A (not so) brief historical overview of porous skeletal lesions (PSLs)

Uma (não tão) breve contextualização histórica das lesões esqueléticas porosas (LEPs)

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Abstract Porous skeletal lesions (PSLs) — cribra cranii, cribra orbitalia, cribra humeralis, and cribra femoralis — are well-known skeletal alterations that have been described in paleopathology and bioarcheology for more than two centuries. This paper offers a comprehensive historical synthesis of how their study — initially centered on cranial forms — expanded conceptually, methodologically, and anatomically. From early racial classifications of cranial cribra in the 19th century to the consolidation of the anemic models (genetic and iron-deficiency anemia) in the mid-20th century, and their subsequent re-evaluation under broader biosocial and stress frameworks, PSLs research has mirrored the wider evolution of paleopathology. The early 21st century brought the recognition of postcranial cribra, diversifying etiological interpretations and promoting a more integrated understanding of physiological,

Resumo As lesões esqueléticas porosas (LEPs) — cribra cranii, cribra orbitalia, cribra humeralis e cribra femoralis — são alterações ósseas amplamente conhecidas em paleopatologia e bioarqueologia, descritas há mais de dois séculos. Este artigo apresenta uma síntese histórica sobre como o seu estudo — inicialmente centrado nas manifestações cranianas — se expandiu conceptual, metodológica e anatomicamente. Desde as primeiras classificações raciais da cribra craniana no século XIX até à consolidação dos modelos anémicos (genéticos e de deficiência de ferro) em meados do século XX, passando pela sua posterior reavaliação sob perspetivas biossociais e de stresse, a investigação sobre LEPs reflete a evolução da própria paleopatologia. O século XXI trouxe o reconhecimento das cribra pós-cranianas, diversificando as interpretações e promovendo uma integra-

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environmental, and biocultural factors. Moreover, the recent application of imaging and elemental analyses has reshaped interpretations, emphasizing multifactorial and context-dependent mechanisms that include infection and inflammation. By tracing these transformations, this overview highlights how shifting scientific paradigms, technological innovation, and biocultural thinking continue to redefine the interpretation of PSLs. Rather than fixed diagnostic entities, they emerge as contextual expressions of physiology, environment, and adaptation, illustrating how paleopathology contributes to a deeper understanding of disease and human variability in the past.

Keywords: Cribra cranii; cribra orbitalia; cribra humeralis; cribra femoralis; paleopathology.

ção entre fatores fisiológicos, ambientais e bioculturais. Além disso, a aplicação recente de técnicas imagiológicas e de análises elementares reformulou as interpretações, destacando mecanismos multifatoriais, com novas associações a infeções e inflamação. Ao acompanhar estas transformações, esta revisão evidencia como os paradigmas científicos, a inovação tecnológica e o pensamento biocultural continuam a redefinir a interpretação das LEPs, ilustrando como a paleopatologia contribui para uma melhor compreensão da doença e da variabilidade humana no passado.

Palavras-chave: Cribra cranii; cribra orbitalia; cribra humeralis; cribra femoralis; paleopatologia.

1. Introduction

Porous skeletal lesions (PSLs) are well-known skeletal alterations, frequently recorded in bioarcheological studies. Commonly, they are also referred to as cribra and their designation varies according to the affected skeletal region: cribra cranii (Figure 1, example A; cranial vault, including the frontal, parietal, and occipital bones), cribra orbitalia (Figure 1, example B; orbital roof), cribra humeralis (Figure 1, example C; anatomical neck of the humerus, above the physeal line), and cribra femoralis (Figure 1, example D; femoral neck). In this study, the term PSLs — adapted from the concept of porous cranial lesions (PCLs) proposed by O'Donnell et al. (2020) — is used to encompass these four lesions as a descriptive category, rather than as evidence of a single cause or biological process. Although the expression PSLs had already appeared in Stark (2014) and Smith-Guzmán (2015), it was not employed specifically to designate cribra. Furthermore, in some cases, the word cribra will also be used to refer collectively to all four types.

The nomenclature of these lesions has remained almost unchanged since their first descriptions. A few variations exist, particularly for the postcranial lesion — cribra humeri(s), cribra femora, and cribra femori(s) being among the most common. It should be mentioned that a few texts also refer to a cribra fibularis (e.g., Erkelens, 2017; Jasch-Boley and

Wahl, 2022); however, it will not be considered here. Perhaps the main exception is cribra cranii. A significant number of studies refer to porous lesions in the cranial vault as porotic hyperostosis. Yet the term cribra cranii was preferred in this work for two main reasons: 1) to ensure terminological consistency; and 2) because porotic hyperostosis may imply marrow expansion as the mechanism of lesion formation, which is unlikely to account for all the porosity observed in this region (Brickley et al., 2020).

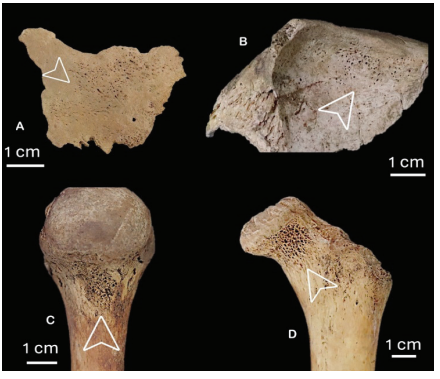

Figure 1. Examples of A - cribra cranii in a 2-year-old individual; B - cribra orbitalia in a 2 to 4-year-old individual; C - cribra humeralis in an 18-year-old female; D - cribra femoralis in an 11-year-old female.

The mechanisms underlying the formation and expression of PSLs remain debated, and nearly 200 years after their first descriptions, no consensus has been reached, as evidenced by recent analyses of current methodological and theoretical trends (Brickley, 2024). This paper therefore aims to contextualize the historical development of PSLs research, elucidating how shifts in scientific and methodological paradigms have shaped its interpretation. By tracing the historical roots of PSLs research, it highlights conceptual and interpretative transitions that have influenced current understanding and continue to inform future directions in PSLs studies.

2. Early research on cranial cribra (mid-19th century to 1960s)

During the 19th century biological (formerly physical) anthropologists were particularly focused on the study of the human skull, predominantly from adult males (Little and Buikstra, 2023), so it is not strange that porosities draw the attention of scholars. For example, Hodgson and Owen (1859: 100) based on the observation of human skulls from Nepal noted that "[…] one shows the hypertrophy of the cranial vault to a great degree, with much density of the thickened bone." A few years later, Rudolf Virchow (1874: 61–62) established a thorough description of porous lesions in two skulls from the Chilean Patagonia and Argentinian Pampa, acknowledging "a peculiar, flat, porous osteophyte formation on the surface of both orbital roofs, as well as several semicircular protrusions, one of which is located on the left parietal."

It was not until 1885 that Hermann Welcker (1885) coined the term cribra orbitalia during the observation of skulls from the Socotra Island (Yemen). The author stated that: "the orbital process of the frontal bone facing the eye socket has

fine fissures and depressions forming an elliptical area up to 3 cm in length. Since these depressions communicate with the diploë, the surface of the bone often presents a very delicate network, from whose meshes small bone spicules and ridges frequently protrude. This formation, which I refer to as cribra orbitalia, occurs in different races." (Welcker, 1885: 93).

In this initial work, little attention was given to the possible etiologies of the lesion, and cribra orbitalia was interpreted as a distinguishing trait of South American populations. Later, Welcker (1887) introduced the first classification of cribra orbitalia into three severity degrees. He noted its characteristic thickening, similar to changes observed in the parietal bones, and its usual symmetry between the orbits. While initially describing cribra orbitalia as a non-pathological phenomenon, possibly linked to vascularization, Welcker later proposed that it might represent a pathological condition, most likely associated with osteoporosis.

Toldt (1886) was probably the first to portray an association between cribra orbitalia and age at death, suggesting higher frequencies in children. This author considers other potential etiologies, such as syphilis, lacrimal gland disease, local new bone formation in juveniles, or predisposition to present higher vascularization. Moreover, based on the observations of Peruvian skulls, he proposed that alterations with symmetrical osteophyte formations could be attributed to artificial modification of the skull. The subsequent investigation of Adachi (1904a, b) consolidates the similarity between the orbital lesions and those found in the parietals, leading him to propose the term "cribra parietallia." Also, the author rejected the idea that cranial modification was responsible for these alterations, since he noted their presence also in non-modified skulls.

Subsequent studies focused primarily on describing the lesions (Le Double, 1906) and assessing their frequency in skulls from different regions (Oetteking, 1909), reflecting the prevailing view that cribra "might potentially serve as an ethnological diagnostic feature" (Ahrens, 1904 in Bartels, 1905).

The publication of Koganei (1913) must be emphasized since he was the first to use the term cribra cranii to describe a "roughness not only on the frontal bone but also on the inner surfaces of other bones […] which had a strong similarity to the cribra orbitalia first described by Welcker, and that these two conditions might be classified under the same category." (Koganei, 1913: 113).

Aleš Hrdlička published in 1914 a study of human skeletal remains from ancient Peru, describing symmetric cranial changes confined to the outer surface. Often beginning on the orbital roofs, these alterations involved increased vascularization and porous tissue deposition, which he termed "symmetric osteoporosis." Although differently named, his descriptions and photographs align with what had been identified as cribra

orbitalia and cribra cranii. Without citing earlier works, he observed that the condition was most frequent in infancy and early childhood, distinguished between active and healed lesions and suggesting a systemic disorder — likely toxic rather than nutritional or degenerative — as a possible cause.

A few years later, the works of Moore (1929) and Williams (1929) were pivotal in shaping cribra etiological interpretations, many of which continue to influence current research. Williams (1929) prefers the term "symmetric osteoporosis" but clearly equates it with cribra cranii and cribra orbitalia. He observed that, although anthropologists were familiar with the condition, it remained little known among pathologists. Noting its higher prevalence in infants and children, and its presence also in non-human primates, he proposed several possible etiologies, including endocrine disorders, disturbances in calcium metabolism, vitamin deficiencies (C and D), and other dietary factors. Additionally, Williams (1929) stated morphological similarities between cribra and those alterations described by Cooley et al. (1927) in their roentgenologic studies of anemic children's skulls. Moore (1929) extended this argument by reporting similarities between bone changes in radiographs of individuals with sickle cell anemia and those in ancient Mayan skulls with cribra. The author suggested that sickle cell anemia, or a related condition, might account for the lesions, further speculating that the downfall of the Maya was tied to widespread malarial infection. This was the first explicit connection between cribra, anemia, and malaria, setting an important precedent for subsequent research.

In his doctoral thesis, Pales (1929) reviewed thoroughly the literature on cranial cribra, detailing macroscopic, radiologic, and histologic evidence. Referring to it as cranial osteoporosis, he suggested vascular-mechanical disturbances — possibly linked to cranial modification or localized pressure — as its underlying cause.

After a period of continuous growth in cribra research, the number of publications declined markedly. Yet, in 1955, Hamperl and Weiss revisited the state of the knowledge, still drawing heavily from the works of Hrdlička (1914) and Williams (1929). Their publication focused on detailed lesion descriptions and a systematic review, ultimately proposing "hyperostosis spongiosa cranii" as the most appropriate designation for these porous alterations. The work of Møller-Christensen (1953), even if previous to Hamperl and Weiss (1955), marked a new precedent by associating cribra orbitalia — referred to here as "usura orbitae" — with leprosy. It is also worth noting that in a subsequent investigation, Møller-Christensen and Sandison (1963: 181) were perhaps the first to dismiss the potential of cribra as an "ethnic index" and unequivocally recognized its pathological nature, even though their etiology "is at present obscure."

The 1960s ushered in a renewed perspective on cribra, gradually abandoning

its interpretation as specific racial traits and consolidating its recognition as a pathological condition. For example, Henschen (1961), after examining skulls from two medieval cemeteries from Denmark, observed that despite similarities between the individuals, the rates of cribra were markedly different. He posited that the lesions were more accurately understood as a pathological response, likely associated with nutritional deficiencies and chronic infections, reflecting a generalized poor state of health. Around the same time, the presence of cribra orbitalia was also documented in apes and monkeys (Nathan and Haas, 1966), reinforcing its recognition as a pathological phenomenon and opening possibilities for experimental approaches to its etiology.

3. Exploring the links between cranial cribra, anemia, and nutritional deficiencies (1960s to 1990s)

Angel (1964a; 1966) research was pioneering by offering a robust physiological and population-based argument linking cribra to genetic anemia, particularly thalassemia. While Moore (1929) and Williams (1929) had previously suggested this connection, they did not delve into the underlying mechanisms behind the lesion formation. Angel (1964a; 1966), on the other hand, identified high frequencies of cranial cribra in Mediterranean populations (Cyprus, Greece, Macedonia, Morocco, Turkey), many of whom inhabited swampy environments where Anopheles mosquitoes carrying the Plasmodium were common. He noted that the distribution of cribra overlapped with malaria-endemic regions and with the occurrence of thalassemia in related modern populations, proposing these conditions as the most plausible causes. This hypothesis was further associated with physiological evidence. The diploë thickening, observed in individuals with porosity in the skull, likely reflected increased red cell production and hypertrophy of the red marrow — processes that hindered normal bone remodeling, leading to porous lesion formation (Angel, 1966). On this basis, the term "porotic hyperostosis" was proposed to describe porous lesions in both the cranial vault and orbits.

It should be mentioned that Angel (1966; 1967) recognized that cribra had a much broader distribution than thalassemia and sickle-cell anemia, suggesting also that lesions in skeletons from America were an effect of iron deficiency with prolonged lactation, severely restricted childhood diets, severe dysentery, or even production of abnormal hemoglobin in response to parasites, other than the plasmodium.

Hengen (1971), noting high frequencies of cribra in non-adults from equatorial regions, argued that poor iron intake combined with heavy parasitic load could synergistically contribute to iron deficiency anemia (IDA) and marrow expansion. He emphasized diploë hyperactivity as the key mechanism, thereby excluding vitamin deficiencies, scurvy, and systemic toxic disorders as primary causes. This ar-

gument was further supported in a study of Nubian skulls, where the presence of cribra orbitalia was interpreted as a result of IDA, potentially arising from high rates of parasitic infection, poor iron intake, frequent weanling diarrhea, and multiparity (Carlson et al., 1974). The focus seems to have shifted to IDA as a possible cause of cribra and the factors behind its development, in this case a synergistic interaction between diet and infectious diseases (e.g., Köhegyi and Marcsik, 1976; Cybulski, 1977; Mensforth et al., 1978).

Lallo et al. (1977) examining non-adult skeletons from Illinois and Ohio, proposed that cribra orbitalia was the initial osseous expression of porotic hyperostosis. This author argued that iron deficiency arose not only from infections but also from growth demands and a maize-based diet. Maize is not only low in iron, but it also prevents its absorption (Keigler et al., 2023). Consequently, it is not surprising that higher frequencies of cribra were found among canyon-bottom inhabitants in Arizona, whose diet relied heavily on maize, compared to the sage plain people in New Mexico, who consumed more iron-rich animal products (El-Najjar et al., 1975; 1976). This model gained popularity mainly due to its interpretative simplicity. In the book *Paleopathology at the origins of agriculture* (Cohen and Armelagos, 1984), several chapters mentioned this association. For example, Goodman et al. (1984: 297) state that cribra is the result of "increased adoption of a maize diet, especially among weanlings, as a cause of poor nutrition and an increase in nutrition-related stress indicators." However, the maize-dependent diet hypothesis was contested by Walker (1986). The author found that cribra in crania from a fish-dependent population of the Channel Islands (California), despite a protein- and iron-rich diet, was as frequent as among maize-dependent agriculturalists. This led him to suggest that high nutrient losses associated with diarrheal disease linked to parasite infections were more significant in the etiology of cribra than a low dietary intake of essential nutrients.

The notion that cribra was an indicator of nutritional impairment was even more widely disseminated than the maize hypothesis. One possible explanation is that although the maize-based hypothesis could easily explain the anemic origin, as Walker (1986) rightly points out, it would not fit in all contexts. Buikstra and Cook (1980: 449) noted that "samples with high frequencies of these defects [dental] also show other stress indicators, such as Harris Lines, meningeal reaction, cribra orbitalia, periostitis and early mortality." This idea was also reiterated in several other works (e.g., Huss-Ashmore et al., 1982; Hummert and van Gerven, 1983; Moore et al., 1986; Hodges, 1987; Jerszynska, 1988), emphasizing its widespread recognition within the field.

The connection between IDA and cribra persisted, partially due to the seminal works of Stuart-Macadam. Revisiting various publications, this author provides compelling evidence that IDA causes cri-

bra. In her analysis of juvenile skulls from the Romano-British site at Poundbury Camp, she noted that in children, where red marrow is prevalent, increased production of RBCs (erythroid marrow hyperplasia) puts pressure on the skeletal system (Stuart-Macadam, 1985). Children's bones, more susceptible to changes, react with marrow expansion and bone erosion. Conversely, in adults, marrow expansion can occur without using all marrow space, suggesting that lesions likely reflect anemia experienced in childhood.

Stuart-Macadam (1987a) research integrates evidence from multiple disciplines to strengthen the IDA theory. From an anthropological angle, lesions on skulls resemble clinical symptoms of anemia, marked by thick, porous appearances, particularly in the frontal and parietal bones. These observations are corroborated by histological analyses revealing enlarged marrow spaces and thinned outer bone tables, indicative of marrow hyperplasia. Moreover, Stuart-Macadam (1987b) confirmed earlier radiological observations of the "hair-on-end" pattern, a feature common in genetic hemolytic anemias but also seen in other conditions. She also described subtler features such as changes in bone texture, diploic and orbital thickening, and sinus alterations, which resemble those observed in anemic patients and individuals with cribra (Sebes and Diggs, 1979; Ponec and Resnick, 1984). The study also incorporates demographic data, highlighting the wide variability in anemia prevalence, with IDA notably affecting a large portion of the global population.

While the term porotic hyperostosis was widely used to describe orbital and cranial vault porosity, later studies questioned whether both reflect the same physiological process. Still, Stuart-Macadam (1989), drawing on earlier evidence and their similarities, argued for a common etiology.

The foundations were then consolidated, and from that point onward, several studies considered IDA as the most plausible cause of cribra (e.g., Guidotti, 1984; Goodman et al., 1988). Nevertheless, the work of Stuart-Macadam did not cease here, and she proposed a new perspective for the interpretation of cribra (Stuart-Macadam, 1991; 1992; Kent et al., 1994). She brought back the association between IDA and infections by highlighting the adaptability of iron metabolism when compared to the role of diet in developing IDA. Based on recent clinical data, at that time (Kent, 1986), she argues that hypoferremia is an adaptive response to disease and microbial invasion. In environments with high pathogen loads, individuals become hypoferremic to defend against pathogens, increasing the risk of IDA. Thus, "porotic hyperostosis" is no longer viewed merely as a nutritional stress indicator but as a sign of a population's adaptation to its pathogen load. To some extent, Mensforth (1991) reflects part of this perspective. Based on the observation of crania from Ottawa County, Ohio (850 to 1250

CE), the author suggests that dietary inadequacy and parasitism played a minor role in the etiology of cribra. Alternatively, local environmental circumstances associated with housing and resource exploitation may have played a fundamental role in elevating infectious disease loads, resulting in a greater prevalence of IDA.

Interestingly enough, this proposal did not gain as much attention as the previous argument, probably not only because it would imply a more complex scenario but also because it was rather deterministic. Goodman (1994) mentions that focusing only on one factor, either diet or parasitism, is simplistic and may imply a narrow view of adaptation. The author suggests that porous lesions are a sign of nutritional deficiency, from a variety of systemic consequences. Holland and O'Brien (1997: 191) echo this argument, mentioning that probably, there is not a major factor behind cribra expression; instead, there is "a multitude of more-or-less equally important, and interdependent, factors. It is this interdependency that all too often falls victim to the seductive lure of a simple just-so model." Approximately at the same time, Wapler and Schultz (1996) published an important study where they analyzed histologically ten samples of cranial cribra. The results of the microscopic analysis showed trabecular enlargement that was not only compatible with anemia but also with inflammation and postmortem erosion, emphasizing flaws in the IDA model.

4. Shifting perspectives: IDA challenged and the consolidation of the stress models (2000s to mid-2010s)

In the new millennium, the discussion on cribra's etiology was defined by a back and forth regarding the IDA hypothesis, yet some other possible etiological models have also been proposed. The works of Polo-Cerdá et al. (1999; 2000b) brought an interesting insight, since this is the only experimental study done so far. The authors induced IDA in Wistar rats (n = 29) through bloodletting and nutritional impairment (early weaning and magnesium deficiency). Both the autopsy and the CT scans results show porous lesions on the orbital roof, consistent with those described in humans.

Despite the significance of these results, this study did not particularly resonate within the scientific community, and more arguments that challenged the IDA hypothesis emerged. For example, Rothschild (2000) finds the association between iron deficiency and hyperplastic marrow problematic, as inadequate iron for blood cell production would result in hypo-regenerative marrow. The author proposes to explore the presence of genetic hemolytic anemias, hemoglobinopathies, parasitic infestations, and nutritional data. Additionally, histological analysis of cribra orbitalia in adult individuals from Sudan (2^{nd} – 6^{th} centuries CE) shows that, even if frequent (43.5%, 20/333), anemia was not the only cause of these lesions (Wapler et al., 2004). This author identified other conditions, such

as inflammation (29.4%, 25/85) and hypervascularization (5.9%, 5/85), together with postmortem alterations (20%, 17/85), even in well-preserved bones.

Already critical of some views regarding the etiology of cranial cribra (Walker, 1986), it was not until 2009 that Walker and co-authors published a vital work that refuted, theoretically and empirically, the IDA hypothesis. The authors critically assessed the potential of IDA to induce marrow hyperplasia and propose a biosocial mechanism that considers environmental instability as a result of: 1) populational growth with higher food demands filled by a plant-based diet (lack of vitamin B12 and folate); 2) cultural changes that affect the health condition of mothers whose milk does not suffice nutritional requirements of their children; and 3) climatic changes that conduct to less salubrious living conditions (e.g., poor sanitation and water contamination) resulting in infections and nutrient loses. These authors propose different mechanisms for cribra expression, marrow hypertrophy due to megaloblastic anemia (MA) would lead to cribra cranii, and orbital roof hematomas from vitamin C deficiency producing cribra orbitalia. Despite different processes, both were seen as outcomes of systemic homeostasis disruption. This synergy points to a more realistic scenario, considering the complexity of the human body (Walker et al. 2009).

Shortly after, this argument was contested, particularly regarding the inability of IDA to cause marrow hyperplasia (Oxenham and Cavill, 2010). To these authors, IDA with heightened erythropoietic activity should be included in the differential diagnosis. Conversely, Rothschild (2012) commends the work of Walker et al. (2009) for recognizing and correcting the misconceptions about the nutritional implications traditionally linked to PCLs. This author calls for a disciplinary shift from disproven dietary explanations toward more plausible causes — genetic hemolytic anemias, hemoglobinopathies, and parasitic infections — that may offer deeper insights into the health of past populations.

In a more empirical study, the bone microarchitecture of seven non-adult individuals with cribra orbitalia was evaluated by peripheral quantitative computed tomography (HR-pQCT; Saint-Martin et al., 2015). The authors found that porosity in the orbital roof could be associated with inflammation or even taphonomy, moving away from an anemic origin. The debate is, however, far from being over. McIlvaine (2015) argues that, although the IDA hypothesis may not fully explain cribra, dismissing it risks underestimating the complexity of past health. The author notes that severe nutritional stress, such as iron deficiency, may not always produce cribra, making affected individuals appear healthy. This could bias assessments of past health, mask multiple deficiencies, and require reinterpreting earlier studies. These ongoing discussions over the IDA model continue to shape cribra's research, leading to no definitive consensus.

In parallel with IDA discussions several researchers have interpreted cribra as a "nonspecific indicator of stress", largely due to insufficient evidence linking it to a specific etiology. The concept of stress emerged from Hans Selye's works on the body's responses to endogenous and exogenous factors. He first described a syndrome caused by harmful agents (Selye, 1936), which he later named stress (Selye, 1950). In osteology, Armelagos (1969) operationalized stress as an "index of biological response" influenced by cultural variations. Goodman et al. (1988) further explored how stress could be inferred from skeletal remains, demographic data, and contemporary health indicators, emphasizing the role of sociopolitical and environmental factors. Through studies of Nubian and Dickson Mounds (USA) populations, they distinguished between specific skeletal indicators of stress — such as the ones found for tuberculosis or syphilis — from nonspecific ones like Harris lines, enamel hypoplasia, periosteal reactions, and PCLs. This work set a precedent for using nonspecific indicators as proxies to estimate past health. Consequently, paleopathological interpretations often rely on these markers to provide insights into episodes of disease, infections, nutritional deficiencies, and other health challenges (Kyle et al., 2018; Buikstra, 2019).

It should be recognized that the conceptualization of stress in bioarcheology is dynamic. Hillson (2014) noted the often-ambiguous use of the concept, highlighting the need for consensus. Recently, Edinborough and Rando (2020) emphasized the importance of transparency in understanding the relationship between "nonspecific stress indicators", environmental factors, and human behavior, advocating for precise language. In a study of more than 3,000 skeletons from pre- and post-contact central California (3050 BCE–1899 CE), traditional stress markers such as periosteal reactions and cribra were re-evaluated (Pilloud and Schwitalla, 2020). The authors highlighted methodological and theoretical challenges, arguing that lesions cannot be directly linked to external stressors. Instead, they advocated for interpretations grounded in clinical literature, regionally appropriate contexts, and the integration of archeological and climatic data. Due to the uncertainty around PSLs etiology, broader bioarcheological investigations often drew a straightforward association between PSLs and stress. This line of thought was followed through the years and is still present in some studies (e.g., Kyle et al., 2020; Laffranchi et al., 2021; Wiesinger and Kirchengast, 2021).

5. The postcranial cribra and emerging directions in PSLs research

So far, the studies presented considered solely PCLs. The historical context for porosity on the necks of humeri and femora is harder to trace. Although the postcranial skeleton's involvement in anemia has long been known (Almklov et al., 1950), to the author's knowledge, the association of postcranial porosity

with cribra cranii and orbitalia is more recent. Interestingly, Angel (1964b) describes bone reactions in the femoral neck and recognized this region as a "sensitive reaction area." He highlighted changes like Poirier's facet — extra joint surface near the femoral head rim — and Allen's fossa — removed cortical bone revealing thickened trabeculae with a raised border. Finnegan and Faust (1974) later described these as normal variations. Although Angel (1964b) acknowledged the "cribriform" appearance of this area, characterized by atrophy and inflammation, he never directly connected it with porotic hyperostosis.

One of the first uses of the term cribra femoris was found in the research of Saunders et al. (1980). The authors briefly mention the appearance of this lesion in skeletons from St. Helen's Church (England) and state that "cribra femoris may indicate calcium deficiency or iron-deficiency anaemia." (Saunders et al., 1980: 109). This small reference seems to indicate that the term was used before, yet even after extensive bibliographic research, it was not possible to identify the source. A similar case was found in the work of Conheeney (1990), but the preferred terminology was cribra femoralis. It was just mentioned as being present together with cribra orbitalia in individuals from Southern Etruria (Italy), and no further inferences were made.

The literature seems to be even scarcer when it comes to the first description of cribra humeralis. The exception appears to be that, when studying the frequencies of cribra orbitalia in indigenous people from Hawaii and Australia, Zaino and Zaino (1975: 92) report "in one [individual] sieving was also present in the proximal portion of the humerus." Nevertheless, the lesion did not receive any specific designation.

One of the key contributions to recognizing porosity of the humeral and femoral neck as cribra came from the work of Miquel-Feucht et al. (1999). Steaming from the analysis of 170 non-adult individuals from Spain, the authors define the existence of cribra femoral "as a bone alteration on the anterior and internal surface of the femoral neck, characterized by the presence of numerous small holes, identical to those of cribra orbitalia" (Miquel-Feucht et al., 1999: 5). They recognize likewise an associated "similar cribrous lesion at the humeral level, symmetrically shaped, and located on the anterior and internal surface immediately below the humeral head (anatomically the same area as the femoral neck)" to which they called cribra humeral (Miquel-Feucht et al., 1999: 9). Additionally, alongside macroscopic study, the lesions were examined through radiology, CT, and histology. Their similarities to cribra orbitalia led the authors to propose a "cribrous syndrome" defined by "the presence in subadult subjects of cribra orbitalia, symmetrical cribra femoralis in hyperplatymeric or platymeric femurs, and (variable) cribra humeralis", with a shared etiology related to magnesium deficiency (Miquel-Feucht et al., 1999: 13).

Despite the conclusions presented in this study, few subsequent analyses addressed postcranial cribra (e.g., Polo-Cerdá et al., 2000a; Capasso, 2001; García et al., 2002; Zaragoza et al., 2005). As a matter of fact, these lesions were largely overlooked in paleopathological literature for quite some time, likely due to the language barrier, as most of these works were written in Spanish, and possibly also due to the similarity with normal porosity in early developmental stages. One exception is the study of Djurić et al. (2008) that evaluated the presence of the four cribra in 327 medieval non-adult skeletons (under 14 years old) from Serbia, finding that 33.3% (5/15) of individuals with all three bones preserved exhibited the four types of cribra. A similar pattern was observed among older individuals (11-15 years) in a subsequent study (Djurić et al., 2010). The authors suggested that both cranial and postcranial cribra in these populations may be linked to parasitic infections, leading to anemia and nutrient malabsorption.

One of the main contributions of the inclusion of the postcranial cribra in the etiological studies of PSLs came from the research of Smith-Guzmán (2015). The author revisited the Angel's (1964a; 1966) hypothesis — genetic hemolytic anemias may lead to cribra formation in association with malaria infection. By analyzing documented individuals from Uganda (n = 98), where malaria is endemic, and comparing them with those from the USA (n = 106), the author found higher frequencies of cribra orbitalia, cribra humeralis, cribra femoralis, new bone growth, and spinal porosity in the Ugandan sample, particularly among individuals with an anemic/malaria cause of death. Cribra humeralis and femoralis correlated strongly with anemia and appeared mainly in younger individuals, whereas cribra orbitalia showed no such correlation, suggesting a possible distinct etiology. The discussion also highlighted the challenges of differential diagnosis, emphasizing the importance of carefully considering co-infections.

Studies on postcranial cribra have been increasing in recent years. In Medieval Spain (n = 129), Mangas-Carrasco and López-Costas (2021) found high frequencies of cribra orbitalia (78%) and cribra femoralis (70%), with more active lesions in non-adults. Importantly, 65% of cases showed co-occurrence, suggesting a shared etiology. Schats (2021), analyzing 232 individuals from the Netherlands, also reported high rates of femoralis (38.8%) and orbitalia (26.7%), especially in non-adults, but simultaneous lesions were rare, challenging the "cribrous syndrome" hypothesis. Data from Portugal, both in identified collections (n = 56; Gomes et al., 2022) and archeological samples (n = 96; Gomes et al., 2025), likewise neither confirm nor exclude the existence of the so-called "cribrous syndrome." Nevertheless, it is possible to state that cribra humeralis seem differentiate from the other porosities and if there is a "cribrous syndrome" it involves only cribra orbitalia and femoralis, since this is the most frequent combination found.

Despite the growing body of evidence on cribra humeralis and femoralis, research remains disproportionately focused on PCLs. Furthermore, the inclusion of postcranial cribra, rather than settling the etiological debate, has opened the way for new and broader interpretations.

As summarized in Figure 2, this historical overview shows that, despite the renewed attention PSLs have received from the mid-2010s onwards (e.g., Brickley, 2018; 2024; Papathanasiou et al., 2018; McFadden and Oxenham, 2020; Morgan et al., 2025; Wyatt and O'Donnell, 2025), contemporary debates still revisit long-standing associations with geographic distribution, anemia, parasitism, and diet (e.g., Steyn et al., 2016; Cole and Waldron, 2019). Moreover, even the pathological nature of the lesions remains under discussion, as some researchers argue that they may result from vascular phenomena (Rothschild et al., 2021; 2023; Zdilla et al., 2022).

However, recent analytical advances such as CT scan (Rivera and Lahr, 2017; Anderson et al., 2021; O'Donnell et al., 2023), micro-CT scanning (Morgan et al., 2024), and elemental bone analysis (Gomes et al., 2021; 2025; Kilburn et al., 2021) have refined diagnostic approach-

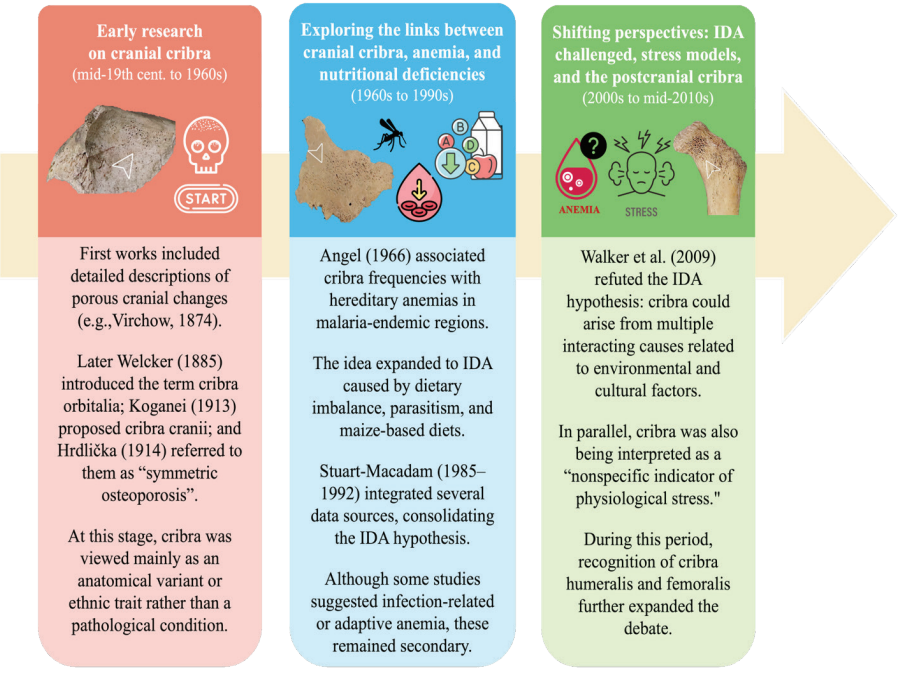

Figure 2. Historical synthesis of research on porous skeletal lesions (PSLs), highlighting the evolution of etiological interpretations of cranial cribra from the 19th century to the early 21st century. The three main phases illustrate the shift from anatomical descriptions to pathological and multifactorial frameworks, culminating in the recognition of postcranial cribra.

es and opened new interpretive possibilities. One good example is the evidence linking cribra cranii and orbitalia with respiratory infections in forensic (O'Donnell et al., 2020), clinical (Anderson et al., 2025), and identified skeletal collections (Gomes et al., 2022; 2024). These findings expand the discussion beyond nutritional and anemic frameworks, suggesting that inflammatory and infectious processes may also play a significant role in PSLs formation. Taken together, these developments illustrate how PSLs research has moved toward increasingly multifactorial and context-dependent interpretations. Despite this progress, several questions remain open in PSLs research. For instance, although some efforts have been made (e.g., O'Donnell et al., 2023), the minimum age at which PSLs first appear is still largely unexplored. Closer integration with clinical research could provide valuable insights into this issue and further advance the understanding of PSLs.

6. Final comments

Over nearly two centuries, interpretations of PSLs have mirrored the broader evolution of paleopathology itself — from typological and racial readings of cranial morphology to increasingly contextual, biocultural, and multifactorial perspectives. Each phase of this history reflects not only shifts in available evidence and analytical methods but also deeper transformations in how disease, adaptation, and variability are understood within human populations.

The trajectory traced here demonstrates that no single etiological model can account for the diversity of PSLs expression. From the mid-20th century onward, successive frameworks, such as genetic and nutritional anemias, infection and inflammation, and more recently biosocial approaches have captured part of a complex picture. While the IDA model dominated for decades due to its explanatory simplicity, subsequent research revealed a much broader range of contributing factors, from physiological and developmental processes to ecological and social determinants. The recognition of postcranial cribra further diversified this discussion, challenging long-standing assumptions that these lesions shared a single origin.

Equally significant is the way PSLs research has been shaped by methodological innovation. Advances in imaging and non-destructive chemical analyses seem to be the key to refine lesions descriptions and to test long-held hypotheses. These techniques allow direct observation of trabecular architecture, marrow space morphology, and elemental composition, bringing new rigor but also revealing the limitations of purely mechanistic explanations. At the same time, comparative and epidemiological studies should also be pursued to integrate environmental, demographic, and socioeconomic dimensions, pointing toward a more holistic understanding of skeletal health.

In this perspective, PSLs emerge not as diagnostic entities but as contextual

indicators — markers through which past health, living conditions, and biological adaptation can be approached. The interpretation of these lesions is a good example of the need to consider the intersections of biology and culture, individual physiology and collective environment, structure and history. Moving forward, PSLs research will benefit from approaches that embrace this complexity, combining standardized recording and imaging with contextual, cross-disciplinary analyses that bridge clinical, archeological, and social data.

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