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Introduction: Scientific rigor in paleopathology

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ABSTRACT

This introductory chapter to the Special Issue on "Scientific Rigor in Paleopathology" serves to orient and introduce the chapters that follow through a detailed consideration of paleopathology as a 21st century intellectual field. In this vein, we first make the significant point that paleopathology is a profoundly interdisciplinary endeavor, encompassing aspects of the biomedical science, the humanities, and the social sciences. Thus, we suggest that no one practitioner can personally command the range of skills necessary for a 21st century paleopathologist. To maintain rigor in differential diagnosis, we emphasize collaborations and consider key concepts that illustrate the basic knowledge from each of these fields that any paleopathologist should command. We then address the manner in which disease diagnosis should proceed as a scientific endeavor. To illustrate scientific rigor in differential diagnosis, we present two case studies drawn from 1970s contributions by Cook and by Buikstra. Finally, we introduce Chapters 2-6, which address differential diagnosis in contexts ranging from specific conditions (scurvy, trepanation) to broader field-wide considerations (paleoparasitology, historical paleopathology, imaging, animal paleopathology).

1. Introduction

The primary motivation for this Special Issue on "Scientific Rigor in Paleopathology" in the *International Journal of Paleopathology* is the senior author's experience as Editor-in-Chief of the *IJPP* since its inception. In addition, both Buikstra and Cook admit to a much longer history of concern for rigorous, reproducible, and scientific differential diagnoses (Buikstra, 1976; Buikstra and Cook, 1980; Cook, 1976). We have invited Bolhofner, a practitioner who has more recently entered the field, to offer insights from the next generation of scholars who study ancient disease.

So, what do we mean by "rigor" in paleopathology? This is not the "rigor mortis" of the newly dead, but rather the need to carefully follow protocols and to exercise objectivity in drawing conclusions. Much is implied here, including not attempting to render a diagnosis beyond the available data. It does mean, however, considering all possible alternatives when constructing a differential diagnosis. Similarly, in evaluating the qualitative information available from historical sources, the researcher must be equally objective in searching out all possible relevant evidence rather than selectively choosing a facile example that supports a favored explanation. Whether scientific or humanistic, quantitative or qualitative, rigorous approaches consider all viable alternatives and thus avoid bias introduced by prematurely narrowing one's search, whether for a historic example or a diagnosis.

This introductory chapter will address a number of important issues. We begin by considering Paleopathology as a **21st century** intellectual field. Here, we make the significant point that paleopathology is a profoundly interdisciplinary endeavor that encompasses aspects of the biomedical sciences, the humanities, and the social sciences. Rather than being "pathology light," that is, a biomedical approach severely limited by the nature of the archaeological record, paleopathology embraces the long term study of people and their diseases. In emphasizing the intimacy of co-evolutionary history, we are reminded of an observation attributed to Hippocrates: "It is more important to know what sort of person has a disease than to know what sort of disease a person has" (Xplore, Inc.). While this statement, viewed in historical context, specifically alludes to the ancient Greek medical belief that good health requires a balance across competing internal forces within individuals (Grmek, 1983/1989), it is also an enduring message that underscores the significance of *people* in the study of ancient disease.

Recognizing that no one practitioner can personally command the range of skills necessary for a 21st century paleopathologist, we further emphasize collaboration and teamwork in advancing the field, and we also briefly consider key concepts that illustrate the basic knowledge that any paleopathologist should command in both the biomedical and the social sciences, as well as the humanities. The acquisition of this knowledge is extremely important in training the next generation of paleopathologists.

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Having established the nature of 21st century paleopathology, we then address the manner in which disease diagnosis should proceed as a scientific endeavor. Two case studies drawn from contributions by Cook and by Buikstra are reframed to serve as examples. The first, a pattern-matching approach by Cook (1976), illustrates the manner in which one can diagnose frequently occurring skeletal changes at a population level by carefully combining clinical and prevalence information. The second, Buikstra's (1976) model for the differential diagnosis of a relatively rare but severely debilitating condition, engages a key diagram in the process of elimination that forms the core of her model. The final section (4.0) introduces Chapters 2–6, which address differential diagnosis in contexts ranging from specific conditions (scurvy, trepanation) to broader field-wide considerations (paleoparasitology, historical paleopathology, imaging, animal paleopathology).

2. Paleopathology in the 21st century: defining and studying "one of the very rarest of things" (Shufeldt, 1892: 679)

In his 1892 essay in *Popular Science Monthly*, auspiciously entitled "Notes on Paleopathology," R. W. Shufeldt proposed the term "paleopathology" (from the Greek, ancient + a suffering) to describe "all diseased or pathological conditions found fossilized in the remains of extinct or fossil animals" (Shufeldt, 1892: 679). He also emphasized that in his experience, primarily with bird remains, fossilized bones showing evidence of disease was "one of the very rarest of things."

The manner in which we define the field of paleopathology affects the way in which we structure research and the questions we ask. This first definition of paleopathology by Shufeldt appears all encompassing; he goes on (p. 683) to discuss healing in modern turkey vultures and a Pliocene fossil specimen provided by paleontologist E. D. Cope, perhaps a medium sized goose. He concludes with a uniformitarian generality that the "interesting fossil specimen, then, goes to provide that the union of fractures of the shafts of the long bones in the vertebrata during the later Tertiary times was identical with what now occurs in the case of existing forms (Shufeldt, 1892: 683). His detailed observations, his uniformitarian assumptions, and his vision of a broad field of paleopathology establish important principles for subsequent scholarship. Therefore, Shufeldt must be recognized as a progenitor of the field of paleopathology, however much we may wish to balance Shufeldt's terminological and uniformitarian prescience with his questionable personal proclivities (*see* Cook, 2012).

Following Shufeldt's definition, the term "paleopathology" began appearing in dictionaries, such as *Funk and Wagnall's Standard Dictionary* (1895, cited also in Jarcho, 1966; Ubelaker, 1982; Aufderheide and Rodríguez-Martín, 1998). In the early 20th century, Sir Marc Armand Ruffer and the American Roy Lee Moodie published general compendia on ancient health (Ruffer, 1921; Moodie, 1923), which are widely cited. Ruffer extended the study of ancient disease to include mummified tissues, while Moodie's work encompassed plants, animals, and humans, thus defining the field in the broadest of terms.

In 1967, Brothwell and Sandison, as paleopathologists and editors of a volume entitled, *Diseases in Antiquity*, lamented that "the past three decades have seen but small advances" in paleopathology (1967: xi). Similarly, medical historian Saul Jarcho (1966:24) lamented that, "[t]he usual pattern has been for the archaeologist to select from his trophies those in which he is able to recognize gross disease and to submit them to a physician. The resultant paleopathologic observations are attached as an addendum or appendix to the archaeological report (Jarcho 1966:24). The subsequent delay in publication and failure to index or otherwise elevate and integrate discussions of ancient medical conditions stimulated Jarcho's dismay, and he called for a "revival of paleopathology" (Jarcho 1966:28).

Following somewhat disgruntled statements of concern (Brothwell and Sandison, 1967; Jarcho, 1966, see also Cook and Buikstra, 1980; Grmek 1983/1989), paleopathology enjoyed increased visibility, including the development of two international and several national/regional professional organizations, two international journals, international training seminars, and professional meetings held across Europe, eastern Asia, and the Americas (Buikstra and Roberts, 2012). While many recent texts continue to define paleopathology as the study of ancient disease (Aufderheide and Rodríguez-Martín, 1998:xv; Ortner, 2003:8), definitions are being broadened to reflect viewpoints drawn from the social sciences and the humanities. Perspectives drawn from the social sciences have, for example, encouraged some scholars to define paleopathology both in terms of disease evolution and human adaptation, thus emphasizing the dynamic interaction between humans, disease and the environment (Campillo, 1992-1994, 2001; Grauer, 2012; Herrin, 2011; Roberts and Manchester, 2005; Rodríguez Cuenca, 2005; Suby, 2012).

Thus, 21st century paleopathology should be profoundly interdisciplinary, occupying a space where the biomedical and social sciences join the humanities. In a field so diverse, we argue that paleopathologists should formally define a core knowledge base essential for practitioners and for training future generations of scholars. Scanning a list of medical specialties drawn from web-based searches (e.g, http://www.aamc.org/cim/ specialty/exploreoptions/list/) leads one to the obvious conclusion that no one person can command the biomedical knowledge necessary for developing truly innovative research in paleopathology, which now includes relatively specialized, intricate fields ranging from molecular oncology to bioinformatics. Further, various social scientific and humanistic specialties are required for answering "big picture" questions about long-term histories. Such questions include, "are cancers truly diseases of the industrialized world," to "how important were animal vectors (or climate change) in the development of infectious diseases in the past, and has their significance decreased or increased over time and with domestication?" It is clearly the social scientist and the historian who will provide contextual data crucial for such investigations. If we are to achieve informed perspectives, teamwork and organization are essential for bringing the necessary biomedical technologies, knowledge, and theories together with those drawn from across the social sciences and humanities.

In this vein, as we advocate for rigor in paleopathology, we must recognize that the humanist, the medical scientist, and the social scientist may not immediately agree upon a working definition of "rigor." Similarly, the medical doctor, while benefitting from the results of many scientific studies and scientific tests, may not necessarily actually "be" a scientist or employ scientific principles in daily practice. In medical practice, matching symptoms and test results through sometimes intuitive methods that involve critical thinking and creativity may actually link the medical doctor more closely with humanists and humanistic approaches than to scientists, especially those following an expressly hypo-deductive research design wherein hypotheses are formally stated and tested.

The Venn diagram illustrated in Fig. 1 illustrates the overlap and specialization of the relevant disciplines. We could argue about the relative contributions from the various fields, but the more important questions is, "what is the core knowledge that each paleopathologist or student of paleopathology should command?

Certainly, understanding basic bone biology, with emphasis upon both normal and abnormal processes is essential for paleopathological research. Clinical knowledge of bone pathology, drawn from both contemporary and historical sources, is also essential. Excellent texts (e.g., Aufderheide and Rodrígues-Martín, 1998; Ortner, 2002; Roberts and Manchester, 2007) should be considered entry points for extensive reviews of the appropriate clinical literatures. Similarly, Baker and Brothwell (1980) and Bartosiewicz (2013) are appropriate references for animal paleopathologists.

We argue, however, that the texts of paleopathology, no matter how detailed, are only introductions to the relevant clinical literatures; they in themselves are not sufficient, nor are their illustrations adequate to illustrate a full range of possible disease expressions, especially considering how variable disease expression can be throughout the life

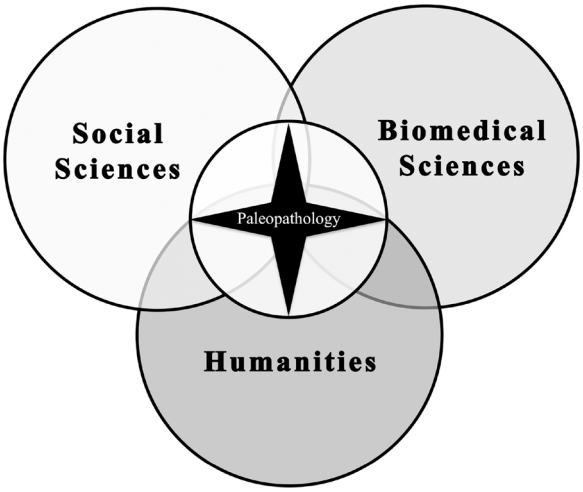

Fig. 1. Schematic of the interaction between the disciplines that interact to form Paleopathology. The central part of the figure emphasizes a core knowledge that all paleopathologists should command.

course. Using images from these comprehensive but secondary texts to identify diseases does not lead to an understanding of disease processes and variable expressions, which may vary depending upon age at the time of pathogen exposure and age at death, for example. This, of course, begs the question: What clinical literature should be used? General texts in orthopedic disease, such as Resnick's multivolume *Diagnosis of Bone and Joint Disorders* (2002) or Volume 1 of Maxie's *Pathology of Domestic Animals* (2007) provide entry points into the literature and inform understandings of disease processes, but primary clinical literature must be consulted, as well.

Equally important is the fact that it will not serve paleopathologists well to model expectations for infectious or metabolic disease in the past based upon western examples, no matter how detailed, when these contemporary cases have been attenuated by effective medical treatment, frequently through antibiotic therapy. Depending on thepathological condition, one may need to focus upon literature from a specific temporal period. Arguably, the most relevant corpus of significant literature is drawn from the period after the disease's causative agent has been identified and before effective treatment has been discovered. For example, for tuberculosis, this would be the period between 1882, the time of Koch's discovery, to ~1950, when antibiotics proved effective. Once a condition can be identified through the presence of bacilli, the medical literature infrequently describes the full extent of tissue changes in detail. Hence, exploring earlier sources may be informative, as these are more likely to extensively describe pathological changes during a period when unifying symptoms are sought and causal agents are as yet unknown.

Another important aspect of the scientific process requires scientists to explicitly state and critically evaluate assumptions. For paleopathology, the uniformitarian assumption is crucial. All else being equal, disease processes in the past operated in the same manner as they do today. Of course, "all else" wasn't necessarily equal in the past – immune responses might have differed for a variety of reasons involving such factors as diet and genetic heritage. Similarly, the virulence of a disease may have changed due to changes in the pathogen's genome. Potential causes of change may be invoked when past patterns depart from the expected, but this is only a first step in furthering discussion and explanation of factors that might have led to the observed deviations. Unsupported assertions are to be avoided, as when deviations are dismissed as "skeletal changes may have differed in the past" (Masson et al., 2015:S16). The researcher must justify why changes would have been different; what identifiable past conditions would have led to this alternative pattern? Rigor in differential diagnosis requires care for details and objective, critical evaluations. Conflicting or mixed results should be carefully evaluated, not dismissed, as it is frequently the outlier or the counterexample that may lead to important new perspectives.

Knowledge from the social sciences is also important for professional and novice paleopathologists alike, and should be integrated into all training programs. Social theories are essential for the contextual interpretation of individual burials, their life histories, personhood, social position, and gender roles, which are often enhanced through knowledge of health. "Cemeteries" are often an archaeological construct, and we must remember that burials may be segregated by health status (Buikstra, 1981) or myriad other factors relating to circumstances of death (Binford, 1971; Murphy, ed 2008; Hodgson, 2013; Reynolds, 2009). This means that the paleopathologist must critically evaluate the nature of each cemetery or burial cluster without assuming that it represents the cumulative dead of a specific social group – community, village, or urban neighborhood. The term "population," as in "population health" requires critical review and explicit definition.

The temptation to use counts of burial accompaniments as a measure of social status should also be avoided. The assumption that durable good counts = social status, even in complex societies, presumes that personal wealth of the deceased will be the persona of an individual most vividly on display at the grave site. The oft-repeated adage that the dead do not bury themselves requires us to recall that kin and friends create the interment facility and attendant rituals, not the corpse (see also Hodder, 1980; Parker Pearson, 2000). Despite these challenges, paleopathologists have provided nuanced life-history and pathology correlates that may shed light on mortuary practices as status markers (Melton et al., 2013; Cook et al., 2017).

Essential knowledge for paleopathologists is also drawn from the humanities. For example, Mitchell (2011; this volume) has argued compellingly that historical sources can enhance the study of ancient people and their diseases, but only if these are referenced critically and contextually. While Shakespeare's Richard III may be very well known, his play – written roughly a century after Richard's death – was not an eye-witness account of the monarch's physique. As humanists, many historians of medicine focus upon literary sources and seldom consider evidence from physical remains. A notable exception is the work of medical historian/medical doctor Mirko Grmek (1969), whose "pathocenosis" focused attention upon the constellation of diseases existing in a specific population at a specific time, including both the pathogens and ecological factors (see also Blondiaux et al., 2012). This concept emphasized the interconnected nature of diseases, arguing that under stable ecological conditions, the pathocenosis would assume a stable condition that could be characterized mathematically.

Similarly, drawing from humanistic critical thought, we must rigorously explore the limits of correlation in proposing causation. Proof by assertion is a flawed method for humanistic and scientific inquiry. The issue of blurring correlation and causation has become increasingly prominent during the 21st century with the development of molecular methods in disease diagnosis. Again, using TB as an example, several workers (Haas et al., 2000; Mays et al., 2002; Masson et al., 2015) have asserted that atypical skeletal features are tuberculosis diagnostics because they occur in individuals who have biomolecular markers of TB, either aDNA or lipid. Researchers should be reminded that co-morbidity can confuse such logic, as can the fact that developmental changes may mimic TB.

The recently proposed "Bioarchaeology of Care," (Tilley and Oxenham, 2011; Tilley, 2012, 2013, 2015; Tilley and Schrenk, 2016) illustrates a successful synthesis of rigorous scientific and humanistic perspectives. Rooted in scientific method, the program of study becomes decidedly humanistic in the interpretative stages, where careful critical thought, coupled with creativity, is required to generate compelling and robust arguments.

3. Terminology, certainty, and differential diagnoses

As stated in the previous section, here we argue that

NOUNS				
YES	YES	YES	???	NO
Addition	Deposit	Hole	Bump	Abrasion
Accepted anatomical names/sites/ locations	Dimensions (height, length, width, etc.)	Layer Marrow Space	Cavitation Flake	Disease name Compact bone
Boundary	End	Overlap	Knife blade	Damage
Build up	Erosion	Pit(s)	Opening	Impression
Cleft	Exostosis	Plateau	Piece	Inflammation
Cortical	Fracture	Reactive bone	Woven bone	Marrow
Crack	Gap	Remnant		Periosteal layer
Curve	Gradient	Ridge		Periostitis
Defects	Groove	Sheet		Remodeling
		Wormian bones		
MODIFIERS				
YES	YES	YES	???	NO
Angular	Elevated	Porous	Angulated	Abscessed
Atrophic	Eroded	Projecting	Clean	Ballooned
Bent	Exophytic	Prominent	Collapsed	Chewed away
Blunt	Fenestrated	Punched out	Crenulated	Degenerative
Bowed	Fine	Ragged	Crinkled	Disrupted
Broken	Flat	Raised	Lucent	Expanded
Carious	Fragile	Robuts	Minor/major	Granulomatous
Coarse	Heavy	Sclerotic	Organized	Is (not) present
Compact	Intact	Sharp	Penciling (-ed)	Is/are noted
Curved	Ivory-like	Smooth	Remodeled	Narrowed
Delicate	Light	Solitary	Worm eaten	Peculiar
Diminishing	Lobulated	Stellate		Periostitis
Dense	Lytic	Straight		Spetic
Depression	Multiple	Undulating		There is/are
Discolored	Narrow	Worn		Traumatic
Eburnated	Overlapping	Widened		
Effaced	Pitted			

Fig. 2. Proposal of standard terminology for practitioners of paleopathology, as recommended by Ortner and Ragsdale (1992:7f).

paleopathologists should characterize abnormal changes in human remains through standard descriptive terminology that are commonly agreed upon and mutually intelligible across the discipline. This standard will allow other scientists to approach the same materials and evaluate description accuracy and completeness. The nature of the full disease process, from first bony changes to those still active at the time of death (if any) must be described during this process using standard terminology, along with descriptions of the process by which she or he arrives at a diagnostic conclusion. This allows requisite critical review by others. Thus, robust conclusions and diagnostic certainty will stand up to scrutiny or will be replaced by alternative and compelling explanations of the evidence. The ultimate goal, of course, is advancing knowledge and not being personally invested in one's own arguments leading to the a priori dismissal of viable alternatives. In this vein, we argue that a crucial component in the development of differential diagnoses is a statement concerning degree of certainty. It becomes essential, therefore, to next discuss the employment of standard terminology and the assessment and reporting of degree of certainty using differential diagnoses.

3.1. Terminology[1]

Concern for consensus and accuracy in the use of terms in paleopathology has been a longstanding focus of the Paleopathology Association. This issue arose frequently in the popular workshops that Don Ortner presented to the PPA membership at the North American annual meeting, beginning in 1985 and intensifying as he partnered with Bruce Ragsdale, starting in 1989 (Powell, 2012). Ragsdale and Ortner, seeking to bring attention to the topics, as well as input, published usage recommendations in the June 1992 issue of the Paleopathology Newsletter (No. 78, p. 7f.), reproduced here in Fig. 2.

At this time Ortner and Ragsdale's main concern was the use of inappropriate terms in describing normal and abnormal structures during the course of paleopathological study, e.g, "ballooned". They emphasized the fundamental importance of descriptive terms that are widely held and used correctly. Ragsdale and Lehmer (2012: 243) have more recently re-emphasized this need: "The approach of agreeing on a few experts to set the terms, and then agreeing on common usage in the

[1] Adapted from "Nomenclature in Paleopathology," https://paleopathology-association.wildapricot.org/Nomenclature-in-Paleopathology by Jane E. Buikstra.

Disease	*Prevalence*	*Age Patterning in Sample*
Scurvy	Common	Juvenile Emphasis
Rickets	Common	Juvenile Emphasis
Osteomyelitis	Relatively Low	Juvenile Emphasis
Tuberculosis	Relatively Low	Young Adult Emphasis
Fungal Infections	Variable	Age Accumulative
Trauma	Common	Age Accumulative
Treponemal Infections		
Yaws	Relatively High	Age Accumulative
Endemic Syphilis	Relatively High	Age Accumulative
Venereal Syphilis	Relatively High	Bimodal

Fig. 3. Expectations for periosteal reactions of common prevalence in an archaeologically recovered skeletal sample (after Buikstra et al., 1993; Cook, 1976).

major journal in the field, will likely help paleopathology, as it has in other fields… With conscientious authors and reviewers working alongside diligent, strong- willed editors, rules will become habits, and manuscripts using uncanonized terminology will go unpublished."

Jane Buikstra, as Inaugural Editor-in-Chief of the IJPP, fully endorsed the need for standard terminology, and encouraged Keith Manchester to expand upon the earlier effort. Manchester, ably aided by Alan Ogden and Rebecca Storm, with input widely invited from across the paleopathology community, has produced a document entitled "Nomenclature in Palaeopathology," which appears on the Paleopathology Association website.[1] The authors wish it to be widely shared and to be organic, growing with the field. Comments are actively invited!

The earlier "structured lists" of terms have now been appended to "Nomenclature in Paleopathology," recognizing the terminological diversity that cross-cuts our interdisciplinary field. Bioarchaeologists, for example, should be particularly concerned with #12, a list of terms drawn from taphonomy. One finds here such descriptors as "abrasion," "cracked," and "wear", terms for which meanings are ambiguous for those who also consider archaeological contexts. Individuals who choose to use these words in reference to bony changes should be clear in their choice of adjectives: ante-mortem, gperi-mortem, or post-mortem. For example, when recording the impact of taphonomic processes that may have obscured pathological changes, an appropriate descriptive phrase would be, "post-mortem abrasion has obscured features of the distal one-third of the humerus diaphysis, and this portion of the bone cannot be observed for pathological changes."

3.2. Certainty

As Ortner (2003, 2012) and Ragsdale (Ragsdale and Miller, 1996; Ragsdale and Lehmer, 2012) repeatedly caution, paleopathologists should temper their diagnostic goals with the knowledge that there are a limited number of ways in which bone can respond to disease. Adopting the orthopedic pathologist Lent Johnson's system (Ortner, 2012), Ragsdale and colleagues distinguish seven basic disease categories: Vascular, Innervation/Mechanical, Trauma/Repair, Anomaly, Metabolic, Inflammatory/Immune, and Neoplastic, which form the helpful acronym VITAMIN. They argue that placing conditions within these categories is frequently a "less ambitious (but more often correct)" goal than attempting to name a specific disease (Ragsdale and Lehmer, 2012:230). Ortner (2012) also discusses the challenges raised by even creating a listing of disease categories, as paleopathological texts vary widely in the number of categories employed, from Resnick's (2002) 17, to 13 (Aufderheide and Rodríguez-Martín, 1998), or even 12 (Ortner and Putschar, 1981). While Campillo (1992–1994, 2001), Roberts and Manchester (2007), Steinbock (1976), and Waldron, (2009) generally discuss diseases within 6 or 7 chapters, it is clear that they consider more identifications achievable. Even Ragsdale's more limited suite of alternatives does not, however, eliminate possible shared responses by bones affected by diseases from different categories.

Appleby et al. (2015) have explicitly addressed defining levels of certainty in diagnostic processes. They advocate an adaptation of the "Istanbul Protocol Manual on the Effective Investigation and Documentation of Torture and other Cruel, Inhuman or Degrading Treatment or Punishment" (UNESCO, 2004). Their recommendations comprise a five-point scale, as follows.

1. NOT CONSISTENT: the lesion could not have been caused by the condition(s) described
2. CONSISTENT WITH: the lesion could have been caused by the condition(s) described, but it is non-specific and there are many other possible causes
3. HIGHLY CONSISTENT: the lesion could have been caused by the condition(s)described, and there are few other possible causes
4. TYPICAL OF: the lesion is usually found with this type of condition (s), but there are other possible causes
5. DIAGNOSTIC OF: the lesion could not have been caused in any way other than by the condition(s) described, (i.e., it is pathognomonic).

Such concerns for levels of certainty, and the need to appreciate the inherent limitations imposed in disease diagnoses established solely upon skeletal remains, are crucial for any practitioner. Differential diagnoses may lead paleopathologists to conclude that two or more alternative conditions remain as viable prospects; this does not *de facto* mean that the study is flawed. Similarly, specifying levels of certainty forces the observer to appreciate that very few skeletal lesions or even lesion patterns are truly pathognomonic of a specific condition.

3.3. Differential diagnosis

As a science, paleopathology advances through hypothesis testing, frequently through the expression of hypotheses about specific diseases,"the observed pathological condition is x or y or z". This implies a rigorous differential diagnosis, whereby we eliminate the least likely maladies in favor of those that fit the observed pathological changes most closely.

Here we present two distinctive examples of differential diagnoses for different infectious diseases. The first explores the distribution of a common condition in ancient skeletal remains from eastern North America: periostosis. The second refers to more rare and extreme forms

Rheumatoid Arthritis	Actinomycosis
Tuberculosis	Sarcoidosis
Blastomycosis	Histoplasmosis
Coccidioidomycosis	Scheuermann's Disease
Brucellosis	Paget's Disease
Echinococcosis	Traumatic Arthritis
Malignant Tumors	Histiocytosis
Rheumatoid Spondylitis	

Fig. 4. Diseases that may cause lesions in the spinal column (after Buikstra, 1976; Buikstra et al., 1993).

of skeletal changes: focal lesions most commonly observed in the lower back. The nature of these pathologies has stimulated two distinctive, rigorous approaches.

3.3.1. Periostosis (adapted from Cook, 1976; Buikstra et al., 1993)

As emphasized by Cook (1976), there are four broad classes of pathology that may produce periostosis, most commonly observed on the tibiae: 1) developmental disorders, including nutritional conditions and dysplasias, 2) inflammatory diseases, 3) trauma, and 4) tumors. The high prevalence in the Eastern North American Woodland (~2000-1000 BCE) remains that Cook observed led her to develop a protocol delineating conditions expected to produce periosteal reactions in 1% or more of a death sample. These conditions included osteomyelitis, treponemal infections, tuberculosis, and other mycobacterial infections, fungal infections, scurvy, rickets (healing stages), and trauma. Cook then mapped the expected pattern for these diseases in a death sample against age-associated prevalence and overall frequency. Prevalence and demographic expectations for diseases frequently associated with the presence of periosteal reaction in more than 1% of the population appear in Fig. 3 (adapted from Buikstra et al., 1993:35).

Based upon an observed age-accumlative high prevalence, Cook was able to conclude that the observed lesions were highly likely (compare HIGHLY CONSISTENT WITH, Appleby et al., 2015) to have developed from non-venereal treponemal infections, yaws and endemic syphilis (bejel).

3.3.2. Focal lesions (adapted from Buikstra, 1976; Buikstra et al., 1993)

Although the diagnostic model presented here was originally developed and applied to historic period remains of the Caribou Eskimo (Buikstra, 1976), it has also been used to explore diagnostic options for focal lesions centered in the lower back and, less commonly and asymmetrically, on sacro-iliac and other joint surfaces. In this example, the observed condition appears to be associated with disproportionate deaths during the late adolescent and young adult years. Assuming the disease represents a condition present in today's world, Buikstra assembled the list of possible alternatives that may cause focal lesions in the spinal column (Fig. 4).

To narrow this extensive list, a key diagram was developed (Fig. 5) based upon the following dimensions of variability: 1) primary skeletal response; 2) most common locations for skeletal lesions; 3) most common site within the spinal column; 4) sites of most common extra vertebral involvement; 5) expected age-related prevalence; 6) ankylosis as a secondary response. For the observed condition, the responses were 1) focal bone resorption; 2) spinal column; 3) lower thoracic and lumbar vertebral bodies; 4) asymmetrical expression in sacro-iliac and limb joint surfaces; 5) disproportionately high late adolescence and young adult deaths with the condition; and 6) ankylosis as a secondary response.

Thus, considering those diseases for which focal, ovoid destructive lesions are characteristic allows us to eliminate Scheuermann's Disease, Paget's Disease (Osteitis Deformans), Traumatic Arthritis, and Rheumatoid Spondylitis (non-cystic). Histiocytosis, actinomycosis, sarcoidosis, and histoplasmosis can be removed from further consideration as they do not typically have vertebral involvement. Lack of thoraco-lumbar affinities permit exclusion of rheumatoid arthritis and perhaps coccidiodomycosis. Elevated young adult mortality is not anticipated for brucellosis, echinococcosis, malignant tumors, and rheumatoid spondylitis (cyctic). Our attention then focuses upon the two fungal infections, coccidiodomycosis and blastomycosis, along with tuberculosis. Given the wide geographic distribution of the observed malady outside areas where coccidiodomycosis and blastomycosis are endemic and the unusually high frequency of young adult deaths, this exercise leads us to conclude that tuberculosis is the highly likely diagnosis (#4, *sensu* Appleby et al., 2015).

In this section we have discussed the need for explicit statements of certainty and cautioned against attempts at diagnoses that are more specific than the data warrant. We have also presented two models for diagnoses of conditions that are highly likely to have represented a yaws-like disease and tuberculosis. We now turn to the organization of the remainder of this Special Issue on Scientific Rigor in Paleopathology.

4. Summary of chapters 2–6

Following this chapter are six papers designed to illustrate the importance of rigorous approaches in human, animal, and parasitological paleopathology. In Chapter 2, Piers Mitchell encourages paleopathologists to use historical sources responsibly, beginning with knowledge of the authors and their motivation for writing. Case studies focused upon plague, crucifixion, and the spinal deformity of Richard III are used to illustrate key issues in the use of historical sources.

Haagen Klaus, in Chapter 3, advocates for rigor in skeletal differential diagnosis, using scurvy as his focal example. Beginning with an emphasis upon descriptive terminology derived from current international standards promulgated by anatomists, he then turns to the need for improved observation and description of abnormal skeletal features in discriminating between anemia and vitamin C deficiency. A structured decision-making process in differential diagnosis proves essential in Klaus' consideration of two new examples of suspected scurvy from northern Peru.

In Chapter 4, John Verano provides rigorous diagnoses of trepanation and other mechanisms that produce defects in the cranial vault. Here, Verano notes that unhealed trepanations are relatively easy to identify, due to the presence of marks of instruments used to create the defects. More difficult are healed or healing defects, which may be mistaken for congenital and developmental anomalies, infections, trauma, neoplasms, and taphonomic changes. Verano argues for a rigorous approach in approaching vault defects, especially important in

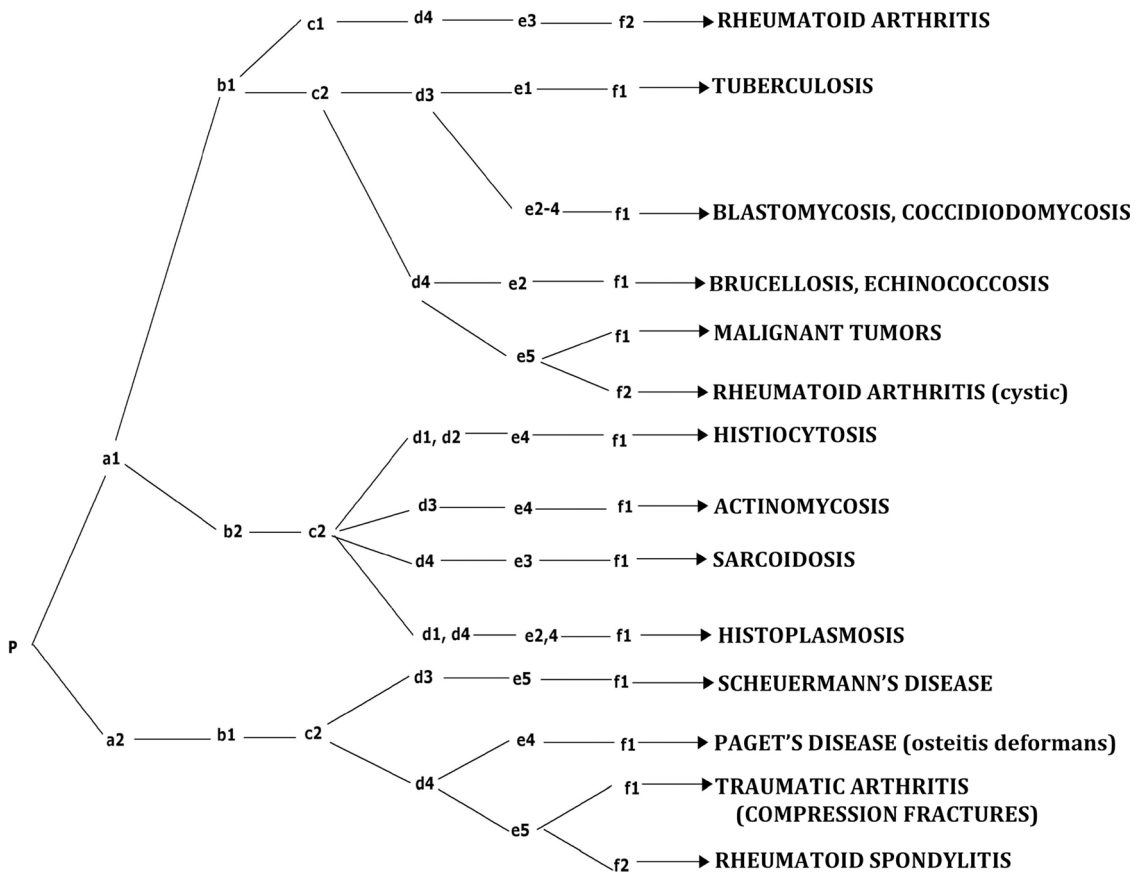

Fig. 5. Key diagram designed to distinguish diseases that may create focal lesions or kyphosis in the spine: a) focal, ovoid destruction, etc. Variable definition: (p) Common or "root" feature: types of pathology associated with vertebral disease. (A) Specific skeletal response: al, resorptive lesion present; a2, resorptive lesion absent. (B) Primary locus of skeletal lesions: bl, vertebral involvement characteristic or common; b2, vertebral involvement rare. (C) Primary foci within spinal column: cl, cervical; c2, thoracic-lumbar or nonspecific. (D) Age of maximum morbidity/mortality: dl, birth-3 years, d2, 3–12 years; d3, 12–35 years; d4, 35 + years or age accumulative. (E) Site of most frequent extra-vertebral involvement: el, limb long bones, articular surfaces; e2, limb long bones, diaphyses; e3, hands and feet; e4, skull; e5, nondiagnostic. (F) Ankylosis: fl, uncommon except as healing response; f2, common in primary phases of pathological change (from Buikstra, 1976).

geographic regions and times where such medical procedures have not been previously reported.

Differential diagnoses in animal paleopathology, where practitioners face the challenge of often incomplete and casually deposited remains, are considered in Chapter 5, by veterinarian Dennis Lawler. Lawler emphasizes the manner in which diagnoses are derived in health care settings as a model for increasing rigor in archaeological examples. He cautions against diagnoses that pretend more precision than the case merits, and he argues for an orderly process that many halt at the identification of a small number of the most likely alternatives, as discussed here in Section 3.2.

In Chapter 6, Karl Reinhard emphasizes the importance of maintaining both scientific rigor and strong links to archaeological and environmental contexts in 21st century paleoparasitology. He asserts that this field, with so much potential in the study of ancient peoples and their diseases, is currently overly specialized, focusing on description rather than context. Reinhard argues that without training in fields related to environmental sciences and archaeology -th contexts from which the ancient parasites derive- paleoparasitology will be scientifically weak and narrowly focused. This parallels the concern we voiced in Section 2, arguing for scientific and humanistic interdisciplinary breadth in paleopathology.

Turning to 21st Century Mummy Science, in the final chapter of this special issue, Ron Beckett discusses the importance of prudently applying paleo-imaging technologies. Beckett reviews various methods and advocates for paleo-imaging as a non-destructive technique whose information capture is essential for a range of paleopathological applications. In focusing upon the strong link between bioarchaeology and Mummy Science, his is a contextual model, one that will benefit greatly from the creation of digital databases.

In closing, we wish to emphasize that rigor is an issue that persistently challenges researchers and scholars in paleopathology, as in other fields. The issues we raise here are not meant as final answers, but rather as stimuli for the consciously rigorous approaches in the research, publications, curriculum development, and conversations essential for advancing our knowledge of ancient disease. The Paleopathology Association began as an informal organization designed to support collaboration, dialogue, and collegial sharing of ideas and expertise. With the growing complexity of technological, medical, and archaeological developments, our challenge is to embrace such complexity as we continue to advance Paleopathology as a discipline characterized by rigorous inquiry, collegial interactions, and mutual respect.

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