peripheral osteophytes was found in 43.0% (n=129) of skeletons with 81.0% affected in the age group >60 years (Table 5.8). Figure 5.27 illustrates the number of bones affected for each skeletal element and a statistically significant difference was observed between skeletal elements ($p<0.001$). The patella, scapula and ulna were most affected with osteophytes (Figure 5.27). The small joints of the hands and feet were also commonly affected (Figure 5.27). Figure 5.28 illustrates the percentage of skeletons with each grading of osteophytes for each skeletal element. Eburnation was observed mostly on the condyles of the femur (24.7%) and tibia (27.1%) involved in the knee joint (Figure 5.28).

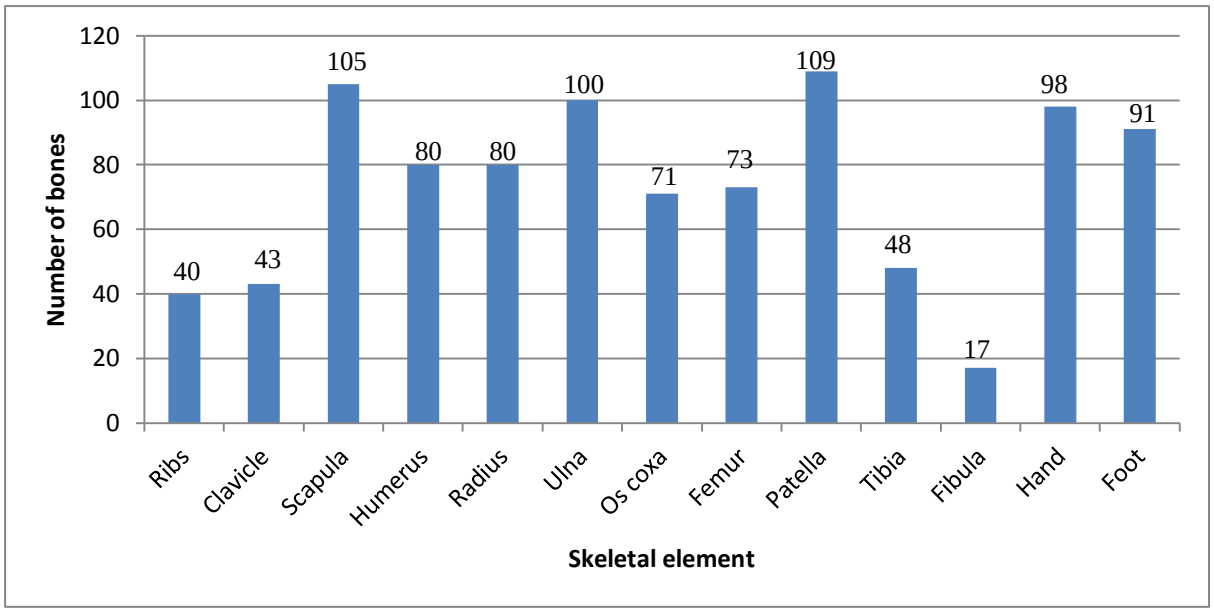


Figure 5.27: Number of bones with osteophytes for each skeletal element
The graph illustrates the number of bones with osteophytes for each skeletal element. The numbers above the bars indicates the number of bones.

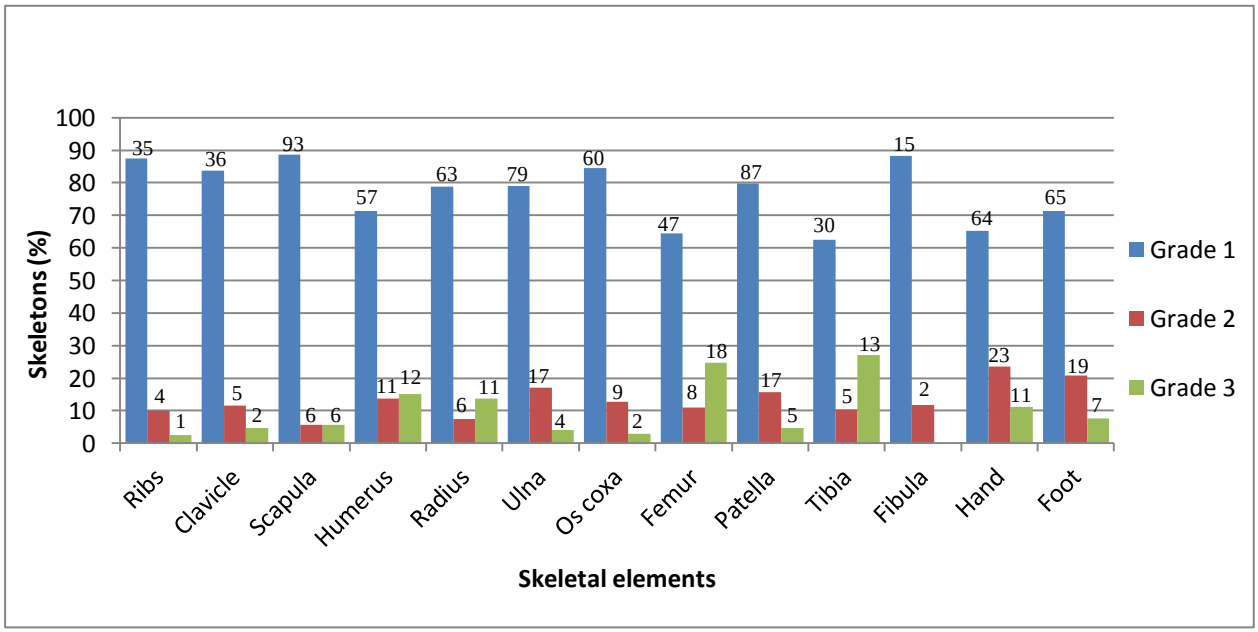


Figure 5.28: Grading of osteophytes for each skeletal element
The graph illustrates the percentage of skeletons presenting with each grading of osteophytes for skeletal elements. The numbers above the bars indicates the number of skeletons.

5.4.3 Schmorl's nodes

Schmorl's nodes were observed macroscopically as indentations in the vertebral bodies. Radiologically a small circular radiolucent area was visible on the vertebral bodies affected (Figure 5.29). Possible Schmorl's nodes were observed in 9.3% (n=28) of the skeletons (Table 5.8). Table 5.9 shows the number of vertebrae in each vertebral group with Schmorl's

nodes. The vertebrae most commonly affected was L3-L5 (n=14) with 42.9% of skeletons with Schmorl's nodes having this region affected. The second most commonly affected region was T12-L2 (n=10) with 28.0% of all skeletons with Schmorl's nodes having this region affected.

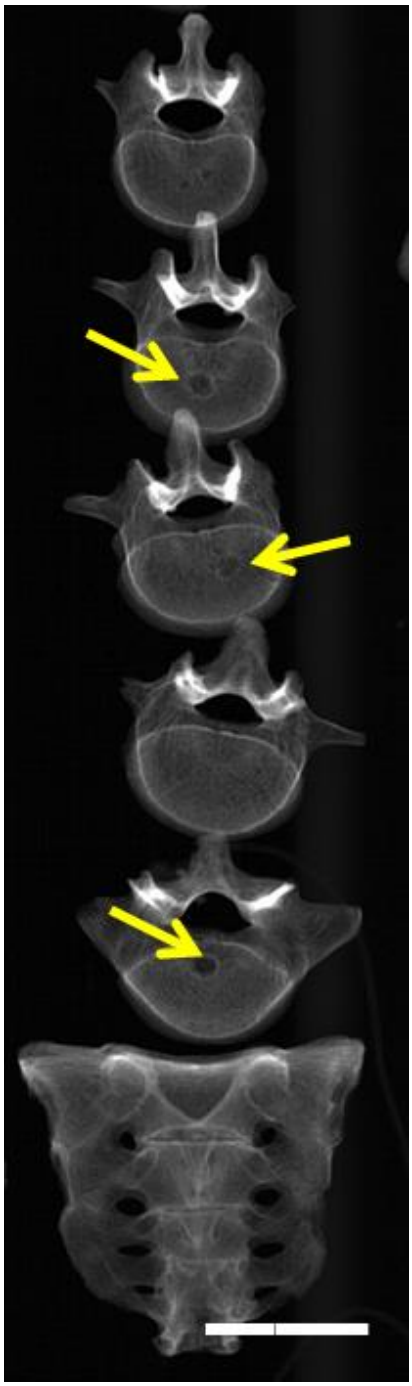


Figure 5.29: Schmorl's nodes
Superior-inferior radiograph (Lodox® scan) of the lumbar vertebrae and anterior-posterior of the sacrum of skeleton AN 657. Arrows indicate Schmorl's nodes on the vertebral bodies. Scale bar=5cm.

Table 5.9: Number of vertebrae with Schmorl's nodes for each vertebral group

Vertebral group	Number of vertebra
C1-C3	0
C4-C6	2
C7-T2	3
T3-T5	1
T6-T8	7
T9-T11	5
T12-L2	10
L3-L5	14

5.4.4 Diffuse idiopathic skeletal hyperostosis

Diffuse idiopathic skeletal hyperostosis was observed in 5.7% (n=17) of vertebral columns with 15.3% of the age group >60 affected (Figure 5.30) (Table 5.8). No skeletons under the age of 31 showed any signs of DISH. Ossification of the anterior longitudinal ligament occurred on the lower thoracic vertebrae in all the cases with the upper lumbar vertebrae also involved in six cases.

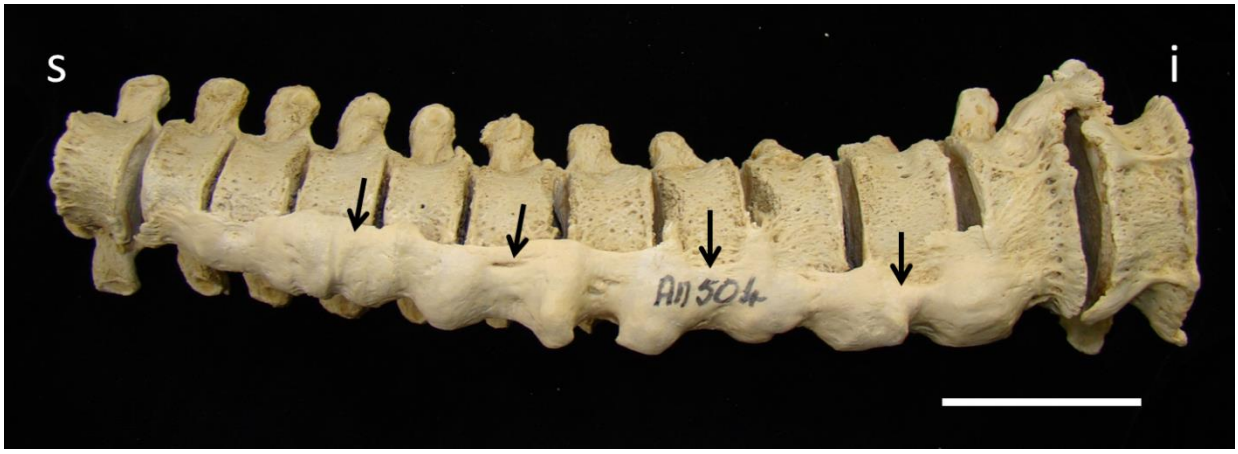


Figure 5.30: Diffuse Idiopathic Skeletal Hyperostosis
Digital image of the anterior aspect of the vertebral column from T6-L5 of skeleton AN 504. Arrows indicate the ossified anterior longitudinal ligament. s=superior. i=inferior. Scale bar=5cm.

5.5 NEOPLASMS

Signs of neoplasms were observed in 23.3% of the skeletons examined. These were divided into primary benign bone tumours, primary malignant bone tumours, and secondary skeletal metastases. Table 5.10 gives the percentage of skeletons with neoplasms for each sex, age, and population group. No statistical significance ($p<0.05$) was observed for neoplasms between any of the sex, age, and population groups.

Table 5.10: Percentage of skeletons with neoplasms for each sex, population, and age group

		Sex		Population group			Age			
Neoplasms	**All**	**M**	**F**	**Black**	**Mixed**	**White**	**<31**	**31-45**	**46-60**	**>60**
Primary benign	17.7	16.8	19.6	27.7	15.8	14.3	12.9	21.7	13.9	20.7
Primary malignant	1.0	1.0	1.0	0.0	1.4	0.0	0.0	0.0	2.8	0.0
Metastases	5.3	5.0	6.2	2.1	5.7	7.1	0.0	6.2	5.6	6.9

5.5.1 Primary benign neoplasm

Primary benign neoplasms were observed on the Lodox® scans as localized small tumours with well-defined margins. Only some of the neoplasms were visible macroscopically (e.g. BO). Possible primary benign neoplasms occurred in 17.7% (n=53) of the skeletons. These include BO (9.7%), osteochondroma (2.3%), geodes (1.3%), bony island/enostosis (3.7%), enchondroma (0.7%), lipoma (2.0%) and ganglia (1.3%) (Figure 5.31). The black population group showed the highest percentage (27.7%) of overall benign neoplasms, however, this was not statistically significant (p=0.051).

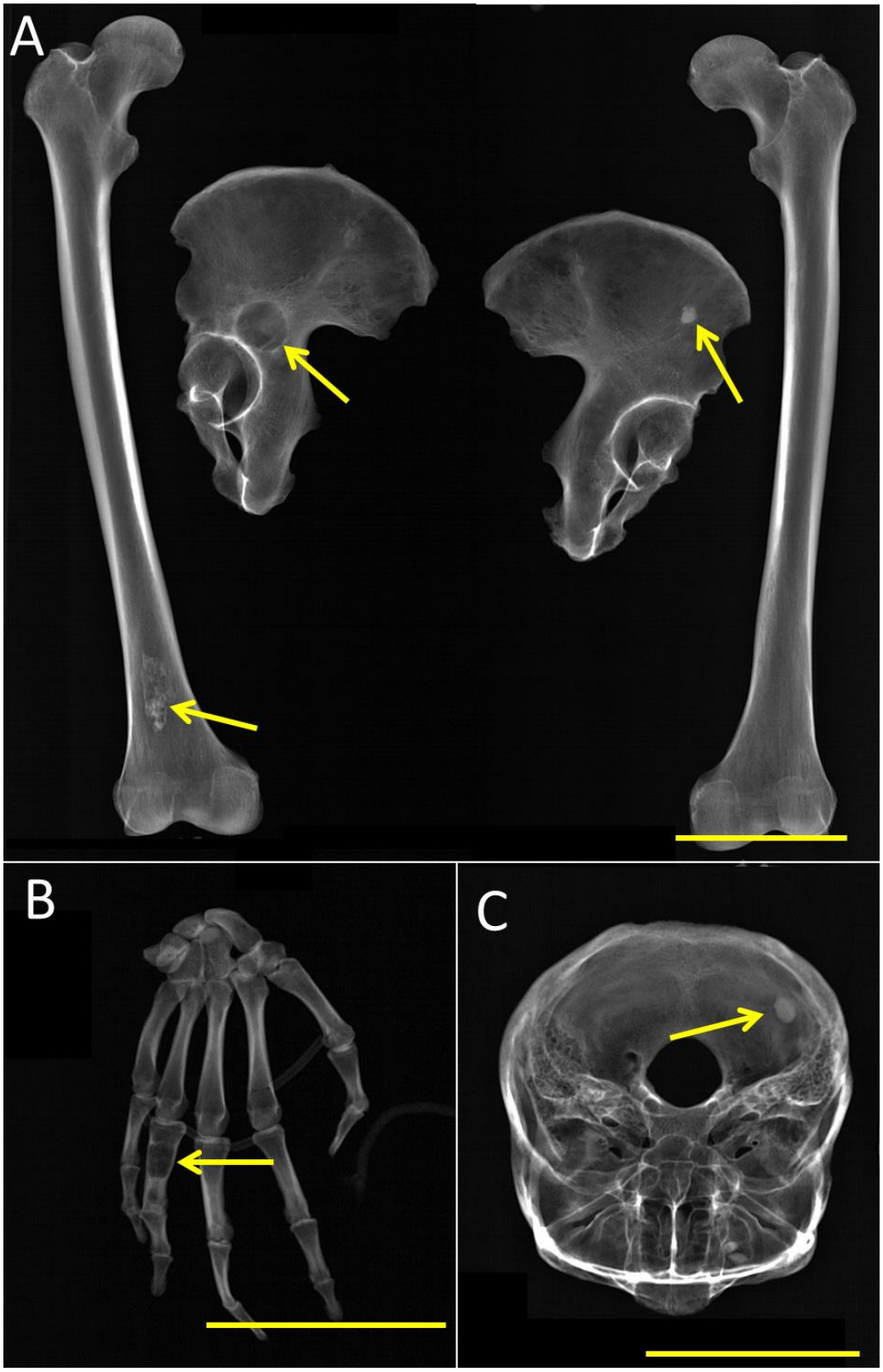


Figure 5.31: Primary benign neoplasms
Radiographs (Lodox® scans) of different primary benign neoplasms. Scale bar=10cm.

A) Anterior-posterior view of the femora and os coxae of skeleton AN 261. Arrows indicate an enchondroma in the distal aspect of the shaft of the right femur, a lipoma on the right os coxa, and bony island on the left os coxa. R=right. L=left.
B) Anterior-posterior radiograph of the right hand of skeleton AN 234. The arrow indicates an enchondroma of the proximal phalanx.
C) Superior-inferior radiograph of the skull of skeleton AN 590. The arrow indicates a BO.

5.5.2 Primary malignant neoplasm

Three cases (1.0%) of primary malignant neoplasms were observed. One case presented with a chondrosarcoma in the proximal shaft of the right femur (Figure 5.32). A second chondrosarcoma was observed in the proximal shaft of the left humerus. Both tumours illustrated cortical scalloping and expansion of the bone. An osteoblastic osteosarcoma of the maxilla was observed in the third case. This presented as a jagged bone growth on the left palate and in the maxillary sinus, protruding into the left orbit (Figure 5.33).

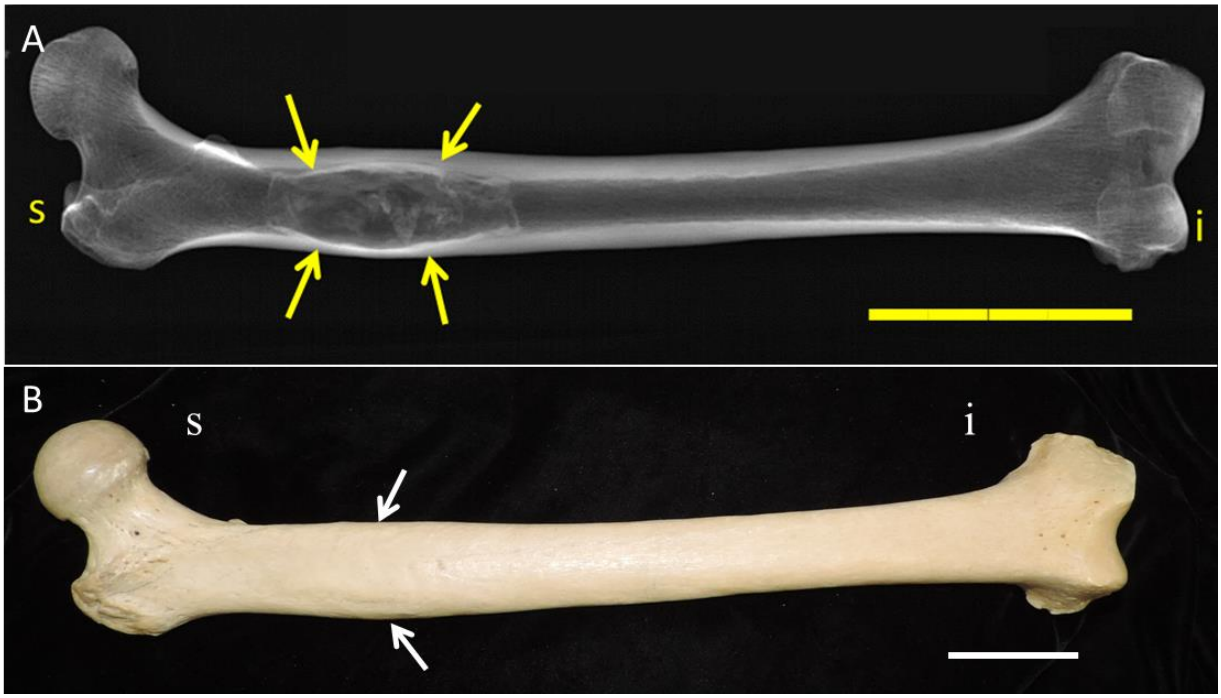


Figure 5.32: Chondrosarcoma
Right femur of skeleton AN 645. s=superior. i=inferior.
A) Anterior-posterior radiographs (Lodox® scan) of the right femur of skeleton AN 645. Arrows indicate the chondrosarcoma with cortical scalloping and bone expansion. Scale bar=10cm
B) Digital image of the anterior aspect of the right femur. Arrows indicate a visible expanded area of bone. Scale bar=5cm.

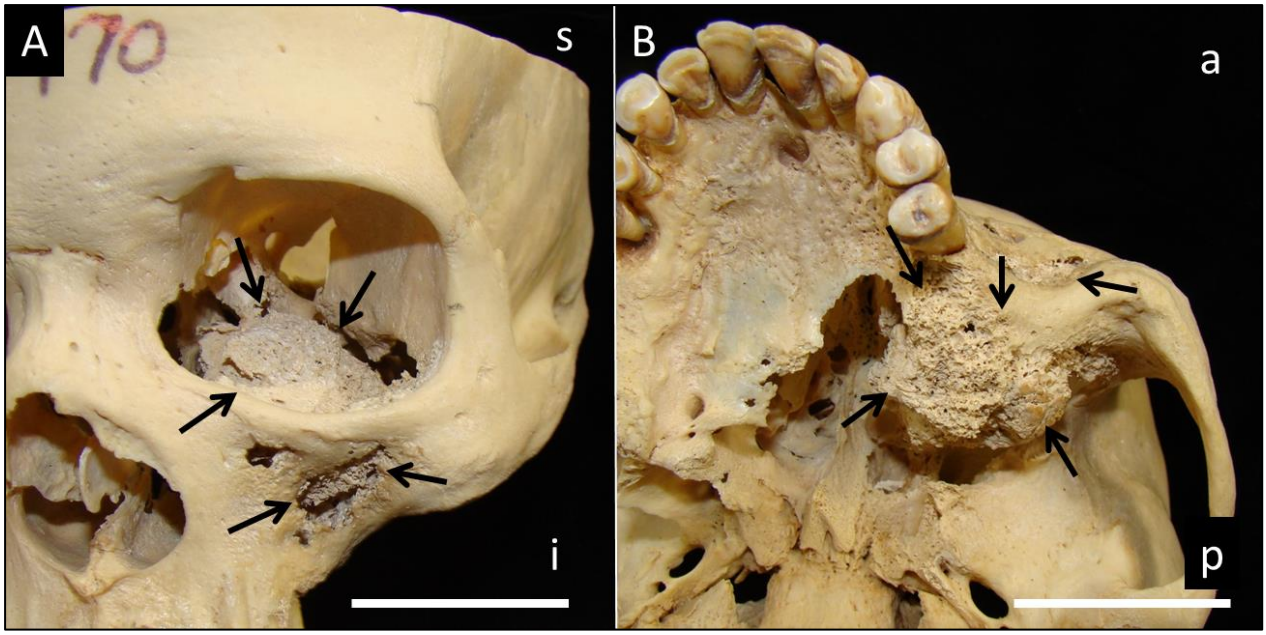


Figure 5.33: Osteosarcoma
Digital images of an osteosarcoma of skeleton AN 770. Scale bar=5cm.

A) Anterior view of the floor of the left orbit and maxilla. The arrows indicate the extent of the osteosarcoma in this view. s=superior. i=inferior.
B) Inferior view of the hard palate and maxilla. The arrows indicate the extent of the osteosarcoma in this view. a=anterior. p=posterior.

5.5.3 Skeletal metastases

Metastases to the skeletal system was observed in 5.3% (n=16) of the skeletons examined. Lesions occurred as either lytic or lytic combined with a sclerotic appearance on radiographs (Figure 5.34). Nine skeletons had a documented COD of cancer in the oral/pharyngeal/laryngeal area of which 55.6% (n=5) showed skeletal metastases. Metastases were located mostly in the skull and mandible with one skeleton also showing lesions on the vertebrae and os coxae. Of the 13 skeletons with bronchus carcinoma as a documented COD, 38.5% (n=5) showed skeletal metastases with the skull, ribs and os coxae affected the most. Skeletal metastases were observed in 21.4% (n=3) of the skeletons with a documented COD of cervical cancer (n=14). All three cases had lesions on the vertebrae and os coxae, and the ribs and scapulae were also affected in two of the cases. One out of five skeletons (20.0%) with lung cancer as a documented COD as well as the only skeleton with a documented COD of breast cancer showed skeletal metastases. No metastases were observed in skeletons with a documented COD of oesophageal or gastro-intestinal tract carcinomas. Table 5.11 summarizes the bones affected by metastases for the different types of primary carcinomas. No statistical analysis was performed between the types of primary cancers or bones affected by metastases due to small sample size.

Table 5.11: Number of skeletons with bones affected by metastases

	Primary carcinoma site						
Metastases site	**Bronchus**	**Tongue/ Pharynx /Larynx**	**Lung**	**Breast**	**Cervix**	**Other**	**All**
Skull	4	2	1	1	1	1	**10**
Mandible	1	3	0	1	1	0	**6**
Ribs	3	0	1	1	2	0	**7**
Vertebrae	2	1	1	1	3	0	**8**
Scapulae	1	0	0	1	2	0	**4**
Os coxae	4	1	0	1	3	0	**9**
Lower extremities	2	0	1	1	1	1	**6**
Upper extremities	1	0	0	0	1	0	**2**

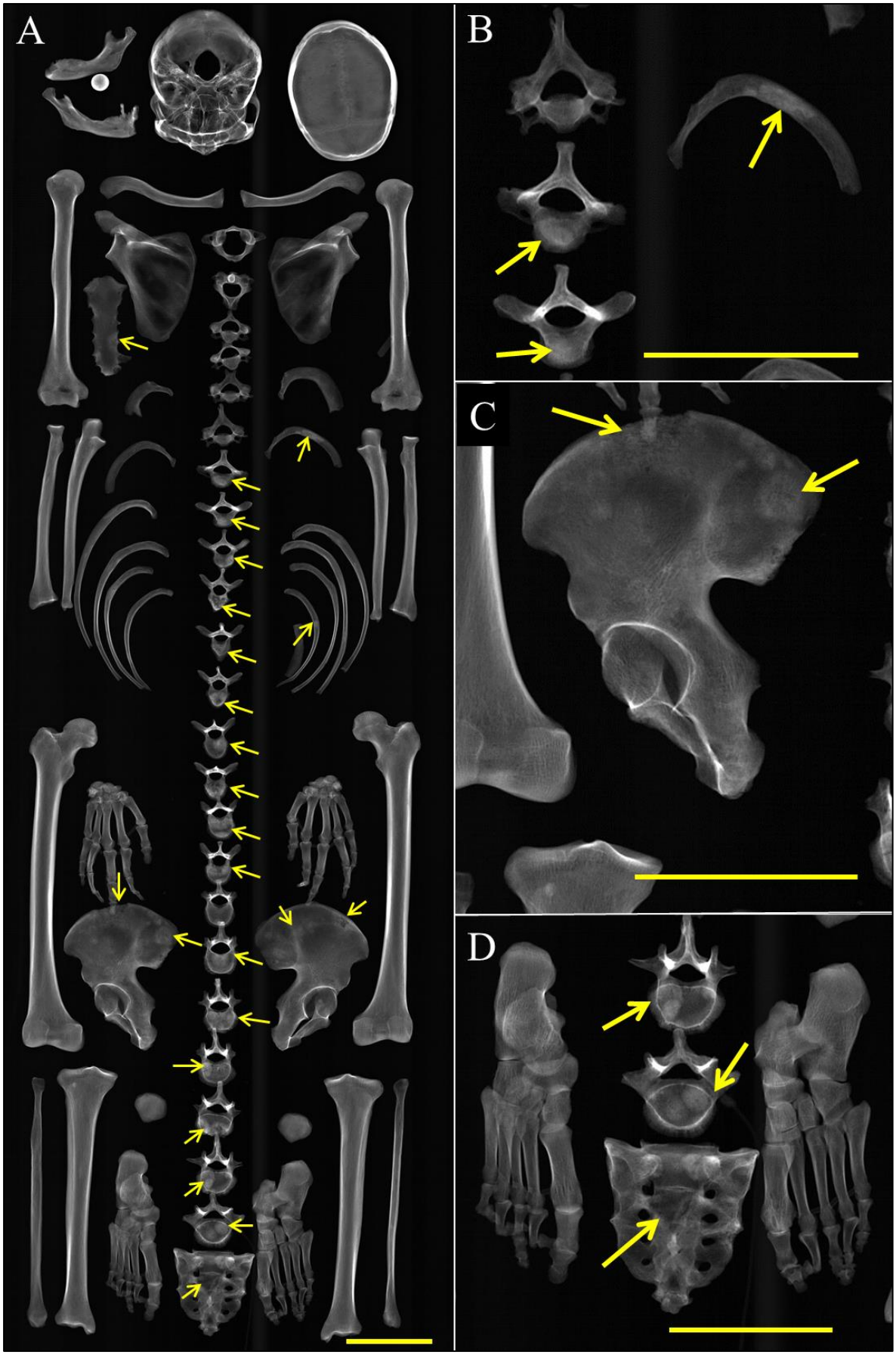


Figure 5.34: Skeletal metastases from bronchus carcinoma

Signs of skeletal metastases from bronchus carcinoma in skeleton AN 666. The arrows indicate lytic and sclerotic lesions of skeletal metastases. Scale bar=10cm.
A) Full body Lodox® scan of skeleton.
B) Enlarged image of vertebrae C7-T2 and left rib 2.
C) Enlarged image of the right os coxa.
D) Enlarged image of vertebrae L1-2, sacrum and feet.

5.6 MISCELLANEOUS CONDITIONS

Only one miscellaneous condition was observed and described namely Paget's disease.

5.6.1 Paget's disease

Signs of Paget's disease, which could be observed radiologically, were found in two cases. A further two cases showed signs of Paget's disease histologically giving a total of four possible cases of Paget's disease. One case was observed in a 50-year-old female and the other three cases in 66-, 63-, and 44-year-old males. The left os coxa was affected in two cases with one case in which the fourth lumbar vertebra was affected as well (Figure 5.35). The os coxae and lumbar vertebra had a "cotton wool" appearance, resulting from combined lytic and sclerotic lesions, on the radiographs. The cranium (frontal bone) was affected in another two cases. Macroscopic thickening of the inner surface of the frontal bone could be observed on the crania. Histologically, Paget's disease was identified by unorganized bone deposition and mosaic appearance of bone structure (Figure 5.36).

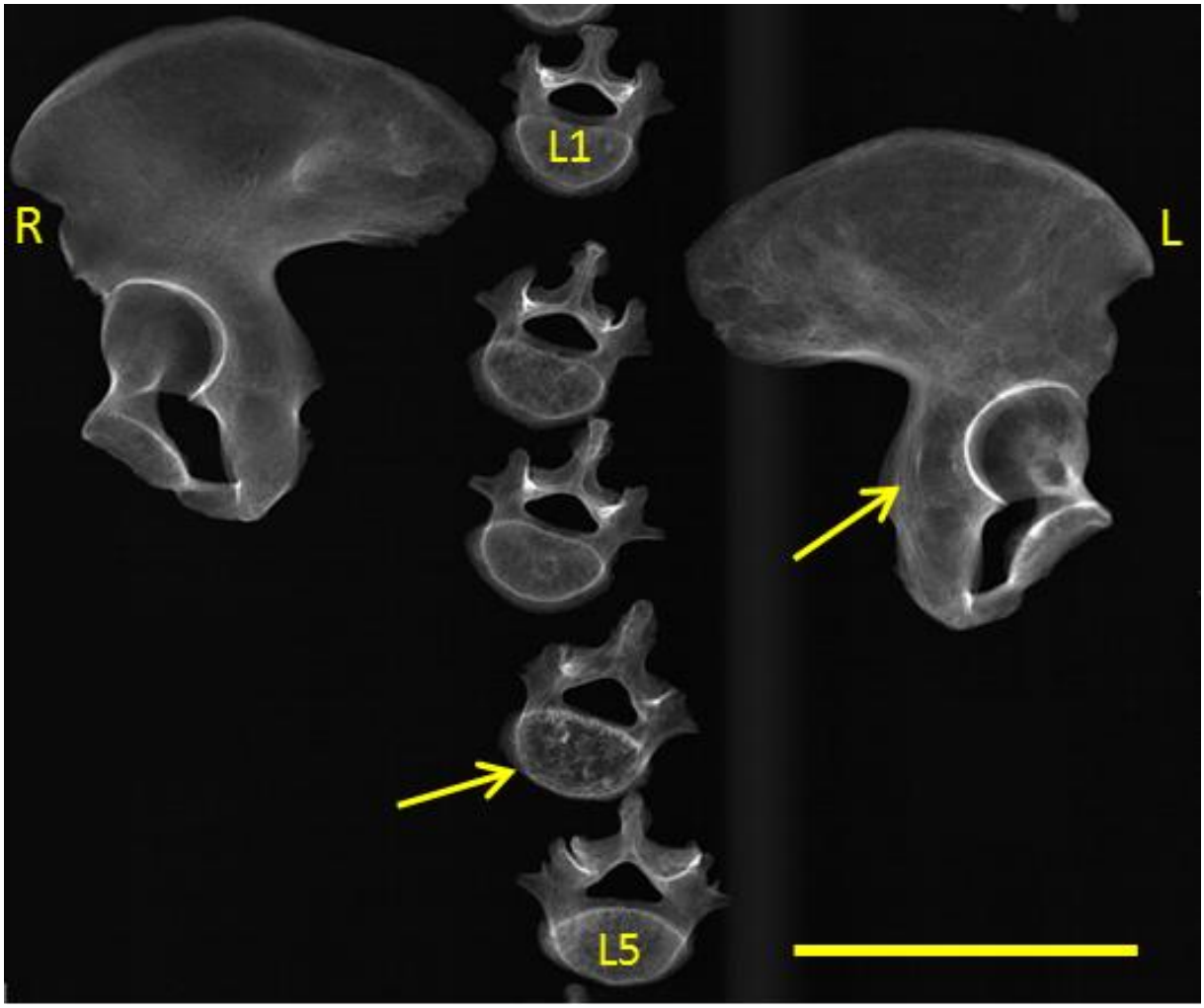


Figure 5.35: Paget's disease
Lodox® scan of skeleton AN 251. The arrows indicate the bones affected by Paget's disease. R=right. L=left. L1=lumbar vertebra 1. L5=lumbar vertebra 5. Scale bar=10cm.

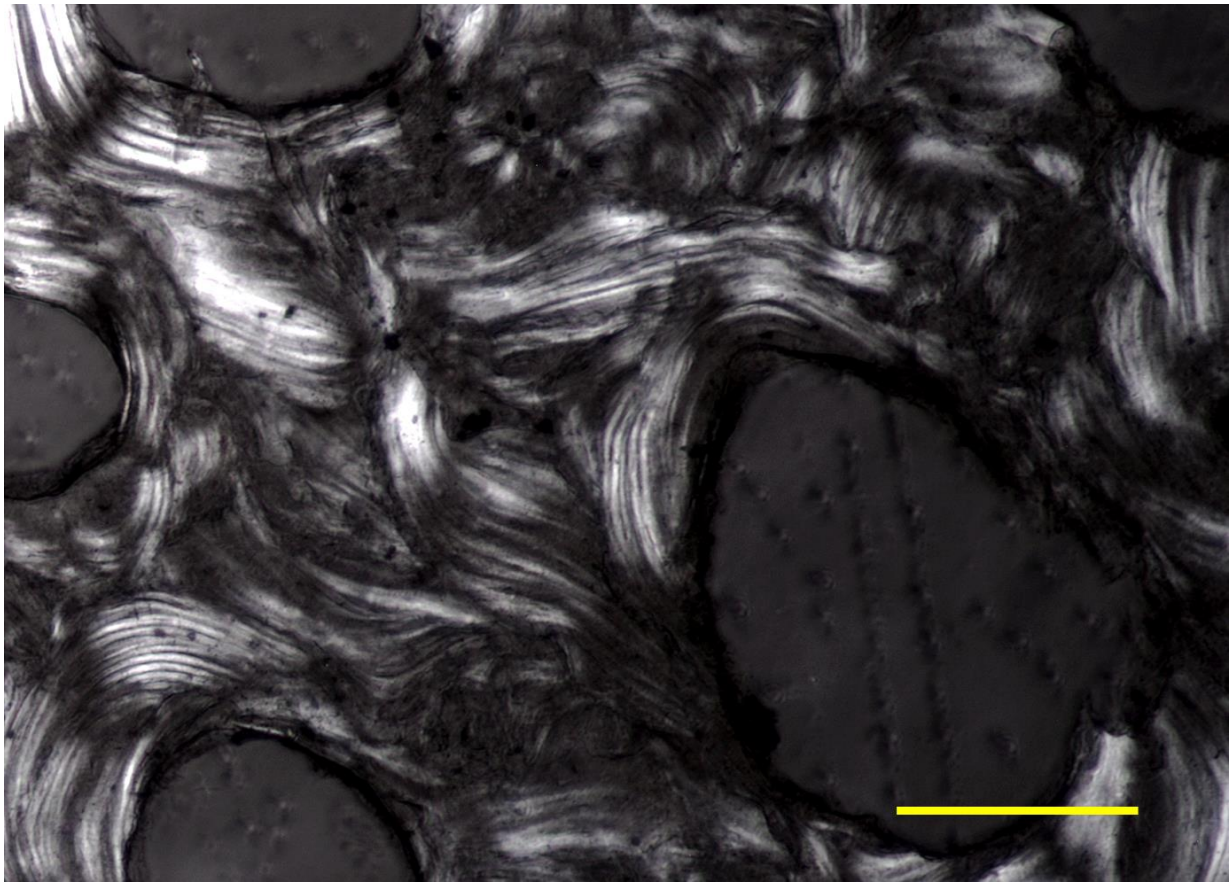


Figure 5.36: Dry bone histology of Paget's disease
Microphotograph of the left os coxa of AN 578 illustrating unorganized bone deposition with few complete osteons. Image taken with a Nikon® light microscope with DCI contrast at 80X magnification. Scale=200µm.

Chapter 6 DISCUSSION

Skeletons in the present study form part of the Kirsten Skeletal Collection at Stellenbosch University and were obtained between the years 1967 and 2000. Most of these skeletons were received from teaching hospitals as unclaimed bodies. The results of this study might, therefore, represent a biased population of low socio-economic status in the Western Cape, rather than the general population of the region (Labuschagne & Mathey, 2000; Pfeiffer *et al*., 2016). Conditions associated with low socio-economic standards include poor and overcrowded living spaces, poor hygiene and sanitation, malnutrition, low levels of education, and alcohol abuse (Labuschagne & Mathey, 2000; Pfeiffer *et al*., 2016).

Between the years 1948 and 1994, it was likely that individuals of the present study lived under the apartheid government where they were separated according to race. The socio-economic standards and living conditions would be expected to have differed between the different population groups of the time. More than two-thirds of the study population represented the mixed population, or indigenous Cape Coloured group. This group show a mixture of genetic influences from Khoisan, Bantu, European and Indian origins (Pfeiffer *et al*., 2016). Few previous studies have been able to compare diseases of a population group of such mixed ancestry and unique to the Western Cape, with other population groups from that region (Labuschagne & Mathey, 2000).

An age bias exists between the different population groups used in the present study as the white group have an older mean age at death than the black and mixed population groups (see Table 4.3). Any diseases that are age dependent were difficult to compare between population groups due to the above-mentioned age bias.

This chapter will further discuss each disease or disorder separately and compare it with previous research.

6.1 CONGENITAL OR ACQUIRED MALFORMATIONS

Congenital or acquired malformations occur generally in the axial skeleton, with preference to the vertebral column due to its complex embryology and structure (Kaplan *et al*., 2005). The results of the current study in which almost all of the defects occurred in the vertebral column, illustrate the common occurrence of defects in the axial skeleton with approximately half of the study population presenting with at least one defect.

6.1.1 Lumbosacral transitional vertebrae

In the current study, lumbosacral transitional vertebrae as an entity were observed in 19.3% of the skeletal sample. This falls well within the range of 4.0%-35.0% for lumbosacral transitional vertebrae observed in previous studies, as summarized by Bron *et al.* (2007). The accuracy of diagnosing lumbosacral transitional vertebrae depends on the method of classification which could have contributed to the wide range in prevalence observed in previous studies (Bron *et al.*, 2007).

A number of studies differentiated between sacralisation and lumbarisation (Leboeuf *et al.*, 1989; Hahn *et al.*, 1992; Kim & Suk, 1997; Peh *et al.*, 1999; Santiago *et al.*, 2001; Chithriki *et al.*, 2002; Steinberg *et al.*, 2003; Taskaynatan *et al.*, 2005; Hughs & Saifuddin, 2006; Sharma *et al.*, 2011; Kubavat *et al.*, 2012). The findings of the present study agrees with most studies in which a higher prevalence of sacralisation than lumbarisation was observed (Hahn *et al.*, 1992; Kim & Suk, 1997; Santiago *et al.*, 2001; Chithriki *et al.*, 2002; Steinberg *et al.*, 2003; Taskaynatan *et al.*, 2005; Hughs & Saifuddin, 2006; Sharma *et al.*, 2011; Kubavat *et al.*, 2012). Only a few studies found the opposite, such as a study by Peh *et al.* (1999) in Hong Kong and a study by Leboeuf *et al.* (1989) in Sydney. Bron *et al.* (2007) calculated a mean prevalence for sacralisation and lumbarisation in existing studies and found the prevalence to be 7.5% and 5.5% respectively. These means are slightly lower than the values found in the current study. This may be as a result of the exclusion of type I lumbosacral transitional vertebrae in some of the previous studies (Vergauwen *et al.*, 1997; Hsieh *et al.*, 2000).

In the present study, type III lumbosacral transitional vertebrae were observed the most, followed by type II (see Figure 5.4). This differed from a study by Hughs & Saifuddin (2006) who observed type II to occur most frequently (54.6%) followed by type III (24.8%), while type I (10.6%) and type IV (10.0%) were observed the least. In studies by Peterson *et al.* (2005) and Quinlan *et al.* (2006) type II also occurred more than the other types of lumbosacral transitional vertebrae. Aihara *et al.* (2005) observed the same number (46.2%) of type II and III lumbosacral transitional vertebrae with type IV only observed in four of their cases (7.7%). Sharma *et al.* (2011) observed type III the most (44.7%) which correlates with the present study; however, in the study by Sharma *et al.* (2011) type III was closely followed by type I (36.4%) which occurred less in other studies. As mentioned above, the prevalence of type I appearing high may be the result of misdiagnosis of type I lumbosacral transitional vertebrae in previous studies.

6.1.2 Spina bifida

Groza *et al.* (2012) stated that spina bifida is the most common congenital malformation of vertebrae. This is reflected in the current study as well, with spina bifida showing the highest prevalence compared to the other congenital malformations. Eubanks & Cheruvu (2009) observed spina bifida occulta in 12.4% of specimens studied with males affected more than females. Males were also affected more than females in several other studies (Lorber & Levick, 1967; Vannier *et al.*, 1981; Fidas *et al.*, 1987). The present study found the opposite, namely that males (12.9%) are affected slightly less than females (16.5%), even with the lower number of females in the current study population (see Table 4.1). This correlates with a statement by Groza *et al.* (2012) that females are more prone to conditions such as anencephaly and spina bifida than men. Several factors may influence the presentation of these defects including a genetic predisposition or maternal nutritional and environmental factors (Groza *et al.*, 2012). Stinson (1985) found that males are more sensitive to prenatal environmental and nutritional factors which suggest that males would be more prone to conditions such as spina bifida.

Shin *et al.* (2008) observed a higher prevalence of spina bifida in their white than their black study group in the USA. The findings of Eubanks & Cheruvu (2009) showed the same predominance for spina bifida in white individuals, which correlates with the present study in which the white group is affected statistically significantly more ($p=0.008$) than the black group (see Table 5.2). The prevalence of spina bifida in the mixed population group (13.4%) is approximately half of that of the white group (28.6%) and three times that of the black group (4.3%), illustrating a possible combined ancestry contribution from both, although, this is not necessarily the only contributing factor to the difference in prevalence.

Boone *et al.* (1985) and Eubanks & Cheruvu (2009) observed a decrease in spina bifida with age. A possible reason for this may either be calcification of connective tissue structures or the formation of new bone, thereby closing off the neural arch malformation as aging progresses (Boone *et al.*, 1985). In the present study, no decrease in the prevalence of spina bifida was observed with an increase in age.

Groza *et al.* (2012) stated that spina bifida occurs more in the lumbosacral region than in the cervico-thoracic region with the sacrum affected the most. This was observed in several previous studies (Carr, 1956; Boone *et al.*, 1985; Shin *et al.*, 2008) as well as in the present study. Due to the high prevalence of spina bifida in the lumbosacral region, most research

focused on this region alone. The current study found 8.3% of sacra with spina bifida which falls in the prevalence range observed in previous studies (1.0%-30.0%), summarized by Albrecht *et al*. (2007). The wide range described by various researchers may be due to a difference in the classification of spina bifida. The present study classified a sacrum as having spina bifida if at least one or more of the neural arches of S1, S2, or S3 were open, while open S4 and S5 segments were seen as normal variations. Some studies classified a sacrum as having spina bifida only if the S1 segment was open, regardless of its presence in any of the other segments (Vannier *et al*., 1981; Saluja, 1988; Avrahami *et al*., 1994; Papp & Porter, 1994; Henneberg & Henneberg, 1999) while other studies included S2 and S3 to the definition (Boone *et al*., 1985; Fidas *et al*., 1987; Schweitzer *et al*., 1993). Few studies included only sacra of which all segments were open (Trotter, 1947). Possible reasons for the different classifications could be the author's opinion (observer error) on what is considered normal anatomical variation, or the ability to visualise the different sacral segments with the methods used.

6.1.3 Scoliosis and Kyphosis

Scoliosis and kyphosis can either be a congenital or an acquired disorder. Congenital kyphosis and scoliosis is uncommon (Aufderheide & Rodríguez-Martin, 1998) and therefore the discussion will focus on scoliosis and kyphosis as acquired conditions. The prevalence of scoliosis can range from 1.0%-42.8% of individuals (Daruwalla *et al*., 1985; Morais *et al*., 1985). It differs depending on the age and population group studied, as well as the degree of curvature considered as diagnostic for scoliosis (Daruwalla *et al*., 1985; Morais *et al*., 1985; Kebaish *et al*., 2011). Several studies observed an increase in the prevalence of scoliosis (Daruwalla *et al*., 1985; Morais *et al*., 1985; Kebaish *et al*., 2011) as well as the prevalence and severity of kyphosis with age (Fon *et al*., 1980). One of the contributing factors to this increase in scoliosis and kyphosis with age is a decrease in bone mineral density (BMD) as age progresses (Milne & Lauder, 1976; Bartynski *et al*., 2005). This allows for compression of vertebrae resulting in increased curvature of the vertebral column (Milne & Lauder, 1976; Bartynski *et al*., 2005; Curate *et al*., 2014).

Several studies indicated that acquired scoliosis is more common in females than in males (Daruwalla *et al*., 1985; Morais *et al*., 1985; Wong *et al*., 2005). Kebaish *et al*. (2011), however, found that the prevalence is similar for both males and females, as also observed in the current study (see Table 5.2). Kyphosis was previously observed more in females than in males after the age of 40 years (Fon *et al*., 1980). In the present study there was a slight

female predominance for kyphosis even with the lower number of females in the current study population. Possible reasons for a higher prevalence for kyphosis in females include physical inactivity, decreased muscle tone, breast weight, and a higher prevalence of osteoporosis in post-menopausal women (Milne & Lauder, 1976; Fon *et al*., 1980). Physical inactivity can be one of the factors leading to decreased ligament and muscle tone which results in decreased soft tissue support to the vertebral column (Milne & Lauder, 1976; Fon *et al*., 1980). Breast weight would increase the strain on the thoracic vertebrae and together with a loss of BMD in osteoporosis, could increase fracture rates (Fon *et al*., 1980).

Scoliosis was observed more in the white than black group in a study by Kebaish *et al*. (2011). The present study however, showed a slightly higher prevalence of scoliosis in the black (8.5%) than the white group (7.1%). This may be as a result of the relative small sample size in both the black and white groups in the present study (see Table 4.1) compared with that of Kebaish *et al*. (2001) who included 2973 individuals in the study group. Environmental factors and lifestyle causing asymmetrical strain on the vertebral column could increase the prevalence of scoliosis (Stehbens, 2003) and may have influenced the higher prevalence in the black group. Kyphosis on the other hand was observed statistically significantly more ($p=0.046$) in the white than the other two groups in the present study (see Table 5.2). As the prevalence of kyphosis increases with age (Fon *et al*., 1980), this can be explained by the older mean age of the white group compared to the other two groups in the present study.

6.1.4 Spondylolysis

A prevalence of spondylolysis ranging from 3.7%-54.0% was observed in previous studies due to differences in environment and lifestyle of different study population groups (Fibiger & Knüsel, 2005). A high prevalence ranging from 15.0%-54.0% was observed in studies on groups in Alaska, Canada, and Greenland (Stewart, 1953; Lester & Shapiro, 1968; Kettelkamp & Wright, 1971; Gunness-Hey, 1980; Simper, 1986; Merbs, 2002). Studies in the United Kingdom showed a prevalence of 3.7%-17.0% (Waldron, 1991a; Fibiger & Knüsel, 2005) and in Japanese studies the prevalence ranged from 7.0%-12.8% (Arriaza, 1997; Suzuki, 1998). A lower overall prevalence of 3.5% was observed in a study by Eisenstein (1978) on a South African population group, which corresponds to the findings of the present study (2.7%). Comparing population groups, Eisenstein (1978) observed a higher prevalence in the white than the black group in a ratio of 2:1; however, the present study observed a similar prevalence for both white (3.4%) and black (2.1%) groups as well as the mixed

population group (2.9%). Differences between the occurrences of spondylolysis in different population groups may suggest difference in lifestyle and strenuous activities associated with that lifestyle.

Most studies, including the present study, found a higher frequency of spondylolysis in males than females (Stewart, 1953; Lester & Shapiro, 1968; Kettelkamp & Wright, 1971; Gunness-Hey, 1980; Merbs, 2002). The higher frequency of spondylolysis in males may be due to differences in the gender roles in a society. Males would generally take part in more strenuous activities which is associated with the occurrence of spondylolysis (Mays, 2006).

According to Merbs (1996) and Mays (2006), clinical studies suggest an early onset of spondylolysis from as young as ages 5-6 years with prevalence increasing with age. Contrary to this, several archaeological studies found a later onset of spondylolysis with children rarely affected (Stewart, 1953; Lester & Shapiro, 1968; Kettelkamp & Wright, 1971; Gunness-Hey, 1980). The present study found no cases of spondylolysis in individuals under the age of 30 years, thereby suggesting onset at an older age. Spondylolysis may occur as fatigue fractures which continue to form a complete separation (Merbs, 1996; Mays, 2006). This is a possible explanation for the increase of spondylolysis with age (Merbs, 2002). Incomplete separation can, however, fuse again which will decrease the prevalence of spondylolysis (Merbs, 1996).

In several studies the fifth lumbar vertebra was observed to be the most affected, followed by L4 and L3 (Stewart, 1953; Eisenstein, 1978; Arriaza, 1997; Merbs, 2002). This was also found in the present study with only two L4 vertebrae affected and the remaining spondylolysis occurring on L5. The load strain on the vertebral column increases from superior to inferior, thus L5 will have the highest load strain and will therefore show the highest prevalence of fatigue fractures (Dar *et al*., 2010).

6.2 INFECTIOUS DISEASES

In the skeleton, infectious diseases present mostly as a periosteal reaction on bones, which occurs due to inflammation in the periosteum and the formation of new bone, all stimulated by the infectious agent (Rana *et al*., 2009).

6.2.1 Periostitis

The overall prevalence of periostitis itself is not discussed in many studies as it is merely a secondary response to a primary condition (Kim *et al*., 2013). Lambert (1993) observed an increase in the prevalence of periostitis and thus infectious diseases in the time period extending from 6000 B.C. to A.D. 1800. The author stated that it can be the result of an

increase in the prevalence of malnutrition, poor sanitation, and increased human contact as a result of a sedentary lifestyle. A high prevalence for periostitis was observed in a late 19th and early 20th century population in the North West Provence of South Africa indicating that infectious diseases were common at the time (Steyn *et al*., 2002).

The present study observed a high prevalence of periostitis (60.7%) in a 20th century population group representative of the Western Cape region of South Africa. This indicates that almost two-thirds of the study population had a pathological infectious process present long enough to involve the skeleton but which was not necessarily the COD. Therefore, the prevalence of periostitis found in the present study is not an indication of the prevalence of people who died from an infectious disease but rather the number of people who lived with an infectious disease over an extended period of time.

In the present study females (62.9%) showed a slightly higher prevalence of periostitis than males (58.9%) from all groups, but not statistically significantly so (p=0.551). The mixed population group had the highest prevalence of periostitis (70.3%) followed by the black group (44.7%). The high prevalence for the mixed population group gives some indication of the life style of this group in the 20th century. Infectious diseases can spread through an unsanitary environment, overcrowded living spaces and increased human contact, and lack of effective treatment of infectious diseases. These differences may be a contributing factor to the black group having a lower prevalence of periostitis than the mixed population group. The white group showed a low prevalence of periostitis (26.2%). It is possible that this group generally were of a higher socio-economic status, and lived in less crowded conditions, with better access to medical facilities (Labuschagne & Mathey, 2000). They may also have lived in a more sanitary environment, had better access to sewage facilities and clean water, which in combination would result in a decrease in infectious diseases. Infections treated early tend not to leave signs on the skeleton which supports the suggestion of access to health services and medication. Another factor that could have influenced the difference in the prevalence of periostitis between the three study groups is diet. As mentioned previously, malnutrition and suppressed immune system can result in an increase in the prevalence of infectious diseases (Lambert, 1993). The white group showed the lowest prevalence for metabolic disorders caused by malnutrition and most likely had a healthier diet than the other two groups and therefore, fewer infections. Alcohol abuse, which is fairly common among low socio-economic groups in the Western Cape, could possibly have contributed to a lower nutritional

status and an increase in infections among the mixed population group (Labuschagne & Mathey, 2000; Geldenhuys, 2014; Pfeiffer *et al*., 2016).

In the present study the age group with the highest prevalence of periostitis was the 31-45 year-old group (70.1%). The prevalence declined in the older age groups with the group older than 60 years showing the least number of cases with periostitis (44.8%). In the authors opinion, a possible reason why the presence of periostitis is lower (54.8%) in the youngest age group (<31 years) may be because of a better resistance to infectious diseases in this group. It can also be speculated that the decline in periostitis in the older age group may be because the people who survive to the age >60 years are those who received better health care and had a healthier lifestyle than individuals who died at a younger age. These "healthier" individuals may, therefore, also show less signs of disease on their skeletons. Another contributing factor to the decline in visible signs of periostitis in the older age group may be bone remodelling which takes place throughout life.

The tibiae and fibulae were affected most by periostitis in the present study, followed by the ribs and femur, in that sequence. The bone least affected was the clavicle. Steyn *et al*. (2013), in a study on skeletal material from individuals with TB, observed similar results with the ribs, tibiae, and fibulae affected most and the clavicle the least. Several other studies also found the tibiae and fibulae affected the most in individuals with infectious disease (Epstein *et al*., 1979: Lambert, 1993; Bourbou, 2003; Christensen *et al*., 2013). Ortner (2003) suggested that a periosteal reaction occurs in the bones positioned closer to the skin (such as the tibia) which are cooler and also more exposed to trauma than the less superficial bones. The ribs are also a common sight of periostitis because a number of infectious diseases can infect the lungs (Geldenhuys, 2014). Airborne transfer of disease is a common form of transmission, resulting in the respiratory system being the primary system to come into contact with the infectious agent.

6.2.2 Visceral rib lesions

There has been a strong focus on periosteal reactions on the visceral surface of ribs in recent literature (Santos & Roberts, 2001; Matos & Santos, 2006; Santos & Roberts, 2006; Steyn *et al*., 2013). The overall prevalence of rib lesions ranged from 1.4%-22.9% (Roberts *et al*., 1998; Santos & Roberts, 2001). The present study showed a higher prevalence (29.3%) than in some previous studies. This may be as a result of the high prevalence of pulmonary infectious diseases, such as TB, in the Western Cape (Western Cape Government Health,

2013; Geldenhuys, 2014). The black and mixed population groups had a statistically higher prevalence ($p<0.001$) for rib lesions than the white group for reasons similar to those mentioned for periostitis above. The trend for rib lesions in the different age groups were similar to those with periostitis, with the 31-45 year-old age group affected the most (see Table 5.4).

According to Matos & Santos (2006), VRL occur more frequently in pulmonary TB than in any other lung disease (Kelley & Micozzi, 1984; Roberts *et al*., 1994). The prevalence of rib lesions in skeletal material from persons who died from TB have been found, in previous studies, to range from 8.8%-90.5% of the population (Kelley & Micozzi, 1984; Roberts *et al*., 1994; Matos & Santos, 2006; Steyn *et al*., 2013). This prevalence may vary according to the severity of infections, treatment received for the disease, as well as accuracy in recording rib lesions. Matos & Santos (2006) found that 90.5% of individuals who died from TB develop rib lesions while they were only present on 36.7% of individuals who suffered a non-tuberculous pulmonary disease as COD, such as pneumonia. The present study found that individuals who died from pneumonia showed a slightly lower prevalence for rib lesions (47.8%) than skeletons with TB as a COD (58.1%). It is possible that individuals with a pneumonia as a COD also suffered from TB and *vice versa*. It is therefore difficult to determine whether rib lesions observed are the response of only the disease documented as the COD or a combination of diseases.

In most of the previous studies, rib lesions were generally observed more on the right rather than on the left in skeletal material with TB as COD, with ribs 3-7 affected the most (Matos & Santos, 2006; Steyn *et al*., 2013). Although Santos & Roberts (2001) observed the opposite with more lesions on the left than the right, it was not significantly higher. The present study correlates with most of the previous studies with more lesions on the right than on the left for both TB and pneumonia. The middle ribs (ribs 4-8) were also found to be most commonly affected. The site for rib lesions correlate with the site where TB and other non-tuberculous pulmonary diseases occur in the lungs. This is due to the direct spread of the infection from the lung to the pleura (pleuritis) which then cause a proliferative inflammatory response in the adjacent periosteum and ribs (Roberts *et al*., 1994; Santos & Roberts, 2006; Geldenhuys, 2014).

As periostitis and VRL are only a general response to a number of infections the diagnosis of a specific disease as primary cause is difficult to determine (Ortner, 2003; White *et al*., 2012).

An indication of Pott's disease was observed on the first lumbar vertebra of only one skeleton in the study population. Until recently, TB infection of the skeleton was diagnosed in the vertebral column as Pott's disease while pulmonary TB diagnosis from skeletal material was rare (Santos & Roberts, 2006). Although rib lesions are frequently used as a tool for diagnosing pulmonary TB, it cannot be used as a specific diagnosis of TB on its own (Roberts *et al*., 1998; Santos & Roberts, 2006; Steyn *et al*., 2013).

6.3 METABOLIC DISORDERS

Metabolic disorders are characterized by decreased osteoid production or decreased mineralization of bone and can be caused by nutrient deficiencies or changes in endocrine function (Huss-Ashmore *et al*., 1982; White *et al*., 2012).

Osteomalacia is caused by a deficiency in vitamin D which can be obtained through dietary intake or exposure to sunlight (Ortner, 2003; Brickley *et al*., 2005; Holick, 2005; Waldron, 2009). Brickley *et al*. (2007) observed a 4.9% overall prevalence of osteomalacia in adults in England. The prevalence of osteomalacia for the present study was lower, namely 1.7%. The Western Cape receives sunlight for most of the year whereas England is known for its cloudy weather conditions throughout most of the year (Monteith, 1977; Edwards, 1996; Le Maitre *et al*., 1996). This may explain the lower prevalence of vitamin D deficiency in the present population, as osteomalacia seldom occurs due to dietary deficiency alone (Brickley *et al*., 2005). The five cases in the present study were all mild without clear macroscopic signs of the disease. Diagnosis was confirmed through histology which also showed only minor defects in the cement lines of the compact bone. All of the cases in the present study fell in the age group between 45 and 60 years. Brickley *et al*. (2007) also observed more osteomalacia in older adults than young adults and suggested a decrease in vitamin D absorption with age to be a contributing factor. Vitamin D deficiency may also be linked to other medical conditions observed in older individuals such as hypertension or cardiovascular heart disease (Holick, 2005). Four of the five cases of osteomalacia were males of the mixed population group while the fifth case was a white female. With only a few cases presenting with possible osteomalacia it is difficult to make any assumptions on predilection of this disease in different sex or population groups.

Secondary hyperparathyroidism results from low levels of calcium in the blood which stimulates the parathyroid glands. This is commonly caused by renal failure (Mays *et al*., 2001a). Over-stimulation of the parathyroid hormones will increase osteoclast activity which

could be observed on the Lodox® scan as a permeative image (Mays *et al*., 2001a). In the present study a permeative appearance and brown tumours (lytic lesions), as observed in hyperparathyroidism, were present in only one skeleton. Periostitis was also present which is a frequent finding in secondary hyperparathyroidism and therefore favours the diagnosis of a secondary rather than a primary disease (Mays *et al*., 2001a).

6.3.1 Porotic hyperostosis/Cribra orbitalia

Porotic hyperostosis and CO are characterized by porosities in the external cranial vault and the orbital roofs respectively. In previous studies, the prevalence of CO was found to range from 14.3%-68.0% in adults (Webb, 1982; Bergman, 1993; Fairgrieve & Molto, 2000). A slightly lower prevalence, ranging from 0.7%-48.0%, was observed in studies on PH (Carlson *et al*., 1974; Facchini *et al*., 2004). The prevalence differed according to the location and time period from which the skeletal material was collected. Lallo *et al*. (1977) observed an increase through the time period of 900-1490 A.D during which there was change from hunter-gathers to agriculture. According to the author, the hunter-gatherers relied on iron rich resources and showed the lowest prevalence for infectious diseases (Lallo *et al*., 1977). With an increase in agricultural lifestyle, there was an increase in maize and a high phosphorous diet which lead to dietary iron deficiency (Lallo *et al*., 1977). Infectious diseases also increased with the agricultural lifestyle (Lallo *et al*., 1977). The overall prevalence in the present study was 35.6% and 10.7% for CO and PH respectively. These values are similar to what was observed in an 8^{th}-12^{th} century population group from Slovakia studied by Obertová & Thurzo (2004).

The black (CO=34.8%, PH=14.9%) and mixed (CO=37.2%, PH=11.5%) population groups showed a higher prevalence for CO and PH than the white group (CO=25.00%, PH=2.4%). This may be a reflection of the living conditions and dietary intakes of the different population groups in the Western Cape. Genetic anaemia is unlikely to explain the high prevalence in the present study since most of the lesions were mild and there is no malaria in this region to favour anaemia mutations. According to the 2013 South African National Health and Nutrition Examination Survey (SANHANES-1) (Shisana *et al*., 2013), dietary iron deficiency has a low prevalence affecting only 1.9% of the population in South Africa, with a prevalence of 8.1% for iron depletion and a prevalence of 10.7% for other causes of anaemia. A diet low in iron may therefore not have been the largest contributing factor for CO and PH. If considering the high prevalence of infectious diseases in the black and mixed population groups, as discussed in the previous section, it might have been an important

contribution to increased anaemia and therefore CO and PH. Since certain infectious diseases, such as TB, uses iron derived from the host for growth and metabolism; it may be advantageous for the body to have lower iron levels when suffering from infectious diseases such as TB (Stuart-Macadam, 1992; Holland & O'Brien, 1997).

Several studies found that CO and PH show a higher prevalence in females than in males (Webb, 1982; Kozak & Krenz-Niedbala, 2002; Facchini *et al*., 2004; Obertová & Thurzo, 2004; Wapler *et al*., 2004). The reason for this lies in the physiology of a female who, during, for example, menstruation, childbirth and lactation can lose iron (Kozak & Krenz-Niedbala, 2002). The present study however, found a higher prevalence of CO and PH in males than in females for both the black and mixed population groups. Additionally, in a study on more recent skeletons (n=124, years of death = 2009-2012) from the same skeletal collection, six cases of CO was observed in males and none in females (Geldenhuys, 2014). The SANHANES-1 reported a 10.0% higher prevalence of anaemia in females than in males (Shisana *et al*., 2013) which contradicts the findings of the present study. This suggests that a factor other than anaemia may contribute to CO and PH. Other factors previously suggested include post-mortem erosion, hyper-vascularisation, osteoporosis and osteitis (Wapler *et al*., 2004). Wapler *et al*. (2004) used histological sections to differentiate between these possible causes. With marrow hypertrophy observed in anaemia, the marrow space appears widened with openings in the orbital lamina (Wapler *et al*., 2004). When vascularisation increases it can create impressions on the orbital roof and inflammation can lead to bone resorption characterized by osteoclast activity (Wapler *et al*., 2004). Post-mortem erosion can be observed as disintegrated collagen fibres (Wapler *et al*., 2004). Only a few other studies found a higher prevalence in males but none of them with significant differences (Fairgrieve & Molto, 2000; Keenleyside & Panayotova, 2006).

In the present study most orbits showed grade 1 severity of CO, some grade 2 and very few grade 3 or 4 (see Figure 5.17). This was similar to most adult studies, although some studies did not find any orbits with grade 4 CO (Kozak & Krenz-Niedbala, 2002; Peckmann, 2003; Facchini *et al*., 2004; Keenleyside & Panayotova, 2006; Liebe-Harkort, 2012). As previously suggested by Stuart-Macadam, (1985), healing or partial healing of CO after a period of stress may result in less severe expression of the condition. The author also stated that CO in adults most likely occurs due to lesions resulting from childhood anaemia which has not completely remodelled.

Previous authors have suggested that bony lesions usually start in the orbits and then spread to the parietal and occipital bones due to a difference in diameter and microstructure of the bones (Stuart-Macadam, 1987; Facchini *et al*., 2004). Porotic hyperostosis is usually associated with CO while CO frequently occurs without PH (Lallo *et al*., 1977). The present study found that 75.0% of skeletons with PH showed signs of CO as well, while only 23.0% of skeletons with CO showed signs of PH.

6.3.2 Enamel Hypoplasia

Enamel hypoplasia is a result of metabolic stress during childhood. The prevalence of EH differs vastly between populations ranging from 17.4% in developed countries or well-nourished populations to 90.0% in developing countries or populations living under low socio-economic conditions (Goodman *et al*., 1980; Malville, 1997; Saunders & Keenleyside, 1999). The prevalence of EH in the present study was 43.8%. There may be two explanations for the high prevalence in this study. Firstly, as most of the skeletons were obtained as unclaimed bodies, individuals might represent the part of the community living under low socio-economic conditions with poor access to health care. In the second place, a high prevalence of infectious diseases was found in the present population. Both malnourishment and infectious diseases contribute to the formation of EH (Aufderheide & Rodríguez-Martin, 1998). During childhood, these conditions place the body under stress which results in energy diverted away from non-vital processes such as enamel formation, and redirect it to physiological processes needed for survival (Aufderheide & Rodríguez-Martin, 1998). These conditions could therefore explain the high percentage of EH observed in the present population.

Similar to what was observed in CO, EH, in this study, also occurred most in individuals from the mixed population group while the white group showed the lowest prevalence. This suggests that the white group may have come from a higher socio-economic status with better nutrition and were less exposed to infectious diseases compared to the black and mixed population groups.

Saunders & Keenleyside (1999) observed a statistically higher prevalence of EH in males than in females and supported the theory that males are more sensitive to external environmental effects during growth than females. In a review by Stinson (1985) on sex differences to environmental sensitivity, it was concluded that this theory is difficult to prove in the postnatal period due to complex environmental differences and cultural differences

between population groups. Prenatal differences in environmental sensitivity show more consistent trends with males showing a higher mortality rate than females prenatally (Stinson, 1985). It was also shown that maternal nutritional supplementation improved growth in males more than females (Stinson, 1985). In the present study the prevalence of signs indicating infections are high for both males and females with the prevalence for females slightly higher. Several other studies also indicated that no difference exists between males and females (Malville, 1997).

In the present study, results showed that the prevalence of EH decreased when age of death increased. Previous studies have not found any correlation between age-at-death and EH (Saunders & Keenleyside, 1999). A possible explanation for the decrease in EH may be that the children developing this defect were exposed to infections and malnutrition not just during childhood but throughout life resulting in death at an earlier age. The individuals without the defect were most likely better nourished and lived under better socio-economic conditions, thereby decreasing the opportunity of obtaining infectious diseases to a similar extent.

6.3.3 Harris lines

Harris lines refer to lines of increased radiodensity extending parallel to the epiphyseal plate across the shaft of long bones. The prevalence of HL has been observed to range from 12.0% to 80.0% in different population groups (Hughes *et al*., 1996; Ameen *et al*., 2005). In the present study the overall prevalence of HL were 24.3%. It has been suggested that HL develop due to a period of stress early in life, such as malnutrition or infectious diseases, which result in growth disruption in long bones (Goodman, 1981; Mays, 1985; Hughes *et al*., 1996). When considering the high prevalence of periostitis in the present study population, infectious diseases most likely contributed to the prevalence observed for HL. Alcohol intake can also influence the formation of HL in subadults (Gonzáles-Reimers *et al*., 2007). Gonzáles-Reimers (2007) found that alcohol intake reduces growth more than malnutrition or illness. It is possible that alcohol abuse by teenagers in Western Cape communities (Flisher *et al*., 2003; Parry *et al*., 2004) could also contribute to the observed HL. In the present study, HL was observed statistically significantly more ($p<0.001$) in the tibiae than the other bones. Although HL can be found on any of the long bones, most authors agree that the distal tibiae are the most commonly affected bones (Hughes *et al*., 1996; Ameen *et al*., 2005).

In several studies, including the present study, no significant difference was observed in the prevalence of HL between males and females (Goodman, 1981; Ameen *et al*., 2005). Possible explanations by previous authors for minor difference in the prevalence of HL between males and females include that females could have received less familial care, males had more responsibility in providing for the family resulting in a more strenuous lifestyle, or higher nutritional needs in growing males than in females (Goodman, 1981; Ameen *et al*., 2005). In the present study a slightly higher prevalence of periostitis, EH, and HL, was observed in females than in males. Even though these differences were not statistically significant, it may suggest that females were under more environmental and other stresses than males during childhood.

It is commonly known that HL is observed less in older individuals than in younger individuals (Hughes *et al*., 1996). This was also observed in the present study sample with the <31 year age group showing the highest prevalence of HL (see Table 5.7). Since HL develops as a result of stressful periods during growth, no new HL is formed after adolescence (Huss-Ashmore *et al*., 1982; Aufderheide & Rodríguez-Martin, 1998). Bone remodelling still continues to take place, however, resulting in the disappearance of HL as individuals grow older (Aufderheide & Rodríguez-Martin, 1998).

The black group showed the highest prevalence for HL (31.9%) followed by the mixed population (23.9%) and white groups (16.3%). The white group also had the lowest prevalence for periostitis, EH, and CO. As discussed previously this may suggest a lower socio-economic standard for the black and mixed population groups which would include malnutrition and a higher prevalence of infectious diseases.

6.3.4 Vertebral compression

Vertebral compression can be related to a decrease in BMD and therefore osteoporosis (Curate *et al*., 2014). The prevalence of osteoporosis differs between population groups depending on factors such as general health and nutrition, level of inactivity during life, oestrogen supplementation after menopause and alcohol intake (Westmacott, 1995; Aufderheide & Rodríguez-Martin, 1998). In the present study the prevalence for vertebral compression was observed in 41.3% of the study group for all age groups. It is well known that osteoporosis increases with age, especially in post-menopausal females (Iskrant & Smith, 1969; Westmacott, 1995; Johnell & Kanis, 2006; Curate *et al*., 2014). Vertebral compression

in the present study followed the same trend with a much lower prevalence in the <31 (19.4%) than the >60 (64.4%) age group.

In the present study the white group had a higher prevalence of vertebral compression than individuals from the black or mixed population group (see Table 5.7). The largest contributing factor to this observation is the distribution of age groups in each population group of the study population. The white group has no individuals in the <31 years age group and the largest number of individuals in the >60 years age group, while the individuals in the black and mixed population groups fall mostly in the younger and middle-aged groups with very few individuals in the >60 years age group (see Table 4.2). Another contributing factor may be lifestyle and level of activity throughout life. It can be speculated that the black group followed a more physical type of occupation during their life than the white group (Labuschagne & Mathey, 2000), however, this may not necessarily be the case. Inactivity was suggested to be associated with decreased BMD (Mack & Vogt, 1971). Alcohol abuse may have been more prevalent in the mixed than the black population group in the present study population, based on more alcohol problems experienced in the mixed population group in South Africa (Parry *et al.*, 2005). Westmacott (1995) suggested that there is an increased risk of osteoporosis with alcohol abuse which could explain the higher prevalence of vertebral compression in the mixed population group than the black group in both males and females. In a study by Conradie (2008) on South African black and white females, the author observed that black females presented with a slower decline in BMD than white females. This may also contribute to differences in vertebral compression observed between the black and white population groups in the present study. Conradie (2008) suggests that the slower decline in BMD in the black population may be due to a lower bone turnover rate in this group. It was also suggested that a greater and better maintained body weight of the black group may contribute to a slower decline in BMD (Conradie, 2008).

Vertebral compression was observed mostly in the middle thoracic vertebrae (T6-8), which also showed the most severe degree of vertebral compression. Osteoporosis is a systemic disorder influencing all the vertebrae similarly (Ortner, 2003). The difference in vertebral compression observed between vertebrae or vertebral groups can possibly be explained by the section of the vertebral column under the most strain during life resulting in compression of that part (Curate *et al.*, 2014). Although there is an increase in mechanical load from T1-L5, the lumbar vertebrae resist mechanical load and strain better than thoracic vertebrae due to a thicker cortex, larger size and decreased movement in that area (Dar *et al.*, 2010).

6.4 DEGENERATIVE BONE DISEASES

Bone markings related to degenerative diseases observed includes vertebral osteophytes peripheral osteophytes, and Schmorl's nodes. Osteophytes are bony outgrowths on the margins of joint surfaces occurring in osteoarthritis, also known as DJD (Rothschild & Woods, 2012). Eburnation or pitting of joint surfaces have been used as an indication of more severe osteoarthritis in a joint, compared to a joint with only osteophyte lipping (Weiss & Jurmain, 2007). In general, osteoarthritis primarily increases with biological age; however, many different factors can contribute to both the development and severity of this disease (Rogers *et al*., 1987; Jurmain, 1991; Waldron, 1991b, 1992; Knüsel *et al*., 1997; Weiss & Jurmain, 2007; Brown *et al*., 2008). These factors include genetics, sex, body mass, mechanical load and range of motion of a joint (Kellgren & Lawrence, 1958; Jurmain, 1977; Knüsel *et al*., 1997; Derevenski, 2000; Meulenbelt *et al*., 2006; Brown *et al*., 2008). The most commonly affected area for osteophyte lipping is the vertebral column, followed by the hip and knee joints (Aufderheide & Rodríguez-Martin, 1998). In the present study, vertebral osteophytes were examined separately from the peripheral joints and will therefore be discussed separately.

6.4.1 Vertebral osteophytes

In the present study vertebral osteophytes were observed in 81.0% of skeletons in the entire study sample which is high compared to some previous studies which found as few as 30.0%-34.0% of adults affected with vertebral osteophytes (Lovell, 1994; Gerszten *et al*., 2001). This high prevalence may be due to the generally older individuals in the current sample compared to some archaeological samples in previous studies. It is well known that the presence of vertebral osteophytes correlate with age and have even previously been used as an indicator of age (Snodgrass, 2004). Snodgrass (2004) also suggested that vertebral osteophytes are always present in individuals older than 45 years of age even though, at that age, the presence may be mild. The present study supports this statement with 95.4% of individuals in the age group 45-60 years and 100.0% of skeletons older than 60 years presenting with some degree of osteophyte formation.

Some studies, including the present study, have observed a higher prevalence of osteophytes in males than in females (Lovell, 1994; Snodgrass, 2004). Several studies have, however, observed the opposite, with females being more affected than males (Waldron, 1997; Gerszten *et al*., 2001). Snodgrass (2004), when only including individuals between 40 and 49 years of age in the study, found no difference in the presence of osteophytes between the

males and females for that age range. When considering the larger age ranges used in previous studies (Lovell, 1994; Waldron, 1997; Gerszten *et al*., 2001; Snodgrass, 2004) than the comparison in Snodgrass (2004) (40-49 years), it may be possible that age bias existed between males and females of previous studies contributing to the different results.

A statistically significant difference in the prevalence of vertebral osteophytes was observed between the population groups in the present study. Similar to vertebral compression, this can primarily be as a result of the large representation of the white group in the >60 years of age group, while the black and mixed population groups have more individuals in the middle age groups.

The distribution of osteophytes observed in the present study showed an increase in the number of vertebrae affected in vertebral groups C4-6 (n=463), T6-11 (n=586/574), and L3-5 (n=636) (see Figure 5.25). This pattern is similar to what was observed by Knüsel *et al*. (1997). Cervical and lumbar vertebrae in the present study showed similar degrees of severity, with the thoracic vertebrae showing less severe lesions (see Figure 5.26).Lovell (1994) found that severe lesions were observed mostly in the cervical vertebrae (31.0%), followed by the lumbar vertebrae (20.0%), with the thoracic vertebrae showing the least severe lesions (4.0%). A possible explanation for the difference in areas affected include increased movement in the cervical vertebral column during head and neck movement compared to the thoracic and lumbar vertebral column, and the increased weight bearing in the lumbar vertebrae compared to the cervical and thoracic vertebral column.

6.4.2 Peripheral osteophytes

The overall prevalence for peripheral osteophytes (43.0%) in the present study was lower than that for vertebral osteophytes (81.0%). A trend for peripheral osteophytes similar in number to that of vertebral osteophytes was observed for age, sex, and population groups in the present study, with, at first peripheral osteophytes increasing with age, secondly, males more affected than females, and thirdly, the white group showing a higher prevalence than the black or mixed population groups (see Table 5.8). This is not surprising as both vertebral and peripheral osteophytes are primarily age dependent and are affected by the similar factors (Lovell, 1994; Knüsel *et al*., 1997; Weiss & Jurmain, 2007; Brown *et al*., 2008). Several studies observed a higher prevalence of peripheral osteoarthritis in males than females (Maat *et al*., 1995; Waldron, 1997; Schrader, 2012). Weiss (2007) suggested that entheseal remodelling tends to be more pronounced in males due to increased body size and muscle

mass. Therefore, increased osteoarthritis in males cannot be explained by activity patters alone without considering body size (Schrader, 2012). In a review of the prevalence observed in different study populations, Rothschild & Woods (2012) noted that South African Blacks showed a lower prevalence of osteoarthritis than white groups in general. The present study also illustrates this prevalence (black=40.4%, white=57.1%); however, with the age bias in the present sample mentioned above, it is difficult to determine whether this difference is statistically significant.

Joints reported to be the most commonly and severely affected by osteoarthritis are the hip and knee joints (Rogers *et al*., 1987). Some authors found the hip joint to be more severely affected (Schrader, 2012), while others, including the present study, found the knee joint more severely affected by osteoarthritis and eburnation (Weiss, 2006). Waldron (1997) suggested that the type and degree of physical labour or occupation could influence which joints (hip, knee or other) would be affected more by osteoarthritis. In the present study, the shoulder, wrists and ankle joints for all groups showed a high prevalence for mild osteoarthritis without eburnation, as was also observed by Schrader (2012). These joints are not major weight bearing joints and would, therefore, not have the same severity of osteoarthritis as the hip and knee joints.

6.4.3 Schmorl's nodes

Schmorl's nodes are a common occurrence in the lower vertebral column and are cause by herniation of the intervertebral disk which then continues to protrude into the vertebral bodies. The prevalence have been reported to range from 5.0%-70.0% (Hilton *et al*., 1976; Frymoyer *et al*., 1984; Hamanishi *et al*., 1994; Stäbler *et al*., 1997). In the present study a low prevalence (9.3%) was observed compared to most of the previous studies. Schmorl's nodes are observed more in males than in females (Fahey *et al*., 1998; Wagner *et al*, 2000; Faccia & Williams, 2008). Only a slight difference (<1.0%) was observed in the present study between males and females, which is not statistically significant (p=0.972). A possible reason for males showing a higher prevalence for Schmorl's nodes may be increased load bearing on the vertebral column resulting from the type of occupation followed by the individual. Previously suggested theories regarding the development of Schmorl's nodes included a genetic influence, developmental defects, degeneration, trauma and pathological infections (Fahey *et al*., 1998; Wagner *et al*., 2000; Peng *et al*., 2003; Williams *et al*., 2007).

Dar *et al*. (2010) found that Schmorl's nodes are more prevalent in the T7-L1 region of the vertebral column with the prevalence declining from L2-L5. The author suggested that although mechanical load on the vertebral column increases from T1 to L5, the lumbar vertebrae are more capable of tolerating the load with a thicker cortex, less movement and general larger size than the thoracic vertebrae. Several other studies also found the lower thoracic vertebrae were affected more than the lumbar vertebrae (Fahey *et al*., 1998; Williams *et al*., 2007; Faccia & Williams, 2008). In the present study, Schmorl's nodes were found to be more prevalent in the lumbar vertebrae (L3-L5) than the lower thoracic vertebrae which differ from most previous studies. Hilton *et al*. (1976) graded endplate lesions and observed that more mild lesions occurred in the lumbar than the lower thoracic region while the opposite was true for more severe lesions. Schmorl's nodes of the cervical column are not reported frequently; however, in the present study, and a number of other studies, it was observed (Faccia & Williams, 2008).

6.4.4 Diffuse idiopathic skeletal hyperostosis

Diffuse idiopathic skeletal hyperostosis is known to occur in older individuals (>50 years) with males being more commonly affected than females (Cammisa *et al*., 1998; Hannallah *et al*., 2007). The prevalence in the present study correlated with the figures above, since only 1.0% of skeletons under the age of 45 years showed signs of DISH. Males in the present study, have a slightly higher prevalence of DISH than females; however, it was not statistically significantly (p=0.784). The overall prevalence of DISH has been reported to range from 2.9%-23.7% (Kim *et al*., 2004; Olivieri *et al*., 2009; Kim *et al*., 2012). Although the overall average prevalence in the present study was low (5.7%) the prevalence increased to 15.2% in the age group >60 years.

In the present study, the white group (9.5%) showed a higher prevalence than the black (4.3%) and mixed (5.3%) population groups. Due to the larger number of older individuals in the white group this could be expected. A genetic influence cannot be disregarded since, as previous studies have also observed, European population groups tend to have a higher prevalence for DISH than Asian, Black, and Native American groups (Weinfeld *et al*., 1997; Rogers & Waldron, 2001; Kim *et al*., 2012). Another factor that is important to consider is the difference in dietary intake among different population groups. Type II diabetes, obesity, and gout are considered risk factors in the development of DISH (Mader, 2002; Hannallah *et al*., 2007). Besides these risk factors, a protein rich diet has also been suggested to increase the prevalence of DISH in a population group (Rogers & Waldron, 2001). In a study by

Jankauskas (2003), it was observed that DISH was more prevalent in individuals with a higher social standard (27.1%) than the individuals from a low socio-economic background (7.1%) in a Lithuanian population group. Kim *et al*. (2012) also observed a higher prevalence in upper class individuals from the Joseon people (4.2%) compared to other Korean population groups. It is possible that in the present study, dietary differences between the different population groups could contribute to the higher prevalence in the white group, however, due to the age distribution in each group, it is difficult to indicate the exact extent to which diet and lifestyle may have contributed to the prevalence of DISH.

6.4.5 Other

Possible Reiter's syndrome was observed in one case in the present study. This disease occurs after enteric or venereal infections and is associated with the antigen HLA-B27 (Winchester *et al*., 1987). Calin & Fries (1976) found that white individuals are more frequently B27-positive than black individuals. The individual in the present study was from the mixed population group and there is a possibility that the individual may have carried the HLA-B27 antigen; however, due to restrictions of the present study, could not be confirmed. The disease was found to be more prevalent in males than females (Fox *et al*., 1979), with the case from the present study also a male. The skeletal changes observed in the present case are all commonly observed signs in patients with Reiter's syndrome. Fox *et al*. (1979) reported sacroiliitis in 40.0% of cases with 22.0% being bilateral symmetric, while Winchester *et al*. (1987) reported asymmetrical arthritis of the large joints, specifically lower limb joint, in all cases studied.

Rheumatoid arthritis is a chronic inflammatory disorder affecting approximately 1.0%-2.0% of the world population (Anderson *et al*., 1985; Kim *et al*., 2011). In the present study only one skeleton presented with clear signs of RA which gives a slightly lower prevalence for the disease in this study. The individual in the present study was a 23 year old female and falls into the age and sex group most commonly associated with the development of this disease (Anderson *et al*., 1985). In general, females are more affected than males with a ratio of 3:1 and individuals in the age group 20 to 50 years are more commonly affected than other age groups (Anderson *et al*., 1985; Arnett *et al*., 1988). Skeletal changes previously considered to be significant to RA includes erosion and destruction of joints, narrowing of joint spaces, hands and feet involvement, coupled with radiological findings (Kim *et al*., 2011; Kilgore, 1989; Rothschild & Woods, 1990; Blondiaux *et al*., 1997). The case in the present study

showed all the skeletal changes mentioned above and falls into the criteria set by Leden *et al*. (2008) (see section 2.4.4.4).

Diagnosing AS, Reiter's syndrome and RA can be difficult since some features of the diseases overlap (Kim *et al*., 2011). Reiter's syndrome is the only one of the three diseases characterized by unilateral arthritis of the knee joint or ankle joint and occurs more commonly in males (Jacobson *et al*., 2008; Kim *et al*., 2011). Rheumatoid arthritis occurs more commonly in females than in males and has a symmetric distribution which differs from the asymmetric lesions seen in Reiter's syndrome and AS (Rogers *et al*., 1987; Kim *et al*., 2011). Ankylosing Spondylitis occurs more commonly in males than in females and is characterized by bone formation on the vertebrae; both factors excluding RA as a differential diagnosis (Gottlieb *et al*., 2008; Kim *et al*., 2011). Vertebral fusion also occurs in AS, starting from the lumbar region and moving upwards along the vertebral column (Rogers *et al*., 1987; Kim *et al*., 2011). This differs from Reiter's syndrome in which patches of ossification takes place along the vertebral column (Rogers *et al*., 1987).

6.5 NEOPLASMS

6.5.1 Primary benign neoplasms

Benign neoplasms are characterized as localized small tumours with well-defined margins (Aufderheide & Rodríguez-Martin, 1998; Ortner, 2003; Marks & Hamilton, 2007; White *et al*., 2012). The prevalence of benign tumours is not well documented as they may stay asymptomatic throughout life (Geirnaerdt *et al*., 1997; Cerase & Priolo, 1998). In the present study the most prevalent benign neoplasm was a BO occurring in 9.7% of the study sample. The prevalence of BOs have been described by some authors as rare, ranging from 0.5%-3.7% (Brothwell, 1961; Bullough, 1965; Ross & Sasake, 1995; Haddad *et al*., 1997), while other authors observed a high prevalence for this disease ranging from 37.3%-50.0% (Schuller, 1950; Eshed *et al*., 2002). Although, in general, BOs were observed more in females than in males (Ross & Sasake, 1995; Tucker and Nasser-Sharif, 1997) some studies observed a slight male predominance (Eshed *et al*., 2002; De Chalain & Tan, 2003). The present study showed a slight female predominance, but, as in most of the previous studies, this was not statistically significant.

Few studies compared the prevalence of BOs between population groups. The present study observed a higher prevalence of BO in the black than in the white or mixed population groups but the differences are not statistically significant. Eshed *et al*. (2002) also observed no

difference between African-American and European-American groups. Eshed *et al*. (2002) suggests that BOs are the result of the rapid growth of the human skull to accommodate the increase in brain volume and the continuous growth throughout life. This might explain the lack of difference between sex, age and population groups. Other suggested causes of BOs include irritation of the periosteum, inflammation and trauma which can occur in any sex, age, or population group (Perou, 1964 as cited by Eshed *et al*., 2002).

Osteochondromas were reported as the most common primary benign neoplasm observed in the skeleton, representing 40.0%-45.0% of all benign neoplasms of the skeleton (Vyhnánek *et al*., 1999; Villanueva *et al*., 2006). This was not found in the present study where only 13.2% of all benign neoplasms were identified as osteochondromas. No significant difference was found between males and females in either the present or any previous study; however, a slight male predominance was observed in some population groups, e.g. in a study in Massachusetts (Chin *et al*., 2000).

Enchondromas were reported to represent 3.0%-17.0% of all primary neoplasms on the skeleton (Unni, 1996; Geirnaerdt *et al*., 1997). In the present study only 3.8% of benign neoplasms were identified as enchondromas, the lowest of all benign neoplasms. Enchondromas can occur at any age and previous studies showed no statistically significant difference between males and females (Kendell *et al*., 2004). The most common site identified for an enchondroma to occur is the phalanges of the hand (Geirnaerdt *et al*., 1997; Shimizu *et al*., 1997). In the present study, only one of the two cases showing enchondromas occurred in the above mentioned site, while the other occurred in the femur, which is also a common site for enchondromas to develop (Geirnaerdt *et al*., 1997).

6.5.2 Primary malignant neoplasms

A benign enchondroma can develop into a chondrosarcoma, which is a malignant tumour (Garrison *et al*., 1982; Björnsson *et al*., 1998). It is important to be able to distinguish between the two as treatment of the tumours differs (Geirnaerdt *et al*., 1997). Radiological characteristics indicative of a chondrosarcoma include ill-defined margins, cortical scalloping, lobulated tumour contours, and expansion of the bone (Brien *et al*., 1997; Geirnaerdt *et al*., 1997; Wang *et al*., 2001). A chondrosarcoma is one of the most prevalent malignant tumours in the skeleton, with only osteosarcomas showing a higher prevalence (Björnsson *et al*., 1998; Pring *et al*., 2001). Larson & Lorentzon (1974) observed osteosarcoma and chondrosarcoma in 28.8% and 22.9% of all malignant neoplasms,

respectively. They do not only develop from enchondromas but can also arise from osteochondromas or develop as a malignant tumour from the beginning (Garrison *et al*., 1982; Björnsson *et al*., 1998). It was not possible to determine the exact origin of these tumours in the present study. The bone most frequently involved in the human body is the ilium, followed by the femur and humerus (Henderson & Dahlin, 1963; Garrison *et al*., 1982; Buirski *et al*., 1986; Healey & Lane, 1986; Nakashima *et al*., 1986). Of the chondrosarcomas observed in a study by Pritchard *et al*. (1980), the pelvis, femur, and humerus were affected in 35.0%, 24.3%, and 10.4% of cases respectively. In the present study one chondrosarcoma was located in the femur, and one in the humerus, both common locations for this neoplasm. Other bones that can also be affected include the fibula, tibia, vertebrae, ribs, scapula, mandible, skull, and in rare cases the hands (Garrison *et al*., 1982; Nakashima *et al*., 1986; Müller *et al*., 2004) but, as stated above, none was observed in the current study.

In the present study both cases of chondrosarcomas was observed in the age group 46-60 years, of which one is a male and the other a female. This disease can occur at any age although previous studies have shown that most cases occur in the age group 20-50 years (Lichtenstein & Jaffe, 1942; Garrison *et al*., 1982). Most previous studies have not found a statistically significant difference between males and females; however, some observed a slightly higher occurrence in males (Lichtenstein & Jaffe, 1942; Garrison *et al*., 1982; Kendell *et al*., 2004). As only two skeletons in the present study showed the presence of chondrosarcoma, no conclusions could be drawn on the predilection for a specific age or sex group.

One case of a maxillary osteosarcoma was observed in the present study in a 55-year-old male. According to Picci (2007), osteosarcoma is the second most common primary malignant neoplasm of the skeleton and comprises 15.0% of all primary bone tumours. The age group with the highest prevalence of osteosarcoma range from 15 to 25 years however, it can occur at any age (Picci, 2007). As the current case is an older individual, it is possible that the observed osteosarcoma developed secondary to dedifferentiated chondrosarcoma or radiation (Picci, 2007). Although no interpretations can be made on the male to female ratio of the disease in the current study population from only one case, previous studies observed a male predominance (Picci, 2007). The maxilla is not the most common location for an osteosarcoma as it has a predilection for the metaphysis of long bones (Picci, 2007). Previous studies that have described maxillary osteosarcomas stated that only 5.0%-6.5% of all

osteosarcomas occur in the maxilla or mandible (Clark *et al*., 1983; Doval *et al*., 1997; Mardinger *et al*., 2001).

6.5.3 Skeletal metastases

Even though metastases to bone are common for cancers in general, the frequency of metastases differs among the different types of primary tumours. The highest frequency of skeletal metastases is observed in breast and prostate cancer with approximately 70.0% of patients showing skeletal metastases at the time of death (Coleman & Rubens, 1987; Kim *et al*., 1987; Coleman, 2006). In the present study only one skeleton had breast cancer registered as a COD and skeletal metastases was observed. Metastases from carcinoma of the bronchus are also common with an incidence of 30.0%-40.0% (Coleman, 2006). The findings from the present study correlate with the Coleman study with an average of 38.5% of the study population showing skeletal metastases with bronchus carcinoma as a COD. Radiological evidence of skeletal metastases in lung cancer patients is observed in approximately 27.0% of patients (Coleman & Rubens, 1987). The present study found that 20.0% of skeletons with a documented COD of lung cancer showed skeletal metastases. The clinically documented prevalence of skeletal metastases in cervical cancer patients ranges from 3.0% to 6.6% (Abdul-Karim *et al*., 1990). This prevalence is lower than what is observed in post-mortem studies. In autopsy studies the prevalence was found to range between 8.0%-20.0% (DiSibio & French, 2008). The findings of the present study correlate with previous post-mortem studies with 21.0% of skeletons with cervical carcinoma as a COD showing signs of metastases. According to Coleman (2006) skeletal metastases are rare in GIT carcinomas, and no skeletal metastases could positively be linked to individuals with GIT carcinomas as a COD in the present study.

In the present study, the axial skeleton was affected most by skeletal metastases regardless of the type of primary carcinoma it resulted from. Previous studies suggested that metastases occurred mostly via a haematogenous route to more vascularised areas of the skeleton such as the red bone marrow found in the axial skeleton (Kim *et al*., 1987; Mundy, 1997; Rybak & Rosenthal, 2001; Coleman, 2006). Other well vascularised sites include the vertebral column, ribs and proximal long bones (Mundy, 1997). Batson's vertebral-venous plexus also contributes to the predilection of metastases for the axial skeleton via haematogenous routes (Rosenthal, 1997; Rybak & Rosenthal, 2001). In the present study, some lesions were observed in parts of the skeleton not mentioned above (e.g scapulae or os coxae). These lesions may be explained by less common modes of spread of cancer namely direct spread

and spread via lymphatic foci (Adbul-Karim *et al*., 1990). Direct lymphatic spread is rare; however, spread of carcinoma from affected lymph nodes is not uncommon and can contribute to metastatic lesions observed on the vertebral column (Rybak & Rosenthal, 2001). Direct spread of cancer to bone situated adjacent to affected soft tissue areas may account for metastatic lesions observed on the ribs from lung cancer, or the os coxae from cervical cancer.

6.6 MISCELLANEOUS CONDITIONS

Paget's disease is a disorder characterized by increased bone resorption followed by unorganized new bone formation (Aufderheide & Rodríguez-Martin, 1998; Ortner, 2003). The prevalence of Paget's disease is commonly known to increase with age and occurs mostly in individuals older than 50 years-of-age (Cooper *et al*., 1999; Cundy & Reid, 2011). In the present study, three of the four cases identified with Paget's disease were over the age of 50, with only one at 44 years-of-age. As was observed in the present study, several studies found a higher prevalence in males than females (Barker *et al*., 1977, 1980; Detheridge *et al*., 1982; Cooper *et al*., 1999; Altman *et al*., 2000; Rogers *et al*., 2002; Whyte, 2006).

The overall prevalence of Paget's disease was found to vary considerably between population groups. The highest prevalence was found in the United Kingdom (2.3%-10.8%) followed by Australia and New Zealand (Collins, 1956; Barker *et al*., 1977; Gardner *et al*., 1978; Reasbeck *et al*., 1983; Cooper *et al*., 1999). A lower prevalence (1.1%-3.9%) was observed in Germany, France, and the USA (Schmorl, 1932; Guyer & Chamberlain., 1980; Ringe *et al*., 1984; Rénier *et al*., 1995) and Paget's disease was rare (0.2%-1.7%) in Japan, Scandinavia, Ireland and black South Africans (Pompe Van Meerdervoort & Richter, 1976; Detheridge *et al*., 1982; Dokoh *et al*., 1985; Lyles *et al*., 2001; Rogers *et al*., 2002). In the present study the overall prevalence was observed to be 1.3% of the study population which is relatively low compared to some of the previous studies. It should be taken into consideration that most studies only determined the prevalence for individuals older than 50 years-of-age. If only individuals older than 50 years-of-age are considered, the prevalence for the present study is slightly higher at 2.3% for that age group.

The exact cause of Paget's disease is unknown; however, both genetic and environmental factors have been proposed (Whyte, 2006). Siris (1994) found that 12.0% of individuals affected with Paget's disease have a close relative also affected by this disease, suggesting a genetic contribution to the aetiology of Paget's disease. Environmental factors suggested to

increase the risk of developing Paget's disease include low calcium levels during childhood and viral infections (Rogers *et al*., 2002). Barker *et al*. (1977, 1980) conducted a study in the United Kingdom in 14 different towns and observed a high prevalence of Paget's disease in six towns clustered close in Lancashire. This cluster of towns supports a hypothesis of a possible environmental factor being responsible for the development Paget's disease (Barker *et al*., 1977, 1980). A second factor suggested to influence this cluster of towns is genetic isolation. Gardner *et al*. (1978) observed a decline in the prevalence of Paget's disease with migration of inhabitants, for example, from the United Kingdom to Australia, thereby giving preference to the environmental hypothesis. In two studies by Guyer & Chamberlain (1980, 1988) in the USA and South Africa, it was observed that the prevalence for Paget's disease in the black population group was slightly lower but not significantly different from that observed in the white groups in both countries. Altman *et al*. (2000) also observed a similar prevalence for both black and white groups. This lack of difference between population groups further supports an environmental aetiology. In the present study, all four cases of Paget's disease were from the mixed population group. The 2.3% prevalence observed for the mixed population group of individuals over the age of 50 is similar to that observed in white South Africans (2.4%) and slightly higher than that observed in black South Africans (1.3%) by Guyer & Chamberlain (1988).

The bone most commonly affected by Paget's disease is the pelvis followed by the vertebrae, femur, and skull (Lyles *et al*., 2001). The pelvis was found to be affected in 54.0%-79.0% of Paget's disease cases (Cooper *et al*., 1999; Eekhoff *et al*., 2004). In the present study the pelvis was affected in two of the four cases with one of them also showing affected lumbar vertebrae. Few studies included the skull to determine the prevalence of Paget's disease, as most diagnoses were made from abdominal radiographs. Studies that have included the skull found 6.8%-65.0% of patients with the skull affected (Collins, 1956; Franck *et al*., 1974; Mirón-Canelo *et al*., 1997; Tiegs *et al*., 2000).

6.7 LIMITATIONS

Some limitations existed in the present study which could have impacted on the quality of the results. The first limitation encountered was the incompleteness of some skeletons. With certain skeletal elements missing, some diseases or malformations were difficult to diagnose. This would have reduced the sample size for comparison of certain diseases thereby decreasing the quality of statistical results. To minimize this limitation, skeletons for the present study were, as far as possible, chosen according to completeness to ensure minimal

missing bones throughout the study. Unfortunately some of the bones were damaged post-mortem due to frequent handling. In cases where a bone was damaged to the point where diagnosis of certain diseases were not possible, that bone was excluded from statistical analysis.

A second limitation was the unequal distribution of skeletons in different population and sex groups which could have resulted in bias with regards to results. Almost twice as many males than females were examined and the majority of skeletons were from the mixed population group. The results most likely influenced by bias are those which take age distribution within the population groups into consideration. The white population group had a mean age approximately 13 years older (59.8 years) than the black (46.7 years) and mixed (46.8 years) population groups resulting in biased results for diseases influenced by aging. This age bias was, however, considered when interpreting results throughout the discussion section.

The diagnosis of different diseases was mostly made through visual examination, whether macroscopically, microscopically or radiologically. Even when certain guidelines were followed in the diagnosis or grading of some of the diseases, it could still be influenced by observer bias. To minimize incorrect diagnosis or grading, other observers were consulted (e.g. radiologists) for confirmation on certain diagnosis. Figures in the results section would aid the reader to observe how the author graded or diagnosed certain diseases.

Information on the sex, and population group was not available for one skeleton and age not available for six skeletons in the present study. Although biological profiling could be done to estimate which group the skeleton belongs to, it is not a 100.0% accurate method. Population group estimations mostly focus on white and black South African groups. Considering that the majority of the skeletons in the Kirsten Skeletal Collection are from the mixed population group, the possibility exists that a skeleton from a mixed ancestry could incorrectly be classified as either black or white. Age estimations can be difficult and inaccurate and may to some extent influenced by level of experience of the observer (Buikstra & Ubelaker, 1994). In order to ensure the accuracy of results, skeletons with unknown age, sex, or population groups were, where possible, excluded from the statistical analysis of these groups instead of including possibly inaccurate estimations in the analysis. However, due to the small number of skeletons with missing information, excluding these skeletons should not have had a major influence on the statistical results. These skeletons

were still included for statistical analysis comparing different skeletal elements for certain diseases.

The extent to which diagnosis of diseases is influenced by the embalming and skeletonising processes of cadavers are uncertain. Disease presentation on the bones of the present study may differ somewhat from untreated archaeological skeletal remains which could influence comparisons between studies.

Lastly, time constraints had to be taken into account and therefore, only certain diseases were examined thoroughly in the present study. Most of these diseases were chosen prior to examining the skeletons based on what the author (after an extensive literature study) expected to find in the current population.

Chapter 7 CONCLUSION

This study gives a comprehensive evaluation of diseases, malformations and metabolic disorders in the Kirsten Skeletal Collection through macroscopic, microscopic and radiological techniques. One of the most important findings of this study was the generally high prevalence of periostitis in the mixed population group indicating a high prevalence of chronic infectious diseases in this group. This high prevalence was ascribed to a combination of factors included unsanitary living environment, overcrowded living spaces, lack of access to or effective medical treatment, malnutrition, and alcohol abuse (Lambert, 1993; Labuschagne & Mathey, 2000; Geldenhuys, 2014; Pfeiffer *et al*., 2016). The prevalence of visceral rib lesions was also high among the black and mixed population groups. A possible reason given for this is the acknowledged high prevalence of pulmonary infections such as TB in the Western Cape (Geldenhuys, 2014) in association with other lung infections. The present study, however, presented evidence to support the theory that rib lesions by itself are not pathognomonic of TB (Roberts *et al*., 1998; Santos & Roberts, 2006; Steyn *et al*., 2013).

Metabolic disorders (such as CO, EH and HL) were also observed indicating periods of metabolic stress experienced throughout life. Possible stresses that were suggested to have contributed in the present study included malnutrition and infectious diseases (Goodman, 1981; Mays, 1985; Hughes *et al*., 1996; Aufderheide & Rodríguez-Martin, 1998). The most contradictory finding on metabolic disorders in the present study was the statistically significantly higher prevalence of CO in males. Several previous studies observed a higher female prevalence supporting an iron deficiency anaemia theory (Webb, 1982; Kozak & Krenz-Niedbala, 2002; Facchini *et al*., 2004; Obertová & Thurzo, 2004; Wapler *et al*., 2004). The present results, however, suggests that factors other than iron deficiency anaemia contributed to the presentation of CO.

The present study illustrates the efficacy of the Lodox® Statscan® imaging system when examining skeletal pathology. This was illustrated particularly with the identification of benign neoplasms, metastatic lesions or HL, which are otherwise not visible macroscopically. Features of Paget's disease could also be identified on the full body x-rays and, together with histological examination, allowed for correct diagnosis. Histological techniques also proved useful in the diagnosis of osteomalacia.

Several other pathological conditions were described and evaluated, which included lumbosacral transitional vertebrae, spina bifida, scoliosis, kyphosis, spondylolysis,

osteoporosis, vertebral/peripheral osteophytes, Schmorl's nodes, and DISH. These pathologies showed similar prevalence as described in several studies in the literature.

Taking into account some of the limitations of the present study, it can be recommended that future studies include a larger sample from the Western Cape for which the age, sex, and population groups are evenly distributed to avoid biased results. This would improve the interpretations an understanding of the diseases studied. Secular changes after the end of Apartheid in South Africa may have influenced disease distribution in the Western Cape and throughout the country. For future research the more recent intakes of the Kirsten Skeletal Collection could be examined for pathology and compared with the data from the present study in order to observe possible differences in disease patterns due to secular changes in the Western Cape. This study also showed some observer bias in the diagnosis of certain pathologies emphasizing the need for continuous improvement of diagnostic criteria and descriptions of pathology affecting the skeleton.

By describing and evaluating pathologies in the Kirsten Skeletal Collection, the aim of this study was achieved. To the author's best knowledge, this was the first in depth study using a combination of three different methods (macroscopic, microscopic, and full body x-rays) to evaluate the general disease presentation of a skeletal collection representative of the inhabitants of the Western Cape, amongst them two groups from generally low socio-economic status. The findings of this study, therefore, gave a unique interpretation of the health status of this population adding to the present knowledge and understanding of the spread of disease and pathology in the Western Cape. Using a combination of techniques to examine pathological conditions on skeletal material in different populations throughout South Africa and the rest of the world could be a step forward to a complete and thorough understanding and diagnosis of pathologies on skeletal material.

Chapter 8 REFERENCE LIST

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Chapter 9 APPENDICES

APPENDIX A: LIST OF SKELETONS WITH SEX, AGE, POPULATION GROUP AND DOCUMENTED COD

Table 9.1: List of skeletons used in the present study

AN Nr	Sex	Age	Population group	COD
An 201	Male	42	Black	Unknown
An 202	Male	50	Mixed population	Unknown
An 206	Unknown	Unknown	Unknown	Unknown
An 208	Male	15	Mixed population	Meningitis
An 216	Female	47	Mixed population	Pulmonary Tuberculosis
An 220	Male	31	Mixed population	Unknown
An 224	Male	56	Mixed population	Carcinoma of Lung
An 231	Male	30	Mixed population	Tuberculosis
An 234	Female	38	Mixed population	Pulmonary Tuberculosis
An 239	Male	60	Black	Pneumonia
An 247	Female	43	White	Carcinoma of Breast with Metastases
An 251	Female	50	Mixed population	Cardiac Failure
An 257	Male	Unknown	Black	Pulmonary Tuberculosis
An 261	Male	76	Mixed population	Coronary Thrombosis
An 270	Male	71	Mixed population	Congestive Cardiac Failure, TB
An 280	Male	64	Mixed population	Status Epilepticus
An 281	Male	65	Mixed population	Cerebrovascular Accident
An 284	Male	Unknown	Mixed population	Coronary Thrombosis
An 288	Male	50	Mixed population	Carcinoma of Lung
An 291	Male	78	Mixed population	Emphysema
An 294	Male	71	Mixed population	Bronchopneumonia, Malnutrition, Dehydration
An 297	Male	Unknown	Mixed population	Pulmonary Tuberculosis, Pneumonia
An 298	Female	34	Mixed population	Carcinoma of Cervix
An 299	Female	43	Mixed population	Subacute bacterial endocarditis, Heart failure
An 302	Female	72	White	Unknown
An 303	Male	42	Mongoloid	Carcinoma of Pharynx
An 306	Female	45	Mixed population	Pulmonary Tuberculosis
An 313	Male	63	White	Coronary Thrombosis
An 314	Male	40	Mixed population	Coronary Thrombosis
An 315	Female	45	Black	Carcinoma of Cervix
An 322	Female	65	White	Coronary Thrombosis
An 330	Male	34	Mixed population	Septic Meningitis
An 333	Male	Unknown	Black	Carcinoma of Oesophagus
An 344	Female	23	Mixed population	Cardiac Failure
An 346	Female	45	Mixed population	Pneumonia (lobar)
An 347	Female	60	Mixed population	Natural Causes
An 348	Male	49	Mixed population	Carcinoma of Tongue
An 349	Male	48	Mixed population	Unknown
An 356	Male	46	Mixed population	Cardiac Failure
An 361	Female	75	White	Cerebrovascular Accident
An 366	Male	50	Black	African Cardiomyopathy
An 370	Male	50	Mixed population	Cancer
An 376	Female	45	Mixed population	Carcinoma of Cervix, Stage 4
An 382	Male	Unknown	Mixed population	Tubercular Meningitis
An 384	Male	40	Mixed population	Carcinoma of Bronchus
An 387	Male	58	White	Carcinoma of Lung
An 389	Male	71	Mixed population	Respiratory Failure
An 390	Male	59	Mixed population	Carcinoma of Oropharynx
An 393	Male	45	White	Cardiopulmonary Arrest
An 394	Male	49	Mixed population	Unknown
An 395	Male	20	Mixed population	Pulmonary Tuberculosis

An 398	Male	26	Mixed population	Carcinoma of Tongue
An 399	Female	50	Mixed population	Natural Causes
An 400	Male	52	Black	Cardiac Failure, Mediastinal Tumour
An 401	Female	70	White	Coronary Thrombosis
An 402	Female	42	Mixed population	Hepatic Failure
An 410	Male	69	White	Cerebrovascular Accident
An 411	Male	75	Mixed population	Carcinoma of Bronchus with Metastases
An 412	Male	18	Black	Cardiac and Renal failure
An 417	Female	55	Mixed population	Carcinoma of Cervix, Stage 4
An 423	Male	62	Mixed population	Septicaemia
An 428	Female	26	Mixed population	Cardiac Failure
An 432	Female	43	Mixed population	Subarachnoid Haemorrhage
An 435	Male	55	Black	Subarachnoid Haemorrhage
An 437	Male	53	Mixed population	Cerebrovascular Accident
An 439	Male	31	Black	Respiratory Failure
An 441	Female	66	Mixed population	Cerebrovascular Accident
An 442	Female	41	Mixed population	Unknown
An 443	Male	75	Black	Cerebrovascular Accident
An 445	Male	32	Mixed population	Lymphoma
An 447	Male	44	Mixed population	Peritonitis
An 448	Female	32	Mixed population	Aortic Incompetence, Heart Failure
An 450	Female	53	Black	Amoebic Dysentery
An 454	Male	45	Mixed population	Congestive Cardiac Failure
An 456	Male	33	Black	Chronic Rheumatic Heart Disease
An 457	Female	81	Mixed population	Cardiac Failure
An 458	Male	59	Mixed population	Lung Abscess, Bronchiectasis
An 459	Male	51	Black	Carcinoma of Oesophagus
An 460	Male	39	White	Cerebral Haemorrhage
An 462	Female	60	Mixed population	Bronchopneumonia
An 466	Male	30	Mixed population	Hepatic Coma
An 469	Female	81	White	Cardiac Failure
An 471	Male	55	Mixed population	Hepatic, Kidney and Respiratory Failure
An 476	Male	58	Mixed population	Respiratory Failure
An 480	Male	66	Mixed population	Tuberculosis
An 483	Male	30	Mixed population	Alcoholic Liver Cirrhosis
An 486	Female	65	Mixed population	Carcinoma of Pharynx
An 487	Male	26	Black	Large cell lymphoma of small bowel
An 490	Female	18	Mixed population	Cardiac Failure
An 492	Male	28	Mixed population	Cardiac Failure
An 493	Male	51	Black	Pulmonary Embolism
An 498	Male	43	Black	Bronchiectasis and Lung abscess
An 499	Male	57	Black	Carcinoma of Tongue
An 503	Male	73	Mixed population	Respiratory Failure
An 504	Male	60	Black	Cardiac Failure
An 505	Male	37	Black	Cardiac Valve Lesions, Gastroenteritis
An 506	Female	66	White	Myocardial Infarction
An 510	Male	47	Black	Carcinoma of Colon
An 516	Male	59	Mixed population	Hepatic Failure
An 518	Male	33	Mixed population	Subarachnoid Bleeding
An 520	Female	44	Black	Carcinoma of Cervix and Renal Failure
An 529	Female	45	Mixed population	Hyperkalaemia, Uraemia, Carcinoma of Cervix
An 531	Male	54	Mixed population	Cardiac Arrest
An 536	Female	58	Mixed population	Acute asthmatic attack
An 538	Male	46	White	Bronchopneumonia
An 539	Male	50	Mixed population	Cerebrovascular Accident
An 542	Male	52	Mixed population	Renal Failure
An 554	Male	66	White	Chronic Obstructive Airways Disease
An 555	Male	60	Mixed population	Tuberculosis, Dehydration
An 565	Female	24	Mixed population	Carcinoma of Ovaries

An 567	Female	39	Mixed population	Carcinoma of Bronchus
An 568	Female	38	Mixed population	Infarction
An 569	Male	45	Mixed population	Natural Causes
An 571	Male	56	Mixed population	Respiratory Failure
An 572	Female	64	White	Pneumonia, Carcinoma of Cervix
An 574	Male	60	White	Leukaemia
An 577	Male	66	Mixed population	Congestive Cardiac Failure
An 578	Male	66	Mixed population	Non-Infective Gastroenteritis
An 579	Male	49	Mixed population	Bronchopneumonia
An 583	Male	50	Mixed population	Stomach exit obstruction due to Carcinoma
An 585	Male	52	Black	Renal Failure
An 588	Female	22	Mixed population	Pulmonary Tuberculosis, Cardiac Arrest
An 589	Male	67	Mixed population	Alcoholic Liver Cirrhosis, Hepatic Coma
An 590	Female	56	Mixed population	Epilepsy and Brain Haemorrhage
An 591	Male	34	Black	Renal Failure
An 592	Male	49	Mixed population	Respiratory Failure
An 593	Male	65	Mixed population	Hepatic Abscess
An 594	Female	44	Black	Carcinoma of Cervix
An 596	Male	43	Black	Possible Lymphoma
An 597	Male	35	Mixed population	Natural Causes
An 598	Male	40	Mixed population	Cardiac and Respiratory Failure
An 599	Male	61	Black	Carcinoma of Oesophagus
An 600	Female	24	Black	Cardiac and Respiratory Failure
An 604	Male	52	Mixed population	Carcinoma of Liver
An 606	Female	46	White	Septicaemia
An 607	Female	62	White	Myocardial Infarction
An 608	Male	66	Mixed population	Carcinoma of Bronchus
An 609	Male	56	Mixed population	Carcinoma of Stomach
An 610	Male	60	Black	Pulmonary Tuberculosis
An 611	Male	67	Mixed population	Bronchopneumonia, Respiratory Failure, TB, Lung oedema
An 612	Male	60	Mixed population	Cerebrovascular Accident
An 613	Female	23	Mixed population	Pneumonia (lobar), pleural effusion
An 614	Male	76	White	Coronary Thrombosis
An 615	Female	66	White	Lupus erythematosus, Carcinoma of Pancreas
An 616	Female	38	Mixed population	Acute Renal Failure
An 617	Female	41	Mixed population	Chronic Renal Failure
An 619	Female	42	Mixed population	Carcinoma of Bronchus
An 622	Male	45	Mixed population	Carcinoma of Bronchus
An 623	Male	63	Mixed population	Acute Myocardial Infarction
An 625	Male	61	White	Cerebrovascular Atherosclerosis
An 627	Male	61	White	Coronary Thrombosis
An 628	Female	52	Mixed population	Bronchopneumonia and Pulmonary Oedema
An 629	Male	50	Black	Respiratory failure, Carcinoma of lung
An 631	Male	50	Mixed population	Malnutrition, Pneumonia, Neglect, Anaemia, Liver failure
An 632	Male	54	White	Acute Myocardial Infarction
An 633	Male	45	Mixed population	Mesothelioma
An 636	Male	57	White	Natural Causes
An 637	Male	52	White	Atrial Fibrillation
An 640	Female	42	Mixed population	Carcinoma
An 641	Male	43	Mixed population	Cardiac Failure and Bronchospasm
An 645	Female	50	Mixed population	Carcinoma of Cervix
An 649	Male	55	Mixed population	Congestive Heart Failure, Pulmonary Embolism
An 651	Female	42	White	Septicaemia with Diffusion, Intravascular
An 654	Male	66	White	Acute Myocardial Infarction
An 657	Male	49	Mixed population	Hypothermia
An 660	Male	46	White	Natural Causes
An 661	Female	38	Black	Carcinoma of Bronchus with Brain Metastases

An 662	Male	69	Black	Pneumonia, Kidney Failure
An 663	Female	40	Mixed population	Natural Causes
An 664	Male	38	Mixed population	Subacute bacterial endocarditis
An 665	Female	34	Mixed population	Pulmonary Tuberculosis
An 666	Male	50	Mixed population	Carcinoma of Bronchus ® intermediate
An 667	Male	38	White	Myocardial Infarction
An 669	Female	33	Mixed population	Carcinoma of Cervix
An 670	Male	58	Mixed population	Leukaemia, Chronic
An 674	Male	56	White	Coronary Thrombosis
An 675	Male	56	Mixed population	Carcinoma of Stomach
An 676	Male	31	Mixed population	Hypertension
An 678	Male	41	Black	Massive Bleeding Oesop. Varices, Liver Cirrhosis, Portal Hypertension
An 681	Male	41	Mixed population	Respiratory Failure due to previous TB destruction to lungs
An 684	Female	62	Mixed population	Bronchopneumonia
An 687	Male	56	Mixed population	Septicaemia and Kleb. Pneumonia
An 689	Male	66	Mixed population	Tuberculosis
An 690	Female	50	Mixed population	Pneumonia (lobar)
An 691	Male	59	White	Myocardial Infarction
An 692	Female	66	White	Anterior Myocardial Infarct
An 693	Female	48	Mixed population	Carcinoma of Oesophagus and Bronchopneumonia
An 694	Male	23	Mixed population	Hodgkin's Lymphoma
An 695	Male	44	Black	Lung Abscess
An 697	Male	42	Mixed population	Bronchopneumonia
An 698	Female	52	Mixed population	Carcinoma of Pharynx
An 699	Male	46	Black	Carcinoma of Bronchus, Respiratory Arrest
An 702	Female	38	Mixed population	Cardiopulmonary Arrest
An 703	Male	46	Mixed population	Cerebral Thrombosis
An 704	Male	52	White	Myocardial Infarction
An 706	Female	34	Mixed population	Pulmonary Embolism, Intracerebral bleeding
An 707	Male	41	Mixed population	Carcinoma of Tongue and Pharynx
An 708	Male	55	Mixed population	Cerebrovascular Accident
An 710	Male	48	Mixed population	Natural Causes
An 713	Female	50	White	Cardiac Failure
An 714	Female	65	Mixed population	Hypertension, Gastritis, Pharyngitis
An 716	Male	56	Mixed population	Carcinoma of Bronchus
An 718	Female	46	Mixed population	Aspiration, Pneumonia
An 719	Female	42	Mixed population	Renal Failure with Anaemia
An 721	Male	60	Mixed population	Congestive Cardiac Arrest
An 722	Male	58	Mixed population	Pulmonary Tuberculosis, Respiratory Failure
An 725	Female	48	Mixed population	Congestive Cardiac Failure, Pericardial effusion
An 732	Male	59	White	Myocardial Infarction
An 733	Male	49	Mixed population	Tuberculosis, Massive Haemoptysis
An 734	Male	36	Mixed population	Respiratory Arrest
An 741	Male	56	Mixed population	Cerebrovascular Accident
An 743	Male	58	Mixed population	Cerebral Thromboembolism
An 745	Male	20	Black	Cardiac Arrest, Rheumatic Myocardial Infarction
An 746	Male	41	Mixed population	Spontaneous Subarachnoid Bleeding
An 747	Female	43	Mixed population	Natural Causes
An 749	Male	48	Mixed population	Acute Pancreatitis
An 751	Female	40	Mixed population	Subarachnoid Haemorrhage
An 752	Female	43	Mixed population	Renal and Biventricular Cardiac Failure
An 753	Female	42	Mixed population	Carcinoma of Cervix
An 754	Female	39	Mixed population	Metastatic Cervix carcinoma
An 758	Male	33	Black	Tuberculosis
An 759	Female	28	Mixed population	Bronchopneumonia
An 760	Male	57	Black	Tumour (brain metastases), Anaemia
An 765	Male	41	Mixed population	Bronchopneumonia

An 766	Male	53	Mixed population	Carcinoma of Mouth Floor and Tongue
An 770	Male	53	Mixed population	Carcinoma of Hard Palate
An 771	Male	62	Mixed population	Coronary Thrombosis
An 772	Male	41	Mixed population	Septicaemia
An 774	Female	41	Mixed population	Pulmonary Tuberculosis
An 776	Male	60	Mixed population	Disseminated Carcinoma of Trachea
An 777	Male	52	Mixed population	Pulmonary TB
An 778	Male	42	Mixed population	Liver failure with Encephalopathy
An 779	Female	40	Mixed population	Carcinoma of Cervix
An 780	Female	32	Mixed population	Hypoglycaemia
An 781	Male	55	Mixed population	Carcinoma of Oesophagus
An 782	Male	37	Mixed population	Carcinoma of Lung
An 783	Female	27	Mixed population	Pulmonary TB
An 784	Male	54	Black	Carcinoma of Oesophagus
An 785	Male	47	Mixed population	Meningitis
An 787	Male	45	Mixed population	Chronic destr. Lung disease, TB
An 788	Male	28	Mixed population	Natural Causes
An 790	Male	35	Mixed population	Cardiac Arrest
An 791	Male	58	Mixed population	Carcinoma of Pancreas
An 793	Male	59	Mixed population	Carcinoma of Bronchus
An 794	Male	66	Mixed population	Natural Causes
An 795	Male	45	Mixed population	Disseminated Large cell carcinoma
An 796	Female	54	Mixed population	Intracerebral bleeding with respiratory arrest
An 797	Female	28	Mixed population	Cardiopulmonary Arrest
An 800	Female	81	White	Myocardial Infarction
An 801	Male	48	Mixed population	Alcoholic Liver Cirrhosis
An 802	Male	67	Mixed population	Chronic Obstructive Airways Disease
An 804	Male	44	Mixed population	Respiratory Failure
An 805	Male	53	White	Cardiac Arrest, cardiomyopathy
An 806	Male	64	Mixed population	Carcinoma of Mouth (Squamous)
An 807	Male	41	Mixed population	Natural Causes
An 809	Male	54	Mixed population	Cardiac Failure and Arrhythmia
An 810	Male	60	Mixed population	Pulmonary Tuberculosis
An 811	Male	38	Mixed population	Disseminated Tuberculosis
An 812	Male	40	Mixed population	Pancreatitis
An 813	Male	61	Mixed population	Cerebrovascular Accident
An 814	Male	69	White	Small cell Bronchus Carcinoma
An 815	Female	60	Mixed population	Chronic Renal Failure
An 817	Male	69	White	Cardiogenic Shock
An 818	Male	56	Mixed population	Cerebrovascular Accident
An 819	Male	59	Black	Pulmonary Embolism, Tuberculosis
An 820	Female	61	White	Carcinoma of Cervix
An 824	Female	61	White	Carcinoma of Oesophagus
An 833	Female	23	Mixed population	Cardiopulmonary Arrest
An 837	Male	45	Mixed population	Epilepsy
An 844	Female	27	Black	Upper cervical dislocation and spinal cord compression
An 846	Female	28	Black	Pulmonary Tuberculosis, Keto acidosis
An 847	Female	30	Mixed population	Renal Failure
An 849	Male	27	Mixed population	Pulmonary Tuberculosis
An 850	Male	50	Mixed population	Cardiovascular Accident
An 853	Male	44	Mixed population	Tuberculosis
An 855	Male	44	Mixed population	Diabetes Mellitus
An 856	Male	42	Mixed population	Pulmonary Tuberculosis
An 857	Male	34	Mixed population	Epilepsy, Cardiorespiratory Failure, Epilepsy
An 859	Female	34	Mixed population	Pulmonary Tuberculosis
An 860	Male	42	Mixed population	Cardiopulmonary Arrest
An 861	Male	42	Mixed population	Septicaemia
An 862	Male	41	Black	Cardiopulmonary Arrest, Hepatic coma

An 864	Female	38	Mixed population	Respiratory Failure
An 865	Female	41	Mixed population	Hepatic coma, Hepatic Failure
An 866	Male	55	Mixed population	Pneumonia
An 867	Male	20	Mixed population	Cardiopulmonary Arrest
An 868	Male	49	Black	Pulmonary Tuberculosis
An 869	Male	40	Mixed population	Unknown heart pathology complicated by infective endocarditis
An 872	Female	47	Mixed population	Natural Causes
An 873	Male	39	Mixed population	Pneumonia
An 875	Male	19	Mixed population	Hepatoma with Gastrointestinal bleeding
An 876	Male	34	Black	Cardiopulmonary Arrest, Brain Abscess
An 877	Male	49	Mixed population	Carcinoma of Oesophagus
An 880	Female	55	Mixed population	Carcinoma of Stomach
An 881	Male	40	Mixed population	Pulmonary Tuberculosis
An 884	Female	23	Mixed population	Pulmonary Tuberculosis
An 888	Female	82	White	Coronary Thrombosis
An 895	Female	60	Mixed population	Cardiorespiratory Failure
An 930	Male	81	Black	Multiple organ failure + pneumonia
An 931	Male	67	Mixed population	Cardiovascular Accident

APPENDIX B: LIST OF CONSUMABLES, EQUIPMENT, SOFTWARE PACKAGES AND RESEARCH FACILITIES

Consumables

The following consumables were used for this study:

Abrasive paper (Grit p220, p800, p1200A)

Glass microscope slides and cover slips

Petroleum Jelly

DPX Mountant (SAAR1935000KF, UN1307, uniLAB®, Merck (Pty.) Ltd.)

Xylene

Equipment

A list of equipment utilised for this study is as follows:

Digital Camera (Sony®, Model Number DSC-H7, Zeiss®, 15X Optical Zoom, 8.1 Mega Pixels)

Lodox® Statscan® Imaging system

Light microscope (Zeiss® Axioskop 2, Ser. no. 801452)

Light microscope with phase and DIC contrast (Nikon®)

Magnifying lamp (Model: 8606L, Magnification: 3D/5D/8D)

Small hacksaw

Soft artist's paint brush

Software packages

The software packages used in this study are listed below:

AxioVision® (AxioVs40), Version 4.7.2.0 (Carl Zeiss® Microscopy)

ImageJ® (Image Processing and Analysis in Java)

Leica® Application Suite (LAS)

Microsoft® Excel®, Version 7 (Microsoft Corporation)

STATA® statistical software version 13.0 SE (StataCorp®, College Station, TX)

ZEN® Lite imagine software (2012)

Research facilities

The following facilities were used in this study:

Histology laboratory of Division Anatomy and Histology, Department of Biomedical Sciences, Stellenbosch University.

Microscopy facility of Division Anatomy and Histology, Department of Biomedical Sciences, Stellenbosch University.

Physical Anthropology Research Unit, Division of Anatomy and Histology, Department of Biomedical Sciences, Stellenbosch University.

Western Cape Forensic Pathology Service medico-legal mortuary at Tygerberg Hospital, Cape Town.

APPENDIX C: TABLE FOR INDICATING GENERAL FEATURES OR DISEASES PRESENT

Table 9.2: Table used to indicate general features or diseases present on skeletons

AN :		AN 201	AN 208	AN 220	AN 231	AN 234	AN 261	AN 291	AN 297	AN 299	AN 306	AN 315	AN 344	AN 370
General:	Age													
	Sex													
	Population group													
Congenital:	Sacralisation L5: 0/1/2/3/4													
	Lumbarisation S1: 0/1/2/3/4													
	Spina bifida: -/+													
	Scoliosis: -/+													
	Kyphosis: -/+													
	Other:													
Infectious (non-specific):	Periostitis: -/+													
	Osteomyelitis: -/+													
	Visceral rib lesions: -/+													
	Other:													
Infectious (specific):	Pott's disease: -/+													
	Other:													
Metabolic (non-specific):	Porotic hyperostosis: 0/1/2													
	Cribra orbitalia: 0/1/2/3													
	Enamel hypoplasia: +/-													
	Osteoporosis: +/-													
	Harris lines: -/+													
	Other:													
Metabolic (specific):	Scurvy: -/+													
	Rickets: -/+													
	Osteomalacia: -/+													
	Other:													

Joint (non-specific):	Osteoarthritis (vertebral): -/+													
	Osteoarthritis (peripheral): -/+													
	Schmorl's nodes: -/+													
	Other:													
Joint (specific):	Ankylosing spondylitis: -/+													
	DISH: -/+													
	Rheumatoid arthritis: -/+													
	Other:													
Neoplasms:	All: -/+													
Miscellaneous:	Paget's disease: -/+													

APPENDIX D: BOOKLET CONSTRUCTED FOR EACH SKELETON STUDIED

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KIRSTEN COLLECTION BIOLOGICAL PROFILE SHEET

Individual Information

General Information

Y	Y	Y	Y	M	M	D	D

☐ **Archaeological** ☐ **Forensic** ☐ **Cadaver**

Recorded by: _____ _____
NAME & SURNAME SIGNATURE

Collection ID	Cadaver ID
Sex	Date of Birth
Age	Date of Death
Ancestry	Area / Hospital
Stature	Received
Weight	COD

History

Medical History: _____

_____

Malformation: _____

_____

_____

Dental Records: _____

_____

Suspected antemortem bone lesions: _____

_____

Suspected perimortem injuries: _____

_____

Postmortem injuries: _____

_____

_____

_____

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Skeletal Inventory

Codes:

1 - present complete
2 - present fragmentary/damaged
3 - absent /missing (post-mortem)
4 – ante mortem loss
5 - unerupted (dentition)
6 - congenitally missing

Cranium:

	Left	Right		Left	Right
Frontal:			Maxilla:		
Parietal:			Nasal:		
Occipital:			Ethmoid:		
Temporal:			Lacrimal:		
Zygomatic:			Vomer:		
Palate:			Sphenoid:		
Sutural bone:					

Mandible:

	Left	Right		Left	Right
Body:			Ramus:		

Dentition:

	Left	Right		Left	Right
Max. I1:			Mand. I1:		
Max. I2:			Mand. I2:		
Max. C:			Mand. C:		
Max. P1:			Mand. P1:		
Max. P2:			Mand. P2:		
Max. M1:			Mand. M1:		
Max. M2:			Mand. M2:		
Max. M3:			Mand. M3:		

Post cranial:

	Left	Right		Mid		Left	Right	Count
Clavicle:			Hyoid:		Rib 1-2:			
Scapula:			Manubrium:		Rib 3-10			
Humerus:			Sternal Body:		Rib 11-12			
Radius:			Atlas:		Carpals:			
Ulna:			Axis:					
Femur:			Cervical 3-7:		Metacarpals:			
Patella:			count					
Tibia:			Thor. 1-12:		Phalanges:			
Fibula:			count					
Ilium:			Lumb. 1-5:		Tarsals:			
Pubis:			count					
Ischium:			Sacrum:		Metatarsals:			
			Coccyx		Phalanges:			

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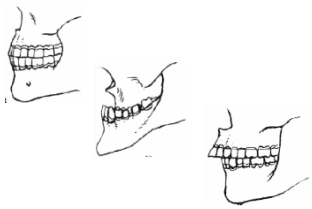
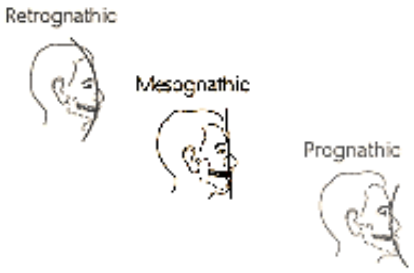
Dental Health Observations

Relationship:



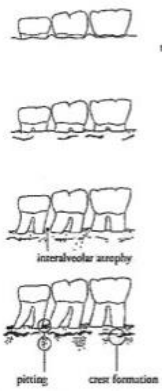
- Normal ☐
- Undershot ☐
- Overbite ☐

Shape of jaws:



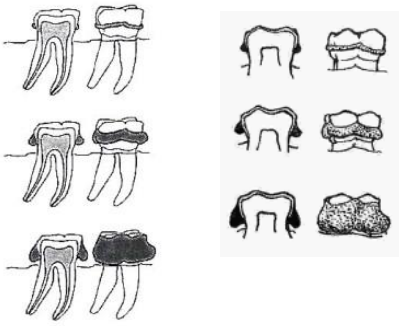
- Retrognathic ☐
- Mesognathic ☐
- Prognathic ☐

Peridontitis:



- \- ☐
- \+ ☐
- ++ ☐
- +++ ☐

Calculus:

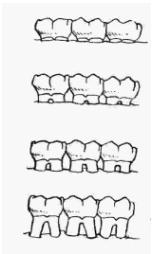


- \- ☐
- \+ ☐
- ++ ☐
- +++ ☐

Stains on teeth:

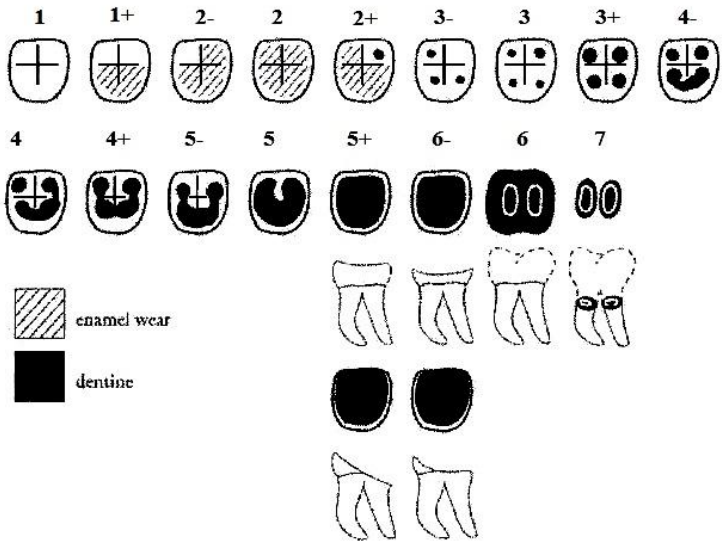
- \- ☐
- \+ ☐
- ++ ☐

Alveolar atrophy:



- \- ☐
- \+ ☐
- ++ ☐
- +++ ☐

Wear/Attrition of molars (see next page)



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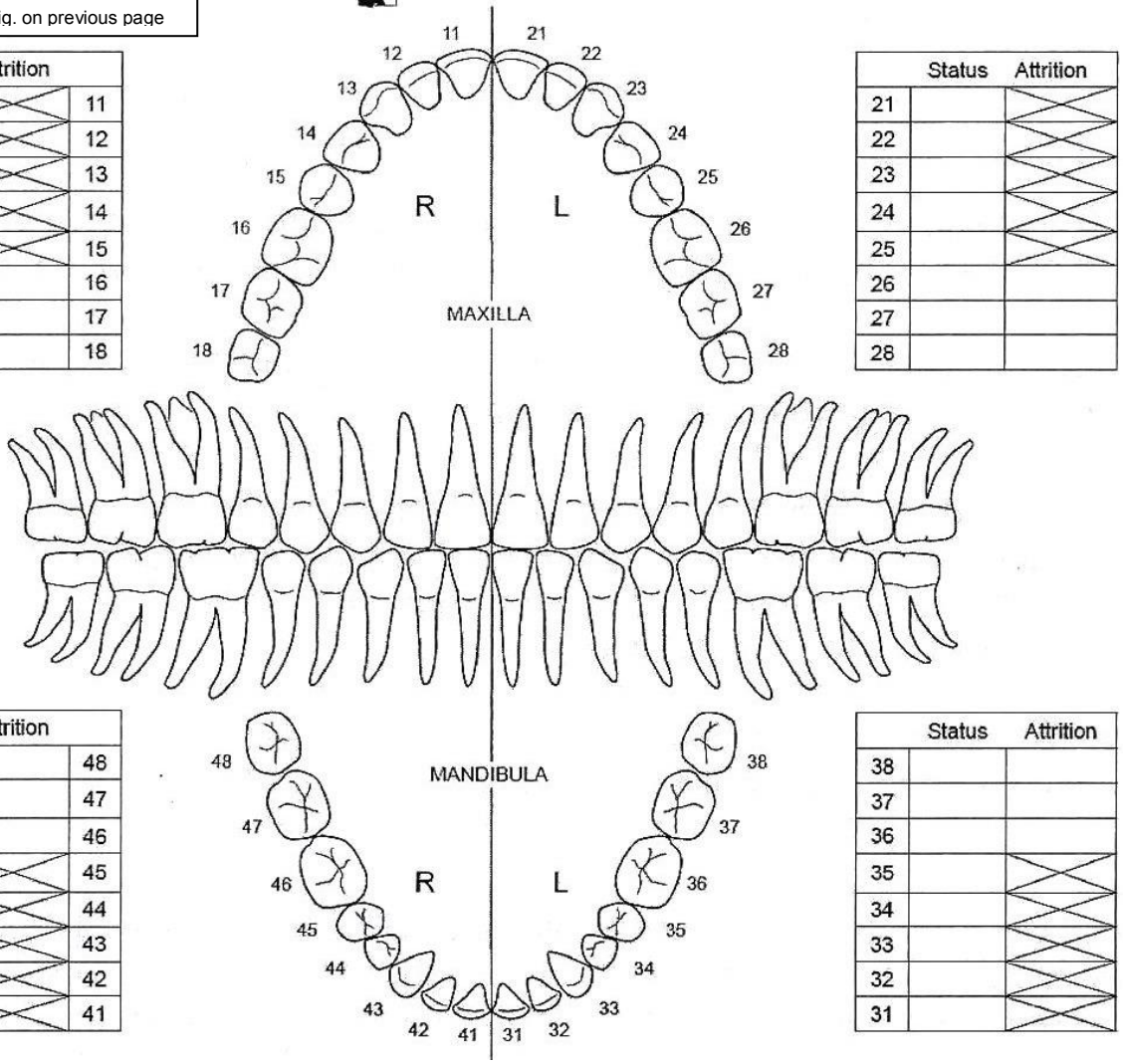
Dental Status of Permanent Dentition

shade indicates absence

Attrition: see fig. on previous page

Status	Attrition	
		11
		12
		13
		14
		15
		16
		17
		18

	Status	Attrition
21		
22		
23		
24		
25		
26		
27		
28		

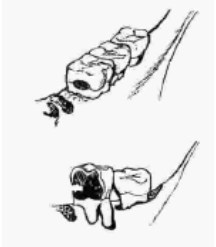


Status	Attrition	
		48
		47
		46
		45
		44
		43
		42
		41

	Status	Attrition
38		
37		
36		
35		
34		
33		
32		
31		

Mark the following on the chart:

- ☐ '**I**' Inspected tooth (whole/part of tooth e.g. only crown during partial eruption can be inspected in position)
- ☐ '**M**' Missing socket (jaw position) and related tooth
- ☐ '**U**' Unerupted tooth (tooth is still in retained position inside jaw)
- ☐ '**C**' congenitally absent tooth (if the tooth failed to develop/agenesis)
- ☐ '**A**' antemortem missing tooth (if the empty socket displays rounded edges or is obliterated)
- ☐ '**P**' post mortem missing tooth (if the empty socket displays sharp unremodeled edges)



Mark and indicate detail of the following on the chart:

- ☐ Outline all caries on teeth
- ☐ Mark enamel hypoplasia lines on teeth
- ☐ Mark diastemas with an arrow (indicate position of teeth apart)
- ☐ Mark mechanical traumas (fractures, remaining roots, wear channels)
- ☐ Mark all restorations (amalgam, gold, silver, porcelain, plastic, bridges etc)
- ☐ Mark the position of supernumerary teeth with an arrow
- ☐ Shade the location of carious lesions on roots and crowns with a pencil
- ☐ Mark with an arrow the position of abscesses (pus cavities)
- ☐ Mark with an arrow the position of fistulas (passage canals for pus release)

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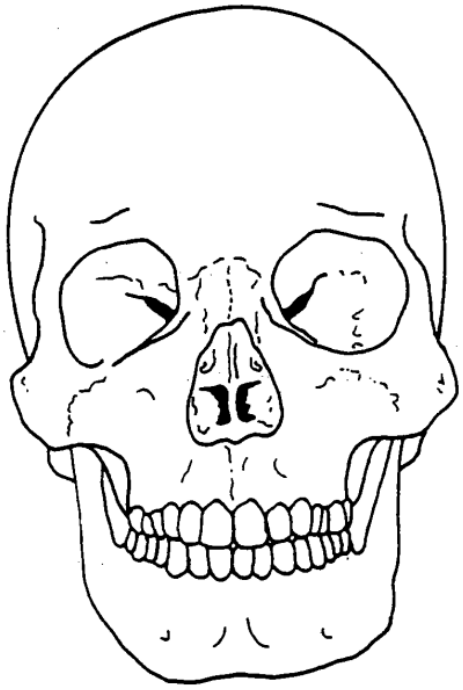
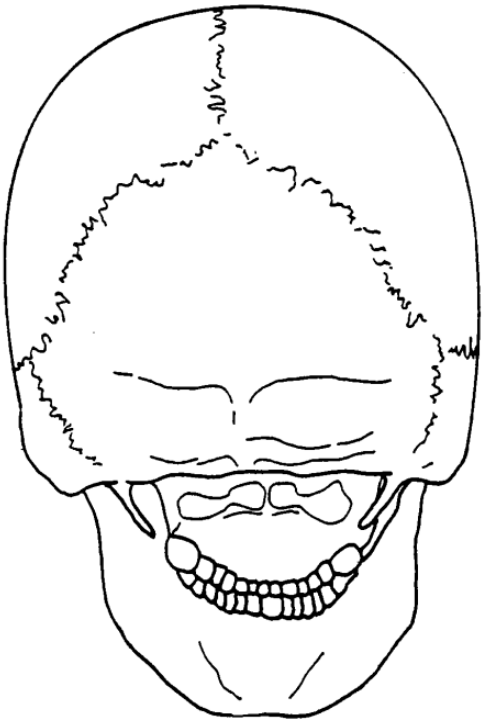
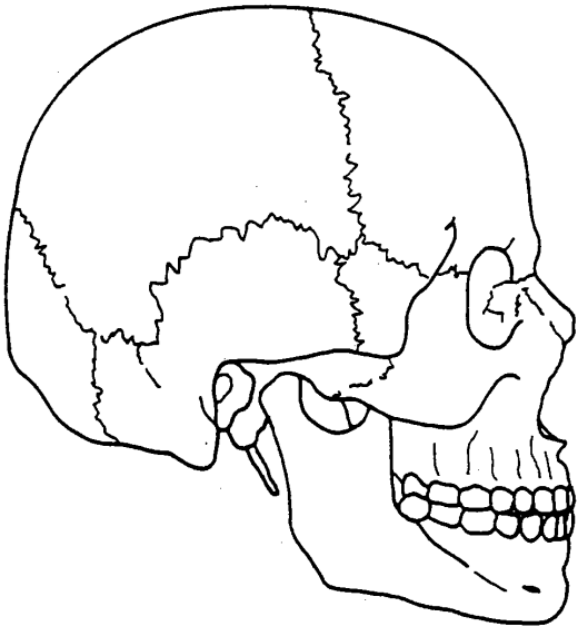
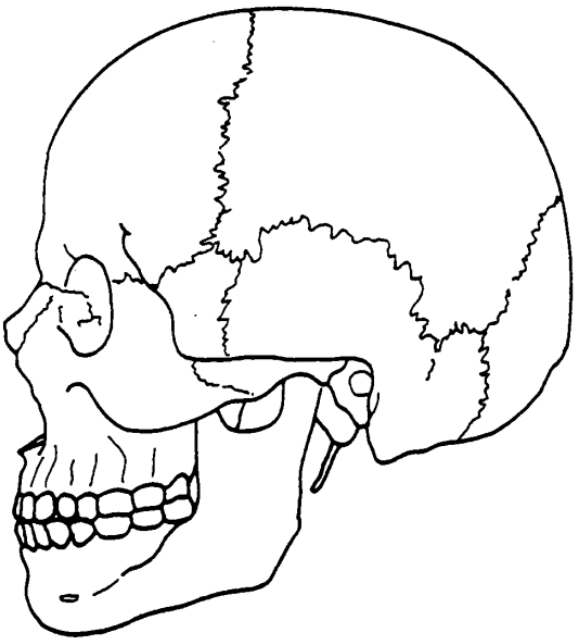
Cranial Trauma & Pathologies









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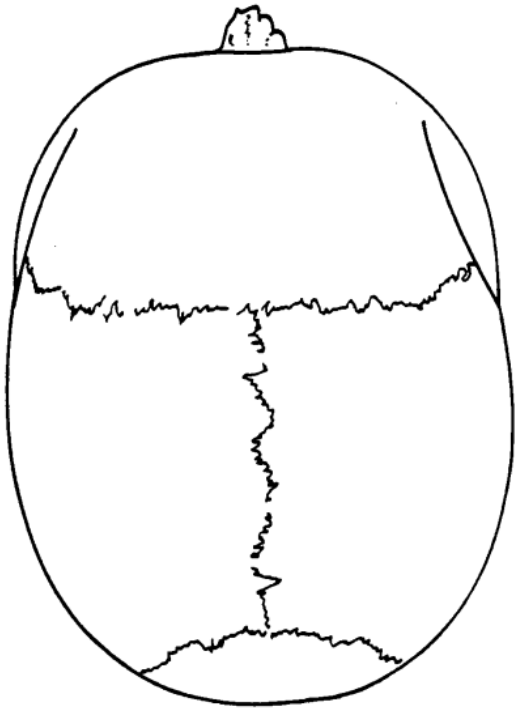
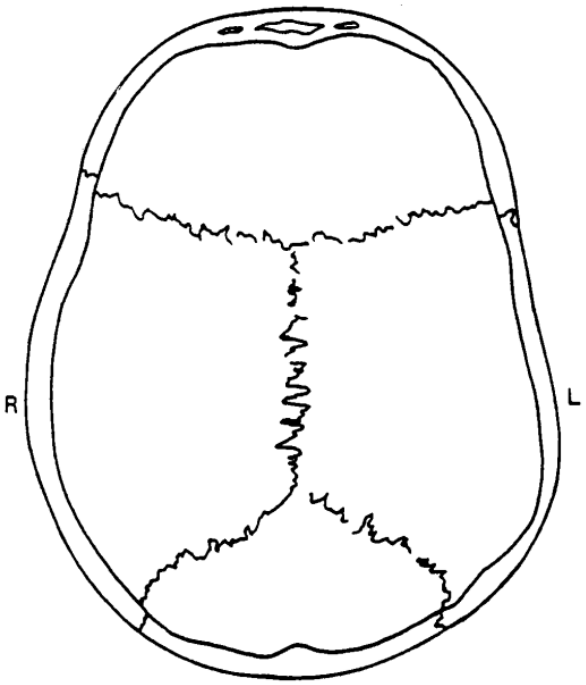
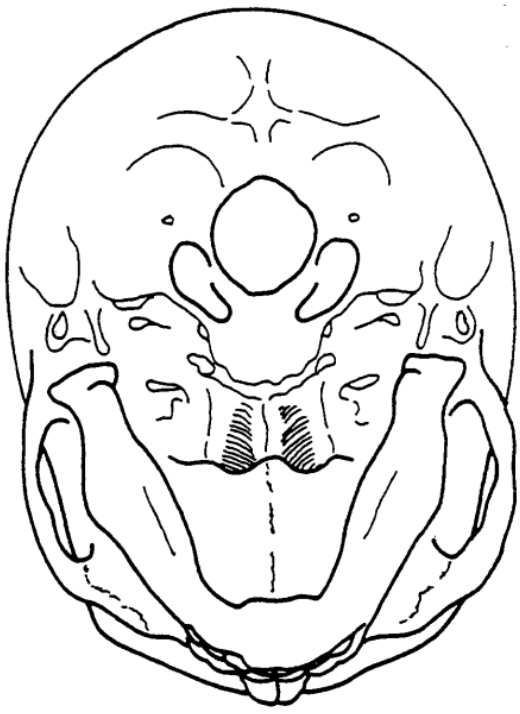
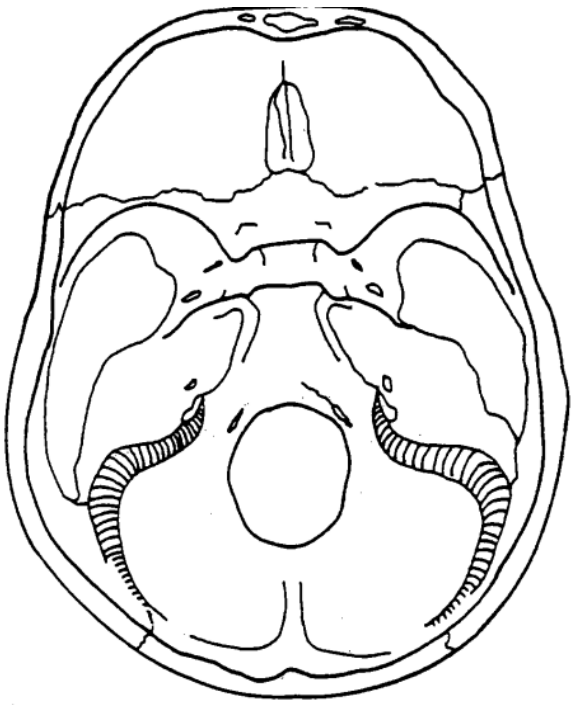
Cranial Trauma & Pathologies





INNER VIEW OF SKULL





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Thoracic Traits

Fill in the blocks if the pathology/trait present and indicate on diagram where pathologies/trauma is present.

Congenital:

Cervical spine:

Spine bifidity ☐ #.....
Accessory Transv foramen ☐ #.....
Open neural arch ☐ #.....

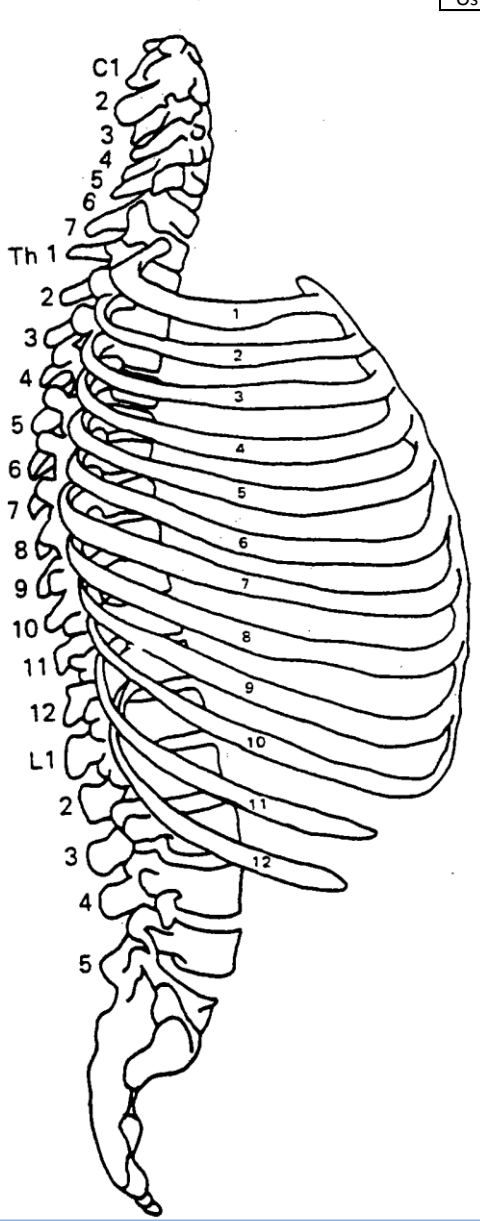
Lumbar/sacral LSTVs:

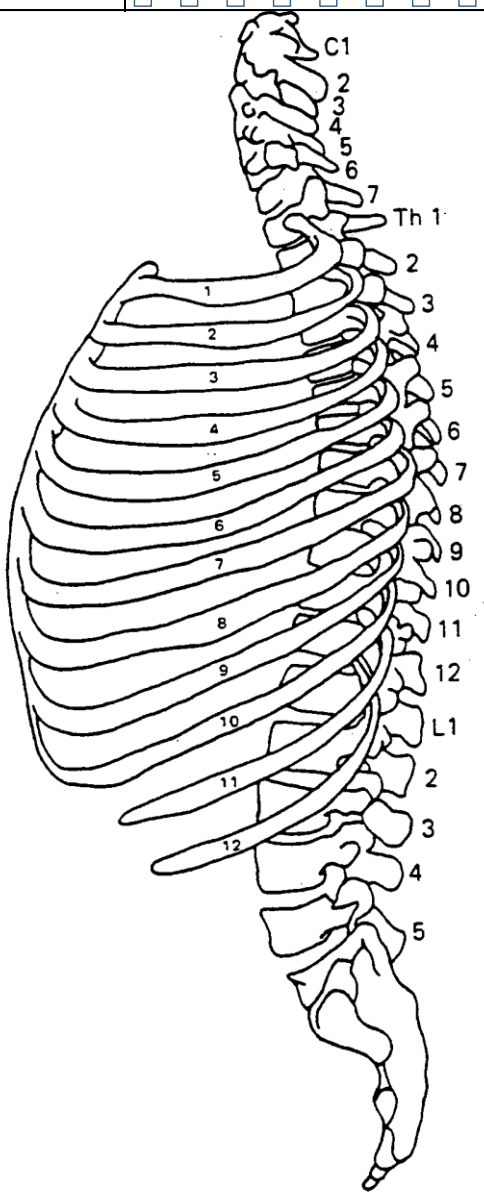
Sacralisation L5 ☐ type.....
Lumbarisation T12 ☐ type.....
Open arch (spina bifida) ☐ #.....

Sacral

Coccyx fused ☐
Number of segments .....
Position of curvature .....

Pathologies	Cervical spine:			Thoracic spine:			Lumbar spine:			Sacrum:		
	-	+	++	-	+	++	-	+	++	-	+	++
Periostitis (nonspecific)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Osteoarthritis (OA)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Ankylosing spondylitis (AS)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Spondylolisthesis	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Spondylolysis	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
DISH	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kyphosis	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Osteophytes	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Osteoporosis	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐





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Post Cranial Trauma & Pathologies

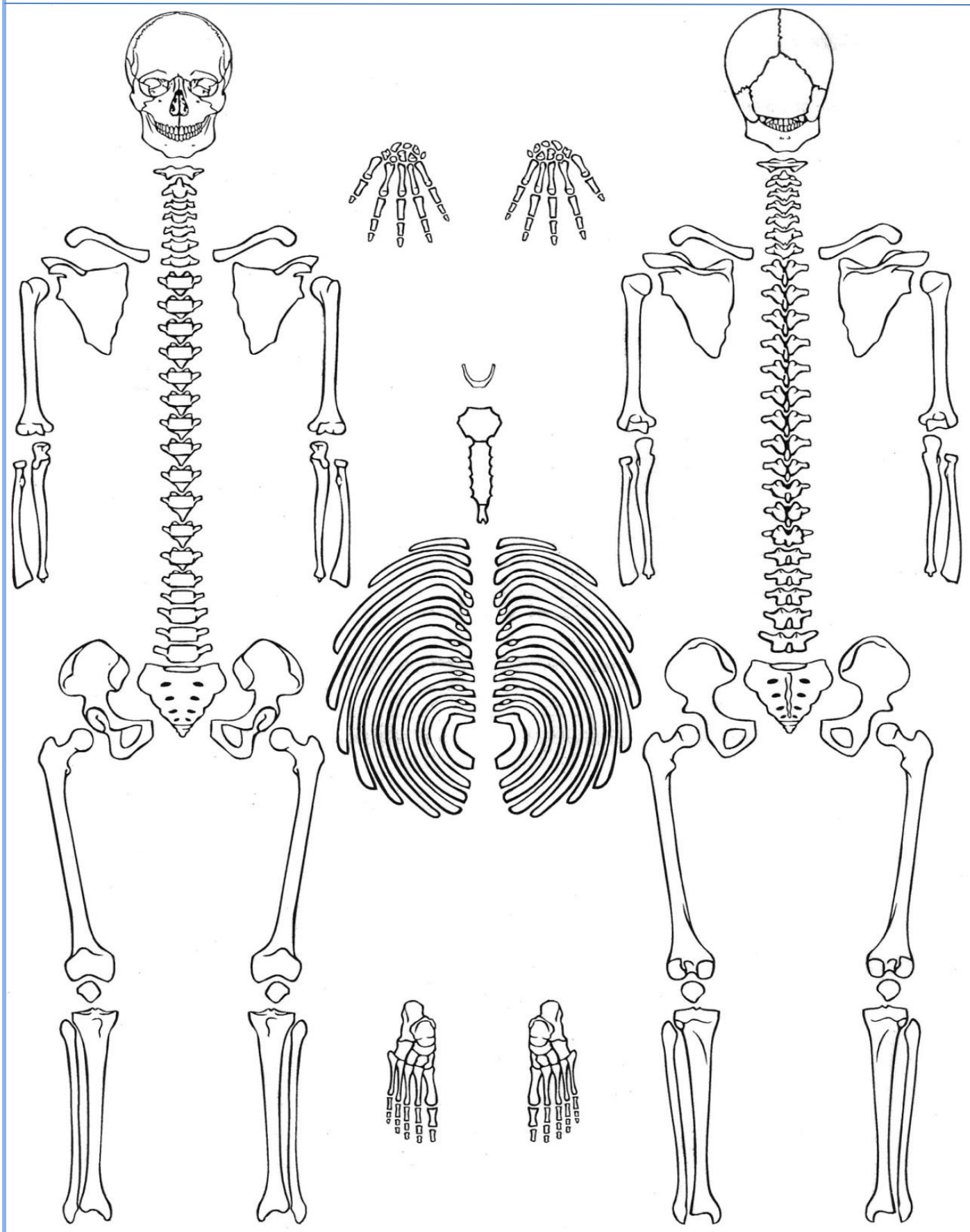

Table 9.3: Table used to indicate disease features and gradings on specific bones of skeletons

			Congen:	**Infec-tious**			**Metabolic**			**Joint**		**Neoplasms:**	**Other:**
Bones		**Inv: -/+**	Spina bifid: -/+	Periostitis: 0/1/2	Osteomy elitis: -/+	Visceral rib lesions: -/+	PH: 0/1/2	CO: 0/1/2/3	Vertebral compression : 0/1/2/3	Osteo-phytes: 0/1/2/3/4	Schmorl's nodes: -/+	All: -/+	Harris lines: -/+
Vert:	Atlas			n/a	n/a	n/a	n/a	n/a					n/a
	Axis			n/a	n/a	n/a	n/a	n/a					n/a
	C3			n/a	n/a	n/a	n/a	n/a					n/a
	C4			n/a	n/a	n/a	n/a	n/a					n/a
	C5			n/a	n/a	n/a	n/a	n/a					n/a
	C6			n/a	n/a	n/a	n/a	n/a					n/a
	C7			n/a	n/a	n/a	n/a	n/a					n/a
	T1			n/a	n/a	n/a	n/a	n/a					n/a
	T2			n/a	n/a	n/a	n/a	n/a					n/a
	T3			n/a	n/a	n/a	n/a	n/a					n/a
	T4			n/a	n/a	n/a	n/a	n/a					n/a
	T5			n/a	n/a	n/a	n/a	n/a					n/a
	T6			n/a	n/a	n/a	n/a	n/a					n/a
	T7			n/a	n/a	n/a	n/a	n/a					n/a
	T8			n/a	n/a	n/a	n/a	n/a					n/a
	T9			n/a	n/a	n/a	n/a	n/a					n/a
	T10			n/a	n/a	n/a	n/a	n/a					n/a
	T11			n/a	n/a	n/a	n/a	n/a					n/a
	T12			n/a	n/a	n/a	n/a	n/a					n/a
	L1			n/a	n/a	n/a	n/a	n/a					n/a
	L2			n/a	n/a	n/a	n/a	n/a					n/a

	L3			n/a	n/a	n/a	n/a	n/a					n/a
	L4			n/a	n/a	n/a	n/a	n/a					n/a
	L5			n/a	n/a	n/a	n/a	n/a					n/a
	Sac			n/a	n/a	n/a	n/a	n/a					n/a
	Coc			n/a	n/a	n/a	n/a	n/a					n/a
Occip:	L		n/a			n/a		n/a	n/a		n/a		n/a
	R		n/a			n/a		n/a	n/a		n/a		n/a
Pariat:	L		n/a			n/a		n/a	n/a		n/a		n/a
	R		n/a			n/a		n/a	n/a		n/a		n/a
Front:	L		n/a			n/a			n/a		n/a		n/a
	R		n/a			n/a			n/a		n/a		n/a
Facial:	L		n/a			n/a		n/a	n/a		n/a		n/a
	R		n/a			n/a		n/a	n/a		n/a		n/a
Mand:	L		n/a			n/a	n/a	n/a	n/a		n/a		n/a
	R		n/a			n/a	n/a	n/a	n/a		n/a		n/a
Ribs:	L 1-3		n/a				n/a	n/a	n/a		n/a		n/a
	L 4-8		n/a				n/a	n/a	n/a		n/a		n/a
	L 9-12		n/a				n/a	n/a	n/a		n/a		n/a
	R 1-3		n/a				n/a	n/a	n/a		n/a		n/a
	R 4-8		n/a				n/a	n/a	n/a		n/a		n/a
	R 9-12		n/a				n/a	n/a	n/a		n/a		n/a
Stern:	Man		n/a			n/a	n/a	n/a	n/a		n/a		n/a
	Body		n/a			n/a	n/a	n/a	n/a		n/a		n/a
Clavi:	L		n/a			n/a	n/a	n/a	n/a		n/a		n/a

	R		n/a			n/a	n/a	n/a	n/a		n/a		n/a
Scap:	L		n/a			n/a	n/a	n/a	n/a		n/a		n/a
	R		n/a			n/a	n/a	n/a	n/a		n/a		n/a
Hum:	L		n/a			n/a	n/a	n/a	n/a		n/a		
	R		n/a			n/a	n/a	n/a	n/a		n/a		
Rad:	L		n/a			n/a	n/a	n/a	n/a		n/a		
	R		n/a			n/a	n/a	n/a	n/a		n/a		
Ulna:	L		n/a			n/a	n/a	n/a	n/a		n/a		
	R		n/a			n/a	n/a	n/a	n/a		n/a		
Os coxae	L		n/a			n/a	n/a	n/a	n/a		n/a		n/a
	R		n/a			n/a	n/a	n/a	n/a		n/a		n/a
Fem:	L		n/a			n/a	n/a	n/a	n/a		n/a		
	R		n/a			n/a	n/a	n/a	n/a		n/a		
Pat:	L		n/a			n/a	n/a	n/a	n/a		n/a		n/a
	R		n/a			n/a	n/a	n/a	n/a		n/a		n/a
Tibia:	L		n/a			n/a	n/a	n/a	n/a		n/a		
	R		n/a			n/a	n/a	n/a	n/a		n/a		
Fib:	L		n/a			n/a	n/a	n/a	n/a		n/a		
	R		n/a			n/a	n/a	n/a	n/a		n/a		
Hand:	L		n/a			n/a	n/a	n/a	n/a		n/a		n/a
	R		n/a			n/a	n/a	n/a	n/a		n/a		n/a
Foot:	L		n/a			n/a	n/a	n/a	n/a		n/a		n/a
	R		n/a			n/a	n/a	n/a	n/a		n/a		n/a