

Pathological cranial lesions in a juvenile cranial collection
By: Hannah Miller

I. Abstract

The purpose of this study is to study the occurrence of cranial defects associated with metabolic disease and inflammatory processes in juveniles. Specific pathogenic changes to be studied are porotic hyperostosis, orbital lesions, endocranial lesions and linear enamel hypoplasia (hence forth referred to as LEH). In some cases, particularly with endocranial lesions, the exact causes and age distributions are still not well documented and further studies of co-occurrence with other lesions of known etiology are needed (Lewis 2004, Janovic *et al.* 2012). In other cases, as with the occurrence and diagnosis of the orbital lesions commonly know as cribra orbitalia and porotic hyperostosis, the data which has been collected and analyzed relies on outdated etiology.

II. Introduction

During the course of this study it is my intent to gain an understanding of the types and co-occurrences of pathological changes to the crania of juveniles. As an anthropologist and an individual interested in paleopathology, I have found that the diagnostic criteria and documentation of pathogenic changes are often lacking. Data available often relies on insufficiently detailed descriptions of the pathological changes of particular diseases. By doing a systematic study with detailed and highly descriptive classifications of pathogenic changes, it is my hope not only to gain a greater understanding of these pathologies and their relation to one-another, but also to make my findings accessible to potentially aid in the creation of a better methodology for the diagnostic criteria of cranial pathologies in juveniles. As such I am utilizing an anatomical collection housed at University of the Pacific.

III. Background

This study expands on previous research conducted by Cynthia Wilczak PhD. On the occurrence and diagnosis of cribra orbitalia in the anatomical specimen collection housed at University of the Pacific Dental School in San Francisco, CA. This study was conducted after the publication of Walker (2012) paper where it was suggested that iron-deficiency anemia was most likely not the cause of the porotic hyperostosis or cribra orbitalia¹, but rather that a complex interaction of malnutrition, sanitation, infectious disease and cultural practices were the most likely causes of porotic lesions in the cranium (Walker *et al.* 2009). This complex etiology harkens back to some of the earliest paleopathology publications on the subject.

The first studies to suggest a potential cause for hyperostotic cranial lesions were published in 1929 (Moore 1929; Williams 1929). Moore compared the crania of ancient Mayan individuals exhibiting porotic hyperostosis to the radiograph of a modern individual diagnosed with sickle cell anemia. Radiographic analysis of both the modern and ancient crania presented an expansion of the diploe, hair on end trabeculae, and the obliteration of the ectocranium of the cranium with a largely unaffected endocranium. The similarities in the radiographs of the ancient and modern crania led the hypothesis that sickle cell anemia, or a similar disease, was potentially the cause of the cranial changes (Moore 1929). While working with Native American remains, Williams compared radiographs of several archaeological specimens to modern clinical cases where he noted that the lesions were similar to clinical cases of sickle cell anemia and

Jaksch's anemia, rickets and scurvy. Williams eliminated rickets as a potential cause as it was believed that Native American populations would have had sufficient exposure to sunlight to prevent the onset of rickets (Williams 1929). Williams (1929) was also the first researcher to propose that cranial deformation, in the form of cranial changes due to cradle boarding, could play a role in the development of the lesions, though it was postulated that these changes would only occur in conjunction with one of the other causative factors.

A later study in the frequency of porotic hyperostosis in two separate cemeteries of similar racial, temporal and geographic distributions showed radically different frequencies of porotic hyperostosis despite the seemingly similar populations. Henschen (1961) proposed that the discrepancy in frequency could be associated with different stresses, specifically nutrition and chronic infection. This was based on the higher prevalence of porotic hyperostosis in the cemetery which consisted of mainly "poor, undernourished and mostly leprous individuals" (Henschen 1961:729), compared to the other cemetery sample. He also used these factors to explain the lack of porotic hyperostosis in the crania he examined that were more recently deposited, as the nutritional and health conditions in modern populations were far superior to those during the medieval period, which would result in far lower frequencies or possibly the absence of porotic hyperostosis in modern remains (Henschen 1961).

In 1966 a highly influential article was published by Nathan and Hass. The authors developed a strict scoring guide for cribra orbitalia and applied it to 718 crania from ancient samples from the Judean desert, native populations from North, South and Central America, Eskimos and modern peoples from India. At least one of the scored

lesions was present in every individual sampled, though they had the highest prevalence in children and were seen more frequently in adult female than adult males. It was the manifestation of cribra orbitalia in all individuals, despite the diverse sample, which indicated that the lesions were most likely, associated with nutritional deficiency (Nathan and Hass 1966). While the scoring methods were developed specifically for cribra orbitalia, the authors noted that porotic lesions of the vault seemed to follow the same characterizations. Three types of porous lesions were classified; porotic which was characterized by small isolated pores, cripeotic in which the pores are larger and more densely distributed without pore coalescence and trabecular in which the pores have become coalesced and resulting in the formation of bone trabeculae. This scoring system was used in the development of later scoring guides still in use today (Buikstra and Ubelaker 1994; Stuart- Macadam 1985), as well as being the foundation for the orbital scoring done in this study.

The first reference to porotic hyperostosis as we refer to it today was published by J. Lawrence Angel (1966, 1967), which is typically defined as abnormal porosity of the outer table with an increase in spongy bone. Angel noted the descriptions of porotic hyperostosis better fit the clinical descriptions of bony change associated with hemolytic anemia than other nutrient deficiencies like rickets or infantile scurvy (Angel 1964). This idea was further developed two years later when Angel noted a higher frequency of porotic hyperostosis in Mediterranean populations who lived in marshy environments, which were the preferred habitat of mosquitos known to carry *Falciparum malaria*. This was linked with the endemic nature of thalassemia within modern Greek populations. Thalassemia, like sickle cell anemia, confers a degree of immunity against malaria caused

by *P. Falciparum*. The overlap in areas exhibiting high frequencies of porotic hyperostotic changes, the range of mosquitos which host the *P. falciparum* protozoan and the endemic nature of thalassemia in the descendent groups of his study populations formed the basis of Angel's conclusion that thalassemia was the most likely anemic condition to cause porotic hyperostosis within the samples from Greece (Angel 1964, 1966). However Angel noted that Thalassemia could not be applied universally as the cause of porotic hyperostosis. Angel proposed that sickle cell anemia was the probable cause of porotic hyperostosis in areas of the world where the disease is endemic today. In the pre- contact New world, where no hereditary anemia's are known to have existed and malaria is thought to be absent, the proposed causative agent was most likely to cause these defects was iron deficient anemia, which could be the result of "prolonged lactation, or of a severely restricted childhood diet, or of severe dysentery" (Angel 1966:761).

Hengen (1971) excluded systemic toxic disorders, protein deficiency, scurvy, A-acitaminosis and panthothenic acid deficiency as potential causes of hyperostotic cranial lesions, in an attempt to locate a specific etiology. It was argued that porotic hyperostosis represented hyperactivity of the diploe; and that any causal condition must have this as a central feature. Anemia, which is known to produce bony changes associated with marrow expansion, was then proposed as the most likely etiology. Given the rarity of hereditary anemia, iron deficiency anemia was postulated as the most likely etiology. He proposed, that while a diet poor in iron could be a cause of iron deficiency anemia, parasitic infection leading to iron deficiency anemia was the likely cause of porotic hyperostosis. Noting that porotic hyperostosis was more common in equatorial

environments, children and in the historical record, Hengen (1971) argued that parasitic infections followed these same trends.

Moving forward the synergistic interaction between diet and disease became a major theme of the literature on porotic hyperostosis. In 1974 Carlson and colleagues published on porotic hyperostosis in prehistoric Nubian remains, where they argued that parasitic infection, an iron poor, cereal-based diet and maternal iron stress interacted in infants to cause weanling diarrhea, which caused iron deficiency anemia within their study population. This would account for the high incidence of porotic hyperostosis observed among children in their sample (Carlson *et al.* 1974). Three years later a study was published exploring the interaction of diet and infection in the pre-Colombian Midwestern United States and the affect that they may have on the development of iron deficient anemia (Lallo *et al* 1977). Citing greater frequency and severity of porotic hyperostotic lesions in agricultural groups that were highly dependent on maize, higher frequency of porotic hyperostosis in infants between the age of one and two and the high co-occurrence of porotic hyperostosis and postcranial pathologies associated with infections disease, Lallo and colleagues concluded that the high prevalence of porotic hyperostosis could be due to growing children experiencing a synergistic interaction between non-specific infections disease and a nutritional deficit of iron due to the maize dominated weanling diet (Lallo *et all* 1977).

In the 1980's Patricia Stuart-Macadam began publishing on porotic hyperostosis combining clinical and anthropological data, and re-asserting early observations which had been largely forgotten or ignored in the literature. Among the conclusions was that porotic hyperostotic lesions were most likely representative of iron deficiency anemia

acquired in childhood and that the lesions visible in adults were the product incomplete remodeling of a condition from childhood (Stuart-Macadam 1985). She combined the anthropological data with the clinical literature to support her hypothesis. The bony changes associated with anemia are the result of diploic expansion to create more space for marrow in response to an increased blood production due to a lack of oxygen-carrying hemoglobin. This expansion of the diploe places pressure on the outer table of the skull, which results in the loss of the outer table and exposure of the diploe. The marrow cavities of children contain high concentrations of hematopoietic marrow, while as adults the amount of hematopoietic marrow contained in the marrow cavities is significantly decreased. In adults an increase in blood production simply requires an increase in the volume of hematopoietic marrow, which does not require diploe expansion as there is sufficient room in the marrow cavities for the increased hematopoietic marrow, thus no lesions form (1985). She would later publish extensively on the theme of porotic hyperostosis being a positive adaptive response and not a sign of dietary stress (Stuart-Macadam 1987a, 1988, 1989a, 1992a, 1992b, 1992c). She argued that their apparent correlation of porotic hyperostosis and the introduction of cereal grains might be due to an increase pathogen load, which accompanied the shift into an agricultural subsistence pattern (Stuart-Macadam 1992a. This view would be challenged by Goodman (1994). Goodman asserted that Stuart-Macadam utilized an over simplistic understanding of physiology which discounted the interconnectivity of the bodies systems. He argues that this led to Stuart-Macadam's view that "signs of stress are seen as adaptation for no other reason than that they exist in stressed but surviving organisms." (Goodman 1993:164). He point out that while the human body may withhold iron in response to a high pathogen

load, this iron deficiency will always have a negative functional impact and should therefore be viewed as an adjustment not an adaptation (Goodman 1993).

As briefly outlined above historically, the etiology of cribra orbitalia and porotic hyperostosis of the cranium has been linked to various anemias. More recent publications have debated this point, instead indicating that these conditions are caused complex interactions between malnutrition, sanitation, infectious disease and/ or cultural practices (Holland 1997; Oxenham and Cavill 2010; Peckman 2003; Rothschild 2012; Rothschild Manzi and Salvadei 2002; Schultz 2001; Wapler *et al* 2004; Walker *et al* 2009), where iron deficient anemia may be secondary. Wapler *et al.* 2004 have further indicated of the 333 individuals exhibiting orbital roof lesions in their study, 56% showed no hypertrophy of the red bone marrow (Wapler *et al.* 2004). This finding eliminates iron deficient anemia as the cause of orbital roof lesions in over half of the study populations. Extrapolating from that idea, it is possible that a number of the cases which have been associated with iron deficiency anemia are actually the result of another condition (Wapler 2004).

In multiple publications Ortner has linked porotic lesions to infantile or childhood scurvy. Ortner asserts that porous lesions in the superior orbits, greater wing of the sphenoid, squamous portion of the temporal, the mandible and maxilla are unlikely to be the result of anemia as they have limited diploic space that would not be affected by increased hemopoiesis (Ortner 1984). The presence of these porous areas are instead attributed to the bodies response to inflammation caused by hemorrhaging (Ortner and Ericksen 1997; Ortner *et al.* 1999; Ortner *et al* 2001) due to weakened blood vessels associated with vitamin C deficiency (Ortner and Eriksen 1997). A hemorrhage between

the periosteum and the bone surface will stimulate production of woven bone, and any hemorrhage can result in bone porosity as the body attempts to diffuse blood accumulation from the hemorrhage. These lesions can result in hypertrophy of the lamellar bone, but do not have any expansion of the marrow space and can therefore be differentiated from porotic hyperostosis. Ortner's publications are notable not only for their contributions in the diagnosis of infantile scurvy, but also as they are some of the few publications which clearly outlines that not all porous lesions on the cranium can be called porotic hyperostosis.

The history outlined above details the manifestation of porotic lesions on the outer surface of the cranium. Cranial defects on the interior surface of the cranium were also being analyzed in this time period. First described in 1912 the endocranial lesions caused by the deposition of new bone was called *cribra cranii* (Koganei 1912). Noting 'web-like' new bone formation of the frontal, parietal and occipital bones Koganei (1912) found these lesions occurred more often in adults than children. These endocranial lesions were linked with porotic lesions on the ectocranium. The link between endocranial and ectocranial lesions resulted in some researchers proposing a common etiology. Two primary etiologies were proposed; the result of nutritional deficiencies (Henschen 1961) or inflammatory processes (Moller-Christensen 1961). Over a decade after the two publications hypothesizing a common etiology for endocranial and ectocranial lesions Mensforth *et al* (1978) proposed that the two types of lesions did not have a common etiology. Instead the endocranial lesions documented on the endocranium were viewed as the result of an inflammatory reaction (Mensforth *et al.* 1978). Trauma,

with resulting epidural haematoma and meningitis² was another hypothesized etiology for endocranial lesions (Shultz, 1989 2001) of the meninges, with no regards to the specific. Multiple strains of bacteria result in the most common form of meningitis, meningococcal meningitis (Rosenthal *et al.*, 1988). Viruses, fungal agents, tumors and lead poisoning (Patterson 1993) as well as various conditions resulting in secondary Phyogenic infections, malnutrition and childhood infections (Hutchinson and Moncrieff, 1944) are all proposed etiologies for endocranial lesions.

Despite the long history of studies of porotic lesions in the cranium, little work has been published on the co-occurrence of these lesions with endocranial lesions, perhaps due to the classification of any porous lesions as porotic hyperostosis within the early literature, in which the endocranial surfaces are unaffected. The relationship between these mostly vaguely understood endocranial lesions and lesions of known etiology is not well not documented in published literature. Inflammatory processes, tumors, hematoma, and vitamin deficiency have all been proposed as possible causes of endocranial lesions (Lewis 2004). It is my hope that by comparing the occurrence of pathological changes of the cranium, both endoendocranial and ectocranial, we can gain a greater understanding of these pathological changes, and their relationship to one another.

IV. Methodology

² Meningitis here refers to any acute inflammation of the meninges, with no regards to the specific etiologies, as they are numerous.

The sample will consist of all individuals housed in the anatomical collection of the University of the Pacific Dental School between the ages of 1 month and 18 years, approximately 350 individuals. All methods of data collection for this study are non-destructive, macroscopic procedures. The ages of all individuals have been previously determined for the collection based on dental development (Richardson 2009).

Individuals age as determined by Richardson will be preferred as multiple radiographic techniques were used to determine the age of the individual (Richardson 2009), though each individual will also have an age determined by standard dental eruption as the first step of analysis.

All crania will be examined for bossing of the parietal and frontal bones. The orbital roof, maxilla, greater wing of the sphenoid, cranial vault, orbital and internal aspects of the zygomatic bones, palate and coronoid process of the mandible will be examined for porotic lesions. Any abnormal porosity will then be scored into one of five categories. Hyperostotic and coalesced lesions where there is porosity with significant pore coalescence and hyperostotic expansion of the diploe are the only lesions that will be called either porotic hyperostosis or cribra orbitalia for analysis. Porotic lesions which exhibit significant coalescence of the pores, but no diploic expansion will be classified as Porotic lesions with coalescence. Porotic lesions which are located in conjunction with abnormal vascular impressions will be classified as porosity with abnormal vascular lesions. In cases where there is appositional bone formation with at least one clear edge of bone formation will be classified not as a porotic lesion, but as woven bone formation. Abnormal porous lesion which do not fit any of these categories as they are just pores will simply be categorized as porous lesions. All porous lesions which are along sutures and

not clearly part of a larger pathological lesion will not be scored, nor will porous lesions on points of major musculature attachments as to avoid misdiagnosing porosity associated with development as pathological conditions. Scoring of porous lesions was based on earlier methods developed by Nathan and Hass (1966), which were adapted into methods used in the field today (Buikstra and Ubelaker 1994; Stuart- Macadam 1985) and further refined by Wilczak and Hopkins (2010).

A flexible pen-light inserted through the foramen magnum will be used to facilitate documentation of endocranial lesions where anatomical cuts have not been made. Lesions will be scored as not present, porosity only, porous or vascular woven bone formation, vascular lesions, erosion and serpens endocranial symmetrica. Scoring was adapted from Lewis' (2004) four lesion types; pitted lesions, deposits of new bone, capillary formations, and hair- on end formations. Due to the nature of the collection, modification of Lewis' (2004) criteria was necessary as the majority of specimen will be analyzed through the foramen magnum, which does not afford a complete or detailed view of the endocranial surface. For each lesion observed in the crania, the bone and approximate percent of the bone affected will be recorded, as well as the lesion type. These lesions along with information on the porotic lesion could provide additional criteria for the diagnosis of specific conditions. This in turn would provide a better understanding of the pathological changes associated with specific diseases, particularly in regards to endocranial lesions. All data will be coded directly into SPSS with observations made in both a notes variable, and a word document to allow for a greater amount of detail in documentation. Direct entry into the statistical program will prevent transcription errors later in the analysis stage. All data will be backed up to a flash drive and places into drop-

box every 1.5 hours to prevent significant loss of data. For a complete scoring guide please reference the appendix.

Expected Results

Because many of the bony changes being studied are more frequently documented in individuals of younger age and undergo remodeling while LEH do not, a higher co-occurrence of LEH and the bony lesions studies at younger ages are expected. Although some of the pathological conditions that will be studied have been documented in adults, all are more commonly manifest in children likely due to their greater susceptibility to infections disease and nutritional stress as well as a greater tendency for bony responses to these conditions in growing bone. As such more pathogenic lesions are expected in the younger individuals from the sample. The study will also be testing whether correlations between LEH, endocranial and ectocranial lesions vary based on the type of orbital lesions presented.

V. Schedule

Primary data collection will begin at University of the Pacific in Fall 2014. Collection of primary data is estimated for completion in December of 2014. Data collection will occur approximately twice weekly, with each visit lasting approximately 7 hours. Simultaneously, research into the specific etiology of pathogenic changes will occur. A complete literature search is estimated to be complete mid-Spring 2015, which shall be done concurrently with data analysis. This will put the beginning stages of the

thesis writing somewhere in late spring or early summer of 2015. Potentially this puts the first complete draft of the thesis in the hands of my graduate committee mid-Fall 2015

VI. Thesis Committee

Cynthia Wilczak-Chair

Mark Griffin- Secondary

Appendix 1

Orbital Lesion Scoring

The right and left superior orbital surfaces are scored.

Anterior 1/3 and Posterior 2/3 are scored separately.

Categories

HCO - Hyperostosis and Coalescence (Cribra Orbitalia on poster)) - Porosity with significant coalescence and hyperostotic expansion of diploe. Concentrated on the anterior orbit but may extend posteriorly.

CO - Porosity with significant coalescence and no hyperostotic expansion.

Concentrated on the anterior orbit but may extend posteriorly.

VP - Vascular Porosis: Porosity with abnormal vascular (capillary) impressions on the anterior or posterior orbit and no evidence of trabeculated hyperostosis.

PO - Porosity without trabeculated hyperostosis or abnormal vascular impressions on the anterior or posterior orbit.

9 = not recordable

Other orbital lesions (Scored separately)

Plaques - Flat, non-porous bone with clear delineated margins.

Record number of plaques

Woven bone - clear, appositional bone formation with thickening may be porous and have some vessel impressions associated but not the significant trabeculated appearance of HCO. List bone surfaces of orbit that are affected, including the superior orbit.

VP and PO not on the superior orbit. List bone surfaces of orbit (other than superior) that are affected.

Ectocranial Lesions Scoring

For each scored list the bone(s) affected and locations.

HCO - Hyperostotic and Coalescence - Porosity with significant coalescence and trabeculated hyperostotic expansion.

CO - Porosity with significant coalescence (trabeculated) but no hyperostotic expansion.

VP - Vascular Porosis: Porosity with abnormal vascular (capillary) impressions.

PO - Porosity only no trabeculated hyperostosis or abnormal vascular impressions.

WB - Woven Bone with clear, appositional bone formation, must show at least one clear edge of bone formation layered onto the periosteal surface.

Other Scoring(present or absent):

Deformation of the mandibular ramus - medial bending

Bossing- Frontal and Parietal bones

Endocranial Lesion Scoring

The endocranial surface is viewed through the foramen magnum using a flex light.

Multiple lesions can be scored

III. Pore Scoring

0 = no lesion

PO = Porosity only

WB = Porous or Vascular Woven Bone Formation (possibly VL)

VL = Vascular (Capillary) lesions (possibly WB)

ER = Erosions

SES = Serpens Endocrania Symmetrica

IV. For each lesion indicate the bones and the approximate % of each affected.

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