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CANCER IN EGYPT AND NUBIA

ABSTRACT: The work of Eugen Strouhal has contributed greatly to the understanding of neoplasms in the archaeological record. His detailed work inspired re-evaluation of a set of remains from a 1960s excavation in Egypt and Nubia. Evidence of metastatic carcinoma is used to highlight the process of differential diagnosis and the changing epidemiology of cancer in the past. Cancer is currently the second highest cause of death in modern America, but relatively rare in prehistory. There are few examples of metastatic carcinoma in the archaeological record. We report a case of metastatic carcinoma in a Meroitic (350 CE – 50 CE) male to highlight both the work of Strouhal and the nature of cancer in Nubia. The frequency of neoplasms is important for the interpretation of the prevalence of the disease and its nature with the increase of chronic disease in the second epidemiological transition.

KEYWORDS: Cancer – Metastatic Carcinoma – Nubia – Epidemiological Transition

INTRODUCTION

Is cancer a disease of modern civilization? David and Zimmerman (2010) note that while cancer is the second most frequent cause of death in industrialized societies, malignancies in ancient populations are considered a rarity. However, there is evidence of cancer in early societies and therefore the question changes to whether there are particular types of cancer that are diseases of modern society? It is well recognized that the nature of disease has shifted during our transition from hunter-gatherers to post-industrial jet setters (Harper *et al.* 2010). The existence of metastatic cancer provides some evidence for the nature of this shift, particularly in one of the most studied ancient societies, Egypt and by extension, Nubia.

Strouhal (1998) has tabulated 176 examples of skeletal malignancies in prehistory. Given the vast number of burials uncovered and studied, this represents a relatively low level of prevalence. The seemingly low rate of cancer may be due to preservation issues, however it may also be that its a rarity in prehistory is related to the differences in life expectancy, diet and environmental factors (David *et al.* 2010). The issue of scarcity will be evaluated through a consideration of Strouhal's previous work and a review of the epidemiological nature of disease. Strouhal's contributions provide an excellent source for comparison with other examples of cancer, specifically metastatic carcinoma in the archaeological record. This will be highlighted through the use of a case study from an area well studied by Stouhal: Nubia. In this paper, we will first present a case of malignant carcinoma from the Meroitic Period (350 BC – 350 CE) excavated from the Wadi Halfa area of Sudanese Nubia. In presenting this case study from Sudanese Nubia, we review Strouhal's role in clarifying and elucidating the instances of cancer in Egypt and Nubia. Finally, we will provide an epidemiological context for understanding the disease transition that has led to the rise in the prevalence of cancer that we observe today.

MEROITIC PERIOD NUBIA

The Nubian population represents one of the most intensively studied archaeological populations in the world, with 36 major excavations of over a 1,000 hectare site in the last 75 years (Adams 1977). These sites in Nubia span broad changes in culture and subsistence practices, encompassing the presence of hunter-gatherer lifestyles through to agricultural intensification.

Lower Nubia is the portion of the Nile River Valley extending from the First Cataract at Aswan to the Second Cataract at Wadi Halfa. The region represented a main line of communication connecting sub Saharan Africa and the Mediterranean (Trigger 1965). Populations from Wadi Halfa represent the Mesolithic (ca. 12000 BC), Neolithic (5000–3600 BC), A-Group (3400–2400 BC), C-Group (2400–100 BC), Meroitic (350 BC – 350 CE), X-Group or Ballana (350–550 CE), and Christian (AD 550–1350) periods. The skeletal material in this study was excavated during the course of the first University of Colorado Nubian Expedition during the 1963–1964 field season.

The reoccupation of Lower Nubia occurred simultaneously with the development of the waterwheel *(saqia)* in Upper Nubia (Adams 1970). The waterwheel increased the productive potential of the region, permitting the support of a larger population than before. Farmers could now grow several crops a year, and the level areas farther back from the Nile (as well as the high banks) could be watered and used for agricultural purposes (Trigger 1965). However, crops grown on these lands required a much greater investment acre-by-acre than did single annual crops grown on the alluvial flood plains. The new system therefore required increased inputs of both time and energy.

The Meroitic culture flourished at this time and Lower Nubia was important for trade and communication between the Mediterranean and sub Saharan Africa. However, most of the settlements were small and relatively poor. The inhabitants of Lower Nubia were being ruled from Upper Nubia and may have been supporting the area with agricultural products (Adams 1977). Even with the waterwheel, agricultural potential was relatively low, and trade accounted for much of the growth (Trigger 1965). The archaeological record shows a farming strategy that involved three growing seasons. The crops harvested included millet, wheat, barley, beans, tobacco, lentils, peas, and watermelon (Trigger 1965). Dates, mangoes, and citrus trees could also be kept watered during dry seasons to produce fruit. Cattle, sheep, and goats were probably herded and animal husbandry may have been only slightly less important than agriculture (Adams 1977). Cattle were used to drive the waterwheel, and were not consumed, though Trigger (1965) suggests that milk and butter may have been important sources of food for trade.

The Meroitic people had a strong incentive for development of the agricultural potential of their region. Immediately to the north lay the wealthy Roman province of Dodekashoenos, a terminus for the caravan trade with sub Saharan Africa. The Lower Nubians, subjects of the Upper Nubian Kingdom of Meroe, traded their surplus agricultural produce to this "industrialized" Roman province (Adams 1970). In return they received a bountiful range of the trade goods of Mediterranean civilization. Toward the later stage of the Meroitic Period, the lower Nubians had achieved a more sophisticated level of cultural development than the area had ever seen before. Settlement patterns indicate that the population size increased and clustered into dense pockets around the irrigated fields (Trigger 1965). Despite this thriving culture, by 350 CE the decline of the Kingdom of Kush and the Kingdom of Meroe brought an end to prosperity in Lower Nubia and eventually the Roman Empire was beset with governmental instability, famine, plagues, and wars (Adams 1977).

SKELETON 42C, SITE 6B16, MEROITIC PERIOD

Cranium

Standard methods of determining age and sex using published standards (Armelagos 1968: 26–28). The postcranial sex determination relied on measurements of the pelvis and long bones. Cranial feature relied on measuring the mastoid process and macroscopic observations of dimorphic features using the ranges of variation that exist in the populations that were being excavated. The skull is a male; it has very pronounced brow ridges and large wide mastoid processes. Both of these features are reliable indicators of sex. The posterior portion of the skull is damaged and the external occipital protuberance cannot be assessed as a sex indicator. There seems to be no external sign of this damage though, meaning his appearance was likely unaffected by the break.

The cranial remains only allow the individual to be aged as an adult. The mandible has erupted third molars, although the left is missing from its socket. The maxilla contains the left third molar and the damaged roots of the right third molar. There is extensive wear on the maxillary premolars and first molar. This level of wear is consistent with the diet and the sandy Nubian environment, and sand introduced during the processing of cereal grains (Thekkaniyil *et al.* 2000). The maxillary second and third molars, however, show very little wear. Though third molars can erupt as many as 10 years after the first molars, the level of disparity between the wear patterns is greater than we anticipate. The original observation recorded at the time of excavation suggests that there was some mandibular alveolar resorbtion, but it does not state which teeth were missing. Therefore it is possible that this individual had no lower second and third molars, which would account for the reduction in occlusion and lower rates of wear. Overall there is very little evidence of dental pathologies. The right maxillary second molar has some staining on the buccal side of the occlusal surface, but there is no evidence of any established carious lesions. There is no dental calculus present.

The anterior nasal spine and what is left of the vomer and the perpendicular plate of the ethmoid seem to be slightly deviated, suggesting that the individual may have broken their nose during their life. There seems to be no external sign of this damage though, meaning his appearance was likely unaffected.

The most prominent feature of the skull is a large erosion of the vertical portion of the frontal bone, extending past the coronal suture onto the right parietal (*Figure 1*). In the 50 years since excavation, damage to the skull makes it

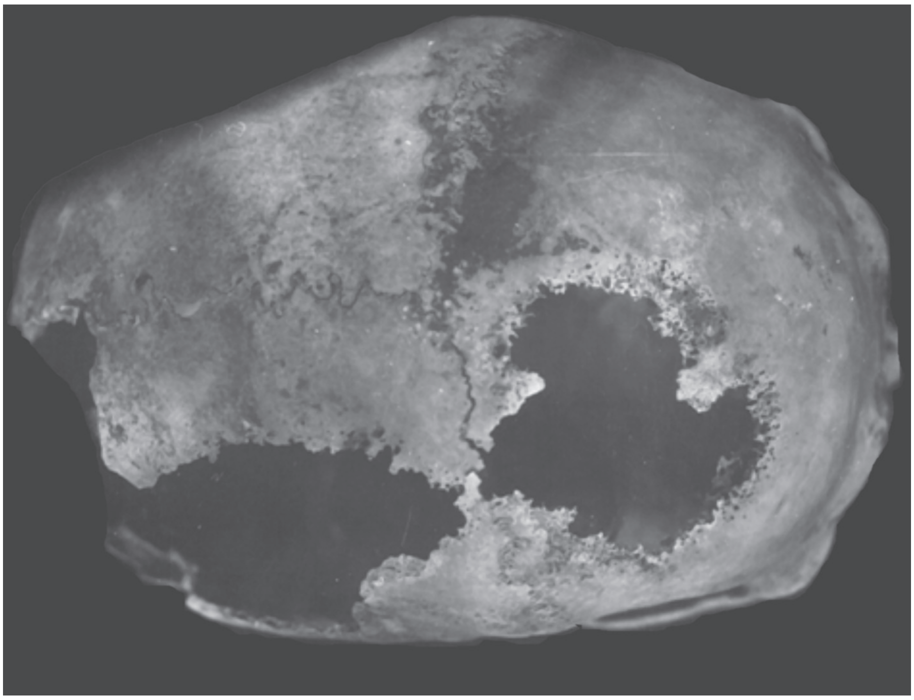

FIGURE 1. The skull of 42C showing the large lytic lesion on the frontal bone and the probable second lesion on the right parietal. This photograph was taken during the excavation and before damage was sustained to the skull removing the secondary parietal lesion.

is exceedingly difficult to determine the full extent of the lesion on the posterior rim. Using the original excavation photographs, the lesion is about 4.5 cm in diameter and exhibits a slightly irregular, circular appearance. A possible second lesion is observable behind the first, eroding a large section of the right parietal from the sagittal suture to 2 cm above the squamosal suture. Though this area of the skull was damaged post excavation, the edges of the lesion appear scalloped and show evidence of periosteal deterioration in the form of a lytic appearance.

There is no sign of any bone remodeling on the outer table of the frontal bone, and the edges of the lesion are flat and thin without any curling or thickening which would suggest bone remodeling. The possible second damaged lesion looks identical in the excavation photographs, and therefore it can be assumed that the two lesions were caused by the same pathology. The inner table of the frontal bone around the lesion depicts some areas of new periosteal, and does not appear to be remodeled; rather, the reaction of the periosteum is likely due to pressure being exerted by the meninges or other soft tissue directly below it. Several depressions are also visible on the internal table of the cranium. There are five present on the inner surface of the left parietal bone, of varying sizes ranging from 0.75 to 2 cm in diameter.

These appear to be the beginning of further erosions of the inner table leaving the outer layer intact. These marks do not have the "moth eaten" edges of the larger lesion, suggesting this appearance indicates advanced erosion of the bone. Finally, the inner surface of the frontal bone adjacent to the eroded area shows more blood vessel grooves than normal, suggesting that something within the frontal area of the brain was commanding a greater supply of blood than is normal.

Post-Cranial

A number of lesions are present on the post-cranial skeleton (*Figure 2*). The right ilia had roughly a 3 cm long erosion on its lateral side behind the auricular surface. One lumbar vertebra has an erosion in the posterior surface of the body, which made it collapse slightly. Finally, the left scapula had two small erosions on the anterior surface, one below the coracoid process and one on the inferior portion of the blade towards the apex. These lesions are no more than 1.5 cm in diameter, and are clearly lytic in nature. While no X-rays have been taken for further confirmation, there were no notable changes in bone weight that would suggest any sclerotic lesions inside the bones.

STROUHAL'S WORK

Strouhal's survey of the observed neoplasms in ancient Egyptians documented a number of tumors of bone, but rarely included soft tissue findings (Strouhal 1976). He was able to diagnose malignant and benign lesions. For example, he and his coworkers (Vyhnánek *et al.* 1999) observed an interesting osteochondroma that are typically found on the long bones of individuals from the Late Period site at Saqqara. In this case, he found a "kissing" osteochondroma of the ulna touching ("kissing") the radius. The osteochondroma grew toward the radius, with their contact causing a reactive impression. They note that the location on the lower arm bones is unusual and may in fact represent a malignant bone tumor (Vyhnánek *et al.* 1999).

Strouhal and coworkers (Strouhal *et al.* 2003) have uncovered neoplasms in notable figures in history. For example, pathological changes of the female lector priest

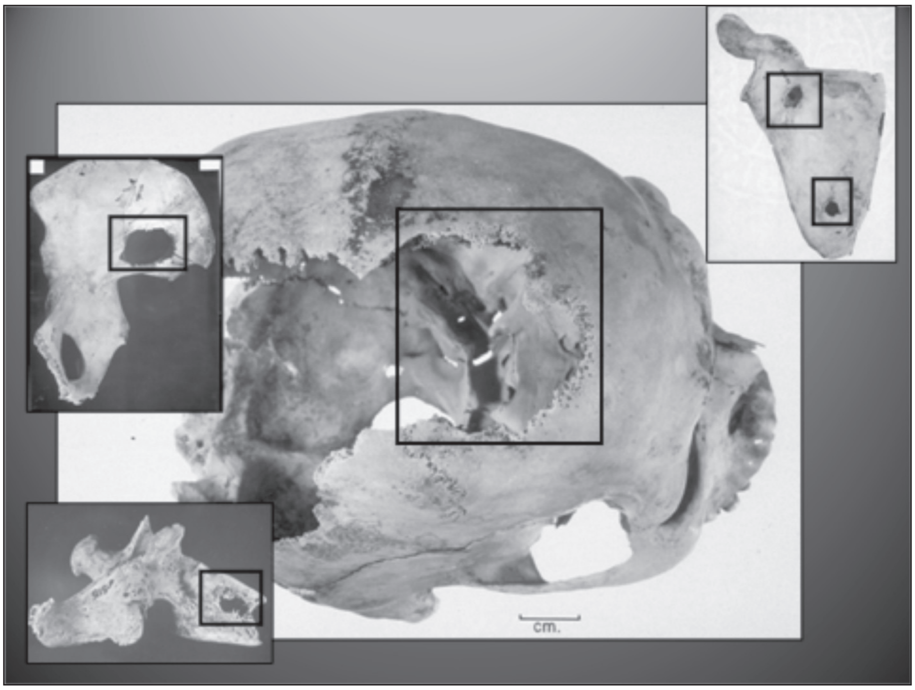

FIGURE 2. These are the only photographs available for the post-cranial skeleton. The lesions are not very clear, but matching them with the descriptions on the data card from the initial excavation it is clear that these were also considered to be lytic lesions characteristic of metastatic carcinoma.

Lufaa from Abusir in Egypt (late 26th Dynasty prior to 535 CE) represent the first palaeopathological evidence of a neurilemmoma, a rare benign neoplasm (Strouhal *et al.* 2003). They describe a large, smooth-walled cavity molded from a relatively hard, globular, and lobulated tissue found inside the sacrum of the Imakhetkherresnet. The origin of the lesion, a nerve sheath, was determined by macroscopic, radiographic, and histological analysis. Strouhal and coworkers speculate that as the mass grew in her sacrum, it hollowed out the bone and eventually compressed her sacral plexus and obstructed two foramina sacralia posterior – potentially having a crippling effect. Macroscopic and radiographic examination, histological analysis, and immunohistochemical testing has led to the unequivocal diagnosis of a benign tumor originating in Schwann cells of the myelin nerve sheath, i.e., neurilemmoma (schwannoma, neurinoma). The sacral location of this tumor has rarely been encountered in the sacra of living patients (Strouhal *et al.* 2004).

Strouhal has been at the forefront of efforts in the differential diagnosis of two difficult lesions (Strouhal 1991). He provided a means of distinguishing lesions caused by the primary osseous myeloma multiplex tumor and the lytic involvement of metastatic carcinoma in dry bones. Using lesions from these conditions he provided a method for separating the two carcinomas. Lesions have also been found that originated in hardened skeletal tissues as well as soft tissue cancers that metastasized to the bone. For example, he reports a case of a female with a calcified myoma uteri and an individual diagnosed with epipharyngeal carcinoma (Strouhal 1976). Another case, from the 6th to 12th Dynasty at Naga-ed-Der, Upper Egypt, was diagnosed as nasopharynx affecting the soft tissue. In this case, a large portion of the facial skeleton was destroyed by the tumor and there was a small secondary deposit on outer surface of the right squamal region of the temporal (Strouhal 1978). In light of his own findings, Strouhal calls for researchers to renew their interest in detailed palaeopathologic evaluation in order to document all potential cases of cancer in material they excavate.

DIAGNOSIS OF INDIVIDUAL 42C

The work of Stouhal has provided ample detailed description of various examples of metastatic neoplasms in archaeological remains. His medical background serves his descriptions well, making them a useful resource when carrying out palaeopathological analysis on potential samples. By comparing the sample described in this paper to Strouhal's work (Strouhal 1976, 1978, 1991) it seems clear that the lesions are evidence of a metastatic carcinoma. However, there are many cancers that can cause similar symptoms and so a differential diagnosis (Marks *et al.* 2007) of sorts must be employed to determine the most likely causes of the lesions observed in skeleton 42C. This is not a differential diagnosis in the strictest sense as the ambiguity lies in the type of cancer rather than the type of pathology as nothing else causes lesions such as those seen in skeleton 42C, but many cancers can cause them; hence the importance of Strouhal's work.

Metastatic cancer is the primary cause of death for people with cancer (Mundy 2002). However, metastasis also only occurs when the cancer is advanced enough, which means that the individual has to live long enough for it to progress to this stage. Therefore, any individual case of metastatic cancer in the archaeological record is evidence that the individual survived for some time with probable pain and discomfort (Mundy 2002). Metastatic carcinoma in bone also weakens the integrity of the skeletal tissue and therefore increases the risk of fracture.

To further elucidate the potential type of cancer experienced by individual 42C, we evaluated modern medical literature and the current prevalence of these cancers. Some cancers affect the bones more than others. Currently in the United States, breast, lung, and prostate cancer are the most common causes of bone metastasis. Breast and lung cancers both cause lytic lesions, as are seen in skeleton 42C, whereas prostate cancer causes sclerotic lesions (Mundy 2002). The modern day prevalence of these three cancers is undoubtedly higher than that experienced in the ancient world, due to the changing epidemiologic nature of cancer over time. While breast cancer is possible in males 1% of all breast cancer cases in the United States occur in men (Giordano *et al.* 2002), it is likely that the condition would have been even less pervasive in ancient times. Thus, breast cancer is eliminated as a likely contender for the lesions observed in individual 42C.

While cancer mortality has begun to decline in developed countries during recent years, the types of cancer most prevalent have shifted from those with infectious origins to those with large lifestyle contributions (Wilmoth 2000). For example, in 2010 it is expected that there will be 222,520 new cases and 157,300 deaths attributable to lung cancer, primarily caused by smoking, while only 21,000 new diagnoses and 10,570 deaths will be related to stomach cancer (Altekruse *et al.* 2010). Three primary cancers with infectious origins include stomach, liver, and cervical cancer. Liver cancer has been tied to infections by hepatitis B and C, and human papilloma virus has been shown to cause cervical cancer (Wilmoth 2000). Stomach cancer, meanwhile, is typically caused by an infection by *Helicobacter pylori* (*H. pylori*), and was known to be much more prevalent prior to the widespread availability of refrigeration (Replogle *et al.* 1996, Asaka *et al.* 1997). *H. pylori* likely transmits among a population through the fecal-oral or oral-oral route (Stone 1999), and therefore should be considered in the case of skeleton 42C. This cancer can cause both lytic and sclerotic lesions (Even-Sapir 2005), though as there are no X-rays available of the skeleton, the presence of sclerotic lesions cannot be excluded.

Schistosomiasis, caused by the bacterium *Schistosoma haematobium/mansoni,* can cause bladder cancer and is well documented in modern day Egypt (Bedwani *et al.* 1998). There is also extensive evidence of schistomes in ancient Egypt and Nubia (Adamson 1976, Miller *et al.* 1992, Miller *et al.* 1993, Kloos *et al.* 2002). Schistosomiasis accounts for 16% of the cases of bladder cancer in modern Egypt (Bedwani *et al.* 1998), though current treatments of the infestation may be limiting the complete expression of cancer and overall prevalence of the cancer may have been higher in the past. The metastatic lesions in the bone caused by bladder cancer are primarily lytic (Babaian *et al.* 1980), and the areas of the skeleton most commonly affected are the lumbar vertebrae, pelvis, ribs, femur, and skull (Bedwani *et al.* 1998). There was no evidence of lesions in the ribs or femur of skeleton 42C, though lesions were evident on the pelvis, one vertebra, and the skull; therefore bladder cancer must be included in the differential diagnosis as a possible and probable cause of the metastatic carcinoma seen in this skeleton.

There are no prevailing theories about the cancer burden in Egypt and Nubia. Strouhal's work highlights the best examples found, and whilst this provides more evidence than is seen in other areas, there is still a limited sample size from which to draw conclusions. This is in part due to the excellent preservation of human remains in Egypt and Nubia as well as the extensive excavation coverage both spatially and temporally. There has been and continues to be substantial excavation in this area along with good documentation. Therefore, if there are so few cases in these areas, does this mean that cancer was this scarce everywhere?

CONSIDERING EPIDEMIOLOGIC TRANSITIONS

David and Zimmerman could have placed the question of cancer in an epidemiological framework. Abdel Omran (1971) models a pattern of disease human history that experienced three disease stages of development. The humans in the Paleolithic lived in an "age of pestilence and famine" (Omran 1971: 516), which gave way to an "age of receding pandemics" (Omran 1971: 516), culminating in "the age of degenerative and man-made diseases" (Omran 1971: 517). Omran (1977, 1983) argued that humans will progress to a state in which infectious diseases are eradicated. With the elimination of early mortality due to infectious disease, the average age of individuals in the population will increase, and a rise in degenerative, chronic, "man-made" diseases will follow. While Omran (1982, 1983) presents his model of epidemiological transition as a comprehensive analysis of human history, abundant bioarchaeological evidence suggests that human populations underwent an earlier disease transition, one that he does not describe. Omran's version of epidemiological transition has been broadened to include an alternative view of the Paleolithic as a relatively disease-free era. Such an expanded epidemiological model (Barrett *et al.* 1998, Armelagos 2004) encompasses three transitions.

The first epidemiological transition occurred ten thousand years ago with the subsistence shift from foraging to agriculture. A dramatic increase in infectious diseases resulted from the subsequent explosion in population size and density, the domestication of animals that served as sources of disease vectors, and the advent of sedentary populations. This dramatic transition to primary food production has been dubbed the "Neolithic revolution" and is marked by the appearance of social stratification, which exaggerated differential risk to disease within a population (Armelagos *et al.* 2002). The emergence of disease that marks the first epidemiological transition accelerates as agricultural land use intensifies and spreads to new regions.

The second epidemiological transition represents Omran's original disease transition. It is a period in which the development of medical practices, improved nutrition, and public health measures resulted in a decline in infectious disease. As the average age of the population increased with the reduced threat of infectious disease, the population began to experience a rise in age-related chronic disease. It is proposed that we are entering the third epidemiological transition, characterized by the reemergence of infectious diseases previously thought to be under control, many of which are now antibiotic resistant, in addition to the rapid emergence of a number of novel diseases (Barrett *et al.* 1998, Harper *et al.* 2010).

The cancers that are most likely to have caused the lesions seen in skeleton 42C are of infectious origin, rather than due to genetic causes or cellular mutations. Therefore they apply to the first epidemiological transition and are not representative of a mismatch between humans and our environment. However, the cancers that cause lytic lesions today are primarily related to aging and therefore more relevant to the second transition. This raises an interesting question about the timings of the transitions and whether ancient Egypt and Nubia were experiencing the first and second transitions at the same time. There is clear evidence of skeletal degeneration in ancient Egypt (Zaki *et al.* 2009) and while the ages of these individuals may not be as great as ages reached today, the examples clearly show advanced degeneration occurring, which would be more likely to align with the disease profile of the second epidemiological transition. However, the transition from the first to the second stage would not have occurred within a discrete time period, and thus individual 42C may represent the transitional nature of such an epidemiological shift where he is not specifically characteristic of either frame. Therefore there is an indication that the mismatch of the second epidemiologic transition was occurring in Nubia during the Meroitic Period. Clearly it is the extent of this mismatch that needs to be established. This is an area we feel deserves further work to amalgamate the existing research on degenerative diseases and their appearance in prehistory.

CONCLUSIONS

Skeleton 42C, excavated from a Meroitic Period burial in the Wadi Halfa region of Nubia shows evidence of osteolytic lesions that are attributable to metastatic cancer. The type of cancer cannot be definitively known from the remains available for analysis. However, careful description and comparison narrows the options, particularly with the inclusion of environmental and epidemiologic information that supports a differential diagnosis.

Strouhal's work focuses on gathering as much information as possible about the skeleton and its appearance. This is of great use to future investigators and provides an excellent basis for analysis of newly discovered analyzed remains. It was Strouhal's work that inspired further analysis of skeleton 42C. The brief description and analysis included here contributes to expanding documentation on the limited examples of metastatic cancer in prehistory. We hope that this paper provides an adequate merging of differential diagnosis and epidemiological theory. Further work is required to fit all the current skeletal evidence fully into a theoretical framework that encompasses epidemiological transition theory. Strouhal's work demonstrates that skeletal evidence provides a great deal of knowledge regarding prehistoric disease trends, and as scientific sampling and testing methods improve more may well be know about the exact causes of the lesions observed in these ancient skeletons.

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