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ARTICLE

New cases of probable skeletal tuberculosis from the Neolithic period in Hungary – A morphological study

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ABSTRACT The aim of this study is to present new data on the occurrence of tuberculosis (TB) in the Neolithic period of Hungary. The authors present results of the paleopathological investigation of skeletal remains from the Tisza culture tell settlement of Vésztő-Mágor, one of the largest Neolithic tells of the Great Hungarian Plain. The remains of 30 individuals were examined using standard macromorphological methods of bioarchaeology. Before the paleopathological examination of the series, sex and age at death of individuals and state of preservation of the observable skeletal elements were also recorded. In spite of the poor state of preservation, the osteoarchaeological series of Vésztő-Mágor showed a wide range of paleopathological alterations: skeletal traces of degenerative articular changes, traumas, haematological and infectious diseases were observed. This presentation focuses on 4 probable tuberculous cases. Most of the detected alterations (rib lesions, superficial vertebral changes/hypervascularisation and endocranial alterations) can be considered as atypical or early-stage TB lesions. Although a positive correlation seems to exist between these alterations and TB, they are not always pathognomonic to tuberculosis. These results contribute to improving our knowledge on the occurrence of TB in prehistoric populations of Hungary. **Acta Biol Szeged 56(2):115-123 (2012)**

KEY WORDS

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tuberculosis
atypical lesions

It is generally agreed that the global warming at the end of the last ice age around 10000 BC created conditions amenable to agriculture in certain parts of the world (Baker 2008). The wide scale transition, including the shift from a largely nomadic hunter-gatherer lifestyle to a more sedentary, agrarian way of living, with the inception of the domestication of various plant and animal species, has been termed the Neolithic Revolution by V. Gordon Childe (Childe 1936). This transition was ultimately necessary to the rise of modern civilization providing foundation for the subsequent development of increasingly complex societies (Weisdorf 2005). However the prehistoric shift from mobile foraging to sedentary farming generated both benefits and costs (Larsen 1995).

It is believed that the emergence of human infectious diseases is linked to population density. Hunter-gatherer populations are thought to have existed as small, nomadic groups of size and density precluding the existence of endemic pathogens. Following the Neolithic Revolution, a dramatic increase in population size and density occurred. (Armelagos et al. 1996; Donoghue 2009) The change to permanent settlements, associated with larger, denser populations, reduced population mobility, general deterioration of living conditions, inadequate sanitary practices and domestication of animals, provided conditions that may promote the spread of infectious diseases, such as tuberculosis (Larsen 1995; Barrett et al. 1998; Hershkovitz et al. 2008; Donoghue 2009).

It has been calculated that about one third of the world's current total population is infected with tubercule bacilli (latent infection). Severity of the situation in 1993 prompted the World Health Organization (WHO) to declare tuberculosis a global health threat. In 2010, approximately 8,5–9,2 million new cases of TB were diagnosed and an estimated 1,4 million people died of tuberculosis globally (Hutás 2007; WHO 2011). The high number of tuberculous cases brought new attention to the research of the disease and the causative agent (Pálfi et al. 2012).

TB is caused by a group of closely related bacteria (*M. tuberculosis*, *M. bovis*, *M. africanum*, *M. canettii*, *M. microti*, *M. caprae* and *M. pinnipedii*) of the Mycobacterium tuberculosis complex (MTBC), most often by *M. tuberculosis* and *M. bovis*. According to recent investigations (Cole et al. 1998; Brosch et al. 2002; Mostowy et al. 2002; Parsons et al. 2002; Gutierrez et al. 2005; Brisse et al. 2006), members of the MTBC all derived from a common ancestor (*M. prototuberculosis*), which may have co-evolved with mankind since at least the time of early hominids between 2–3 million years ago, so tuberculosis is one of the oldest known infectious diseases. In spite of their 99% similarity at the nucleotide level, the causative organisms of TB have distinctive epidemiological and clinical characteristics such as pathogenicity, virulence, host preference or geographic distribution. *M. tuberculosis* is

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the most widespread aetiological agent of human tuberculosis currently, spreading via droplets released from the lungs of an infected person. In certain parts of the world, especially in developing countries, *M. bovis*, the causative organism of tuberculosis in cattle and other mammals can cause human intestinal tuberculous infections trough the consumption of contaminated milk, dairy products and meat (Brosch et al. 2002; Donoghue 2008, 2009).

The manifestation of TB depends on several factors, such as the infecting organism, site of involvement, infected individual's age, condition of the immune system and the acute or chronic nature of illness (Bloom 1994; Aufderheide and Rodríguez-Martín 1998; Madkour 2004). Pulmonary TB is the most common form of the disease: the pathogen first infects the lungs and the lymph system generating the so-called primary complex. In a minority of cases (approximately 15-20%) the bacteria spread from the initial site of infection to other compartments of the human body, including the skeletal system, via lymphogenous and haematogenous dissemination, resulting in extra-pulmonary TB (Ortner 2003; Donoghue 2008, 2009). Data indicate that about 3–5% of patients with chronic tuberculosis suffer from osseous involvement (Ortner 2003; Donoghue et al. 2004; Nicklisch et al. 2012).

TB may cause characteristic morphological alterations in bones (Steinbock 1976; Ortner 2003). Macromorphological diagnosis of skeletal tuberculosis in human remains is based upon the detection of secondary skeletal lesions (Pálfi et al. 2012). The most common representation of skeletal tuberculosis is spondylitis tuberculosa (Pott's disease), which affects the vertebral column resulting in cavitation in the vertebral bodies, particularly in the thoracic and lumbar regions. The process may destroy the entire vertebral body and cause ankylosis (fusion of the adjacent bodies) of several vertebrae as well as kyphosis (Pott's gibbus) of the spine or rarely cold abscess on the ventral surface of the vertebrae. Involvement of the vertebral column appears in 25–60% of skeletal TB cases (Maczel 2003). After vertebral involvement, the second most frequent skeletal lesion in tuberculosis is arthritis of the large, weight-bearing joints, particularly the hip joint (coxitis tuberculosa). Other joints can also be affected with the erosion of the articular surface, possibly followed by subluxation and bony ankylosis (Maczel 2003; Ortner 2003; Kiss and Boda 2007; Kósa and Madách 2007).

The diagnostics of TB in osteoarchaeological samples earlier only focused on the formerly mentioned classical TB lesions, already representing a more or less developed stage of tuberculosis. However, TB may have affected many individuals without classical pathological alterations, and the patients died in an earlier stage of tuberculosis long before these symptoms could have developed. Thus, early-stage TB is not recognizable on the basis of classical TB changes. If we only consider the lesions mentioned above, we may significantly underestimate the prevalance of tuberculosis in the examined historical populations. Because of the problematic nature of TB diagnostics, the importance of establishing diagnostic criteria for early-stage TB has been recognized in the last few years of the 20th century (Maczel 2003; Dutour 2008; Pálfi et al. 2012). Since then a number of researches – mainly based on the study of skeletal collections with known causes of death – have been focusing on searching for atypical or early-stage lesions in connection with tuberculous infection. As a result of these investigations three types of atypical or early-stage TB alterations gained more attention: rib lesions, superficial vertebral changes/hypervascularisation and endocranial alterations. Molecular (ancient DNA and lipid biomarker) analyses also confirmed the diagnostic value of these lesions in a significant number of paleopathological cases (e.g. Haas et al. 2000; Maczel 2003; Raff et al. 2006; Zink et al. 2007; Hershkovitz et al. 2008; Neparáczki et al. 2011).

According to recent studies (Kelley and Micozzi 1984; Roberts et al. 1994; Santos and Roberts 2001, 2006; Maczel 2003; Matos and Santos 2006; Pálfi et al. 2012) based on examination of modern skeletal collections with recorded cause of death, sharply circumscribed lytic lesions and/or diffuse periostitis on the visceral surface of ribs are possible results of a pulmonary infection, and very frequently of TB. Circumferential, irregular pitting and holes especially on the anterior and lateral surface of vertebral bodies also have been described by Ménard (1888) and Baker (1999) in connection with early-stage TB. Small granular impressions or abnormal blood vessel impressions with branched or reticulated appearance as well as plates of newly formed bone in the internal surface of the cranial vault were attributed to tuberculous meningitis in a large number of cases (Schultz 1999, 2001; Hershkovitz et al. 2002; Maczel 2003; Pálfi et al. 2012).

Based on the literature, these two groups of TB related skeletal lesions have diagnostical value: classical TB alterations (TB spondylitis/Pott's disease and TB arthritis of the great joints) (Steinbock 1976; Pálfi et al. 1999; Ortner 2003) and atypical or early-stage TB lesions (rib lesions, superficial vertebral changes/hypervascularisation, endocranial alterations, diffuse periosteal new bone formation) (Ménard 1888; Kelley and Micozzi 1984; Roberts et al. 1994; Baker 1999; Schultz 1999, 2001; Santos and Roberts 2001, 2006; Hershkovitz et al. 2002; Pálfi 2002; Maczel 2003; Matos and Santos 2006; Dutour 2008).

The aim of this paper is to present the results of the paleopathological investigation of TB in the Neolithic (Tisza culture) tell settlement of Vésztő-Mágor in order to improve our knowledge on the occurrence of classical and atypical TB manifestations and the prevalence of TB in prehistoric populations of Hungary.

Materials and Methods

The skeletal material for this study derives from the ar-

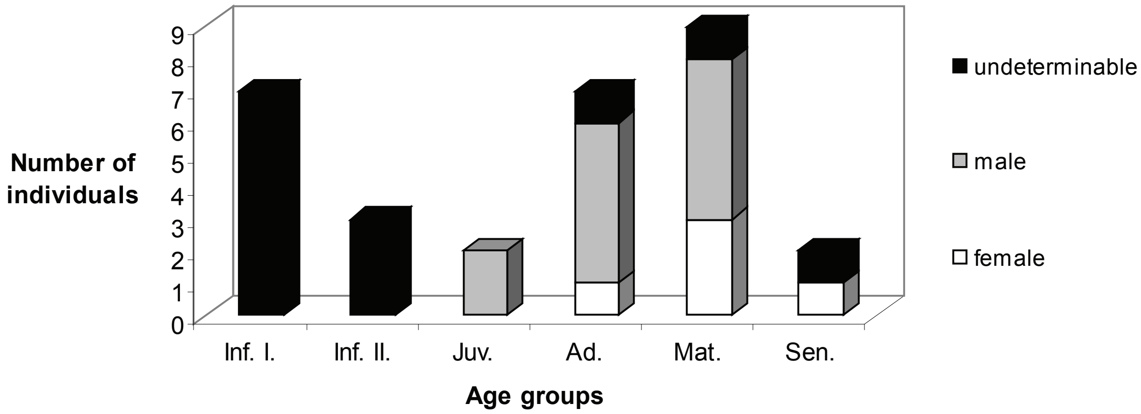

Figure 1. Demographic profile of the examined skeletal series.

chaeological site Vésztő-Mágor, unearthed on the Mágor Hill arising west of the village of Vésztő (a small town in South-Eastern Hungary), on the left side of the oxbow Holt Sebes Körös. Mágor Hill is one of the largest tells of the Great Hungarian Plain first inhabited in the Neolithic period. The hill developed as a consequence of people living a settled life here for thousands of years with shorter or longer interruptions.

The long-running excavation was carried out under the direction of Katalin Hegedűs (1972–1976). The cultural layer is over 700 cm deep divided into nine building layers and was formed of the debris and household waste of the houses rebuilt from time to time (Makkay 2004). Forty nine burials were also unearthed in the site: 1 from the Szakálháti culture (late 6th millennium BC), 30 from the Tisza (ca. 4900–4500 BC) and 18 from the Tiszapolgári cultures (ca. 4400–4000 BC) (MRE, 2003). In Hungary, Neolithic graves containing coffins were first found in Vésztő-Mágor. The dead were buried lying on their left or right side and were painted with reddish ochre, than wrapped in mat and so put into the coffin (Makkay 2004; Siklósi 2010).

The skeletal remains of 30 individuals from the Szakálháti and Tisza cultures, which are housed in the collection of the Department of Biological Anthropology, University of Szeged, Hungary, served as a source of material for this study.

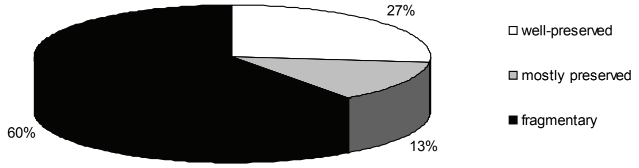

Figure 2. State of preservation of the examined skeletons.

Before the paleopathological examination of the series, sex and age at death of individuals were determined based on standard macromorphological methods (Schour and Massler 1941; Éry et al. 1963; Acsádi and Nemeskéri 1970; Vlček 1974; Stloukal and Hanâkovâ 1978; Brothwell 1981; Ubelaker 1984; Loth and Isçan 1989). State of preservation of the observable skeletal elements was recorded in three stages (well-preserved, mostly preserved and fragmentary). The paleopathological investigation was carried out using macromorphological methods (Steinbock 1976; Pálfi et al. 1999; Ortner 2003) with focus on the previously detailed classical and atypical TB alterations (Ménard 1888; Kelley and Micozzi 1984; Roberts et al. 1994; Baker 1999; Schultz 1999, 2001; Santos and Roberts 2001, 2006; Hershkovitz et al. 2002; Pálfi 2002; Maczel 2003; Matos and Santos 2006; Dutour 2008).

Results and Discussion

Sex and age at death distribution of the examined skeletal series was determined as follows: 12 males, 5 females, 10 infants and 3 undeterminable adults (Fig. 1).

The state of bone preservation is quite bad: 60% of the examined skeletons are fragmentary (Fig. 2).

In spite of the poor state of preservation, the osteoarchaeological series of Vésztő-Mágor shows a wide range of pathological alterations including skeletal traces of degenerative articular changes, traumas, haematological and infectious diseases. This study presents those four cases of the sample that are suspected to present lesions of tuberculous origin.

The skeleton of a 10–12 year old infant (Grave no. 5) was extremely incomplete and fragmentary: only some fragments of the cranium and a few teeth were unearthed. In spite of poor preservation, pathological changes could be clearly identified in the endocranial lamina. Short, serpented abnormal blood vessel impressions surrounded by thin layers of newly formed bone were detected on the endocranial surface

Figure 3. Abnormal blood vessel impressions surrounded by thin layers of newly formed bone on the endocranial surface of the frontal bone (Grave no. 5).

Figure 4. Cribrotic cribra orbitalia of the right orbit (Grave no. 5).

of the frontal bone, most pronounced on the left side, along the sutura coronalis (Fig. 3). Moreover, the internal surface of the parietal bones showed small abnormal blood vessel impressions. The skeleton also exhibited stress indicators: traces of slight periosteal new bone formation on the anterior and posterior aspect of mandible and cribrotic cribra orbitalia of the right orbit (Fig. 4) accompanied the alterations mentioned above.

The endocranial changes observed may refer to increased intracranial pressure possibly due to meningeal reactions induced by intrathoracic infection, particularly TB (Schultz

Figure 5. Signs of widespread periostitis in the right femur (Grave no. 6).

Figure 6. Periosteal new bone formations on the diaphysis of the left tibia (Grave no. 6).

1999, 2001; Hershkovitz et al. 2002). Positive correlation between tuberculosis and stress indicators were also recognized in some studies (Stuart-Macadam 1989; Santos and Roberts 2001; Pálfi 2002; Maczel 2003). Morphology of the detected lesions and their co-occurrence with stress indicators (mandible periostitis, cribra orbitalia) suggest the diagnosis of early-stage TB.

The fragmentary skeletal remains of a mature (50–60 yrs) female (Grave no. 6) revealed severe pathological lesions. The macroscopic features of the upper and lower limb bones included diffuse symmetrical periosteal changes: both femora, tibiae and fibulae showed signs of widespread periostitis along the shaft (Fig. 5 and 6) and the distal radii (Fig. 7) were also affected. Furthermore, traces of pit-like lesions were observed on both ends of the right clavicle (Fig. 8 and 9): at the sternal end a 6x7x8 mm, while at the acromial end a 7x8x6 mm spherical, smooth-walled cystic lesion appeared. In spite of remarkable post mortem damage, the ventral surface of the

Figure 7. Osteo-periostitis on the distal part of the right radius (Grave no. 6).

Figure 8. Cystic lesion on the sternal end of the right clavicle (Grave no. 6).

Figure 9. Pit-like lesion on the acromial end of the right clavicle (Grave no. 6).

Figure 10. Traces of probable cold abscess on the ventral surface of the sacrum (Grave no. 6).

sacrum showed a circular, 17x16 mm lytic lesion accompanied by remodelled, reactive new bone formation (Fig. 10) probably in response to an overlying cold abscess.

Long bone periostitis can be associated with several pathological conditions. However, symmetrical diffuse periosteal new bone formation observed in the limb bones appears to be a general skeletal response to intrathoracic disease, most often tuberculosis (Kelly et al. 1991; Barthurst and Barta 2004; Masson et al. 2012; Sahin et al. 2012). The cystic lesions of the right clavicle may be explained by several aetiological reasons, but their shape, size and the suspicion of TB-related changes in other skeletal elements of the mature female imply tuberculous ostitis. In this case, the lesions suggest the diagnosis of multifocal skeletal tuberculosis.

The skeleton Grave no. 13. belonged to an approximately 30–40 year old male individual. Preservation of the postcranial elements was fairly good, the skull was almost intact. In the vertebral column, signs of hypervascularisation were revealed in the form of multiple, smooth-walled resorptive pits on the anterior and lateral surfaces of the lower thoracic vertebral bodies (from T8 to T11) (Fig. 11 and 12). These lesions sometimes appeared interconnected with wide, horizontal superficial vascular channels. In this skeleton, extra-vertebral pathological changes were also observed. Both tibiae presented evident signs of periostitis: the surface of the cortex was pitted and longitudinally striated (Fig. 13) along the shaft. In spite of the poor state of preservation, very subtle periosteal appositions were noted on the visceral surface of two rib fragments. The alterations appeared near the angulus costae.

Pattern of the superficial vertebral lesions on the anterior and lateral surface of the thoracic vertebrae resembles the

Figure 11. Resorptive lesions on the anterior aspect of the thoracic vertebrae (Grave no. 13).

Figure 12. Signs of hypervascularisation on the lateral aspect of the thoracic vertebral bodies (Grave no. 13).

Figure 13. Pitted and longitudinally striated surface of the left tibial cortex (Grave no. 13).

cases described by Ménard (1888) and Baker (1999), who attributed these alterations to early-stage TB. Previous studies (Kelley and Micozzi 1984; Roberts et al. 1994; Santos and Roberts 2001, 2006; Maczel 2003; Matos and Santos 2006) of osteological collections with recorded cause of death pointed out that periosteal appositions on the visceral surface of ribs are usually indicative of pulmonary infection, and very frequently tuberculosis. In this case the periosteal changes observed in the tibiae also suggest an infectious origin: they might have been induced by TB. The simultaneous occurrence of these lesions suggests the diagnosis of early-stage tuberculosis.

The fairly well-preserved skeleton of an approximately 16–18 year old juvenile male (Grave no. 33.) also showed serious pathological alterations in the vertebral column. Similarly to the previous case, the most significant feature of the remains was the circumferential pitting recognized on the anterior and lateral surface of the thoracic and lumbar vertebral bodies (Fig. 14 and 15). The lesions were sometimes connected with wide, worm-like, horizontal vascular channels. Concerning stress indicators, the examination of the extravertebral bones revealed traces of slight bilateral periosteal reaction in the femora and tibiae. Moreover, in the fragmentary orbits porotic cribra orbitalia was detected.

Hypervascularisation of the thoracic and lumbar vertebral bodies is a suspected sign of early-stage TB based on the studies of Ménard (1888) and Baker (1999). The co-occurrence of the presented superficial vertebral changes with stress indicators (long bone periostitis, cribra orbitalia) suggests the diagnosis of early-stage TB.

Figure 14. Abnormal vascularisation on the anterior surface of the thoracic vertebrae (Grave no. 33).

Figure 15. Hypervascularisation on the lateral surface of the thoracic vertebral bodies (Grave no. 33).

Conclusions

During the paleopathological investigation of the osteoarchaeological series of Vésztő-Mágor, four probable tuberculous cases were found. Most of the detected alterations (rib lesions, superficial vertebral changes/hypervascularisation, endocranial alterations and diffuse symmetrical long bone periostitis) can be considered as atypical or early-stage TB lesions (Roberts et al. 1994; Pálfi 2002). Although there seems to be positive correlation between these alterations and TB, they are not always specific for tuberculosis. Other pathological conditions might also cause similar changes. However, the simultaneous occurrence of several of these conditions – as it was observed in majority of our cases – can increase the probability of the diagnosis of early-stage skeletal TB (Maczel 2003). In order to confirm the supposed diagnosis, further investigations (e.g. DNA and lipid biomarker analyses) are planned.

The paleopathological importance of these cases resides in their prehistoric origin. Neolithic skeletal evidence of TB is relatively rare (e.g. Sager et al. 1972; Dastugue and de Lumley 1976; Formicola et al. 1987; Canci et al. 1996; Bennike 1999; Gladykowska-Rzeczycka 1999; Nuorala et al. 2004; Nicklisch et al. 2012), therefore they deserve remarkable attention in the paleopathological literature. As for Hungary, a probable case of Pott's disease was found by Köhler et al. (2012) in a Late Neolithic (dated to the 5. millenium BC) series of Alsónyék-Bátaszék. Furthermore, five individuals show signs of skeletal TB, with rather atypical symptoms from the Late Neolithic Tisza culture (blooming between 4970-4594 BC) tell settlement of Hódmezővásárhely-Gorzsa. The initial macroscopic investigation of these cases had been confirmed by lipid biomarker analysis and three of them cross-validated by DNA analysis (Masson et al. 2012). Our results contribute to improving the knowledge on the occurrence of TB in Neolithic populations of Hungary.

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References

Acsádi Gy, Nemeskéri J (1970) History of human life span and mortality. Akadémiai Kiadó, Budapest.

Armelagos GJ, Barnes KC, Lin J (1996) Disease in human evolution: the reemergence of infectious disease in the third epidemiological transition. National Museum of Natural History Bulletin for Teachers 18(3):1-7.

Aufderheide AC, Rodríguez-Martín C (1998) The Cambridge encyclopedia of human paleopathology. Cambridge University Press, Cambridge.

Baker BJ (1999) Early manifestations of tuberculosis in the skeleton. In Pálfi Gy, Dutour O, Deák J, Hutás I, eds., Tuberculosis: past and pres-

ent. TB Foundation, Szeged & Golden Book Publisher, Budapest, pp. 301-307.
Baker MJ (2008) A structural model of the transition to agriculture. Journal of Economic Growth 13(4):257-292.
Barrett R, Kuzawa CW, McDade T, Armelagos GJ (1998) Emerging and re-emerging infectious diseases: the third epidemiologic transition. Annu Rev Anthropol 27:247-271.
Bathurst RR, Barta JL (2004) Molecular evidence of tuberculosis induced hypertrophic osteopathy in a 16th-century Iroquoian dog. Journal of Archaeological Science 31:917-925.
Bennike P (1999) Facts or myth? A re-evaluation of cases of diagnosed tuberculosis in Denmark. In Pálfi Gy, Dutour O, Deák J, Hutás I, eds., Tuberculosis: past and present. TB Foundation, Szeged & Golden Book Publisher, Budapest, 511-518.
Bloom BR, ed. (1994) Tuberculosis: pathogenesis, protection and control. American Society for Microbiology Press, Washington DC.
Brisse S, Supply P, Brosch R, Vincent V, Gutierrez MC (2006) „A re-evaluation of M. prototuberculosis": continuing the debate. PLoS Pathogens 2(9):e95.doi:10.1371/journal.ppat.0020095.
Brosch R, Gordon SV, Marmiesse M, Brodin P, Buchrieser C, Eiglmeier K, Garnier T, Gutierrez MC, Hewinson G, Kremer K, Parsons LM, Pym AS, Samper S, Soolingen van D, Cole ST (2002) A new evolutionary scenario for the Mycobacterium tuberculosis complex. Proc Natl Acad Sci U S A 99(6):3684-3689.
Brothwell DR (1981) Digging up bones: the excavation, treatment and study of human skeletal remains. British Museum, London.
Canci A, Minozzi S, Borgognini Tarli SM (1996) New evidence of tuberculous spondylitis from Neolithic Liguria (Italy). Int J Osteoarchaeol 6:497-501.
Childe VG (1936) Man makes himself. Watts & Co., London.
Cole ST, Brosch R, Parkhill J, Garnier T, Churcher C, Harris D, Gordon SV, Eiglmeier K, Gas S, Barry III CE, Tekaia F, Badcock K, Basham D, Brown D, Chillingworth T, Connor R, Davies R, Devlin K, Feltwell T, Gentles S, Hamlin N, Holroyd S, Hornsby T, Jagels K, Krogh A, McLean J, Moule S, Murphy L, Oliver K, Osborne J, Quail MA, Rajandream M-A, Rogers J, Rutter S, Seeger K, Skelton J, Squares R, Squares S, Sulston JE, Taylor K, Whitehead S, Barrel BG (1998) Deciphering the biology of Mycobacterium tuberculosis from the complete genome sequence. Nature 393:537-544.
Dastugue J, de Lumley MA (1976) Les maladies des hommes préhistoriques. In Guilaine J, ed., La préhistoire française: Tome II, Les civilisations néolithiques et protohistoriques de la France. Éditions du Centre National de la Recherche Scientifique, Párizs, pp. 153-164.
Donoghue HD, Spigelman M, Greenblatt CL, Lev-Maor G, Bar-Gal GK, Matheson C, Vernon K, Nerlich AG, Zink AR (2004) Tuberculosis: from prehistory to Robert Koch, as revealed by ancient DNA. Lancet Infect Dis 4(9):584-592.
Donoghue HD (2008) Palaeomicrobiology of tuberculosis. In Raoult D, Drancourt M, eds., Paleomicrobiology: past human infections. Springer–Verlag GmbH, Berlin, Heidelberg, pp. 75-97.
Donoghue HD (2009) Human tuberculosis – an ancient disease, as elucidated by ancient microbial biomolecules. Microbes Infect 11(14-15):1156-1162.
Dutour O (2008) Archaeology of human pathogens: palaeopathological appraisal of palaeoepidemiology. In Raoult D, Drancourt M, eds. Paleomicrobiology: past human infections. Springer–Verlag GmbH, Berlin, Heidelberg, pp. 125-144.
Éry K, Kralovánszky A, Nemeskéri J (1963) Történeti népességek rekonstrukciójának reprezentációja. Anthropologiai Közlemények 7:41-90.
Formicola V, Milanesi Q, Scarsini C (1987) Evidence of spinal tuberculosis at the beginning of the fourth millennium BC from Arene Candide Cave (Liguria, Italy). Am J Phys Anthropol 72(1):1-6.
Gladykowska-Rzeczycka JJ (1999) Tuberculosis in the past and present in Poland. In Pálfi Gy, Dutour O, Deák J, Hutás I, eds., Tuberculosis: past and present. TB Foundation, Szeged & Golden Book Publisher, Budapest, pp. 561-573.
Gutierrez MC, Brisse S, Brosch R, Fabre M, Omaïs B, Marmiesse M, Supply P, Vincent V (2005) Ancient origin and gene mosaicism of the progenitor of Mycobacterium tuberculosis. PLoS Pathogens 1(1):e5.doi:10.1371/journal.ppat.0010005.
Haas CJ, Zink AR, Molnár E, Szeimies U, Reischl U, Marcsik A, Ardagna Y, Dutour O, Pálfi Gy, Nerlich AG (2000) Molecular evidence for different stages of tuberculosis in ancient bone samples from Hungary. Am J Phys Anthropol 113(3):293-304.
Hershkovitz I, Greenwald CM, Latimer B, Jellema LM, Wish-Baratz S, Eshed V, Dutour O, Rotschild BM (2002) Serpens Endocrania Symmetrica (SES): a new term and a possible clue for identifying intrathoracic disease in skeletal populations. Am J Phys Anthropol 118:201-216.
Hershkovitz I, Donoghue HD, Minnikin DE, Besra GS, Lee OY-C, Gernaey AM, Galili E, Eshed V, Greenblatt CL, Lemma E, Bar-Gal GK, Spigelman M (2008) Detection and molecular characterization of 9000-year-old Mycobacterium tuberculosis from a Neolithic settlement in the Eastern Mediterranean. PLoS ONE 3(10):e3426.doi:10.1371/journal.pone.0003426.
Hutás I (2007) A tuberkulózis járványtana. In Magyar P, Somoskövi Á, eds., Pulmonális és extrapulmonális tuberkulózis. Medicina Könyvkiadó, Budapest, pp. 33-46.
Kelley MA, Micozzi MS (1984) Rib lesions in chronic pulmonary tuberculosis. Am J Phys Anthropol 65:381-386.
Kelly P, Manning P, Corcoran P, Clancy L (1991) Hypertrophic osteoarthropathy in association with pulmonary tuberculosis. Chest 99(3):769-770.
Kiss A, Boda A (2007) Csontízületi tuberkulózis. In Magyar P, Somoskövi Á, eds., Pulmonális és extrapulmonális tuberkulózis. Medicina Könyvkiadó, Budapest, pp. 165-186.
Kósa L, Madách Á (2007) Tuberkulózis gyermekkorban. In Magyar P, Somoskövi Á, eds., Pulmonális és extrapulmonális tuberkulózis. Medicina Könyvkiadó, Budapest, pp. 135-145.
Köhler K, Pálfi Gy, Molnár E, Zalai-Gaál I, Osztás A, Bánffy E, Kirinó K, Kiss KK, Mende BG (2012) A late Neolithic case of Pott's disease from Hungary. Int JOsteoarchaeol doi:10.1002/oa.2254.
Larsen CS (1995) Biological changes in human populations with agriculture. Annu Rev Anthropol 24:185-213.
Loth SR, Isçan MY (1989) Morphological assessment of age in the adult: the thoracic region and determination of sex from the sternal rib. In Isçan MY, ed. Age markers in the human skeleton. Charles C. Thomas Publisher, Springfield, Illinois, pp. 105-135.
Maczel M (2003) „On the traces of tuberculosis" Diagnostic criteria of tuberculosis affection of the human skeleton and their application in Hungarian and French anthropological series. Ph.D. Thesis, University of La Méditerranée – Aix Marseille II Faculty of Medicine, Marseille, University of Szeged, Faculty of Science, Szeged.
Madkour MM, ed. (2004) Tuberculosis. Springer, Birkhäuser.
Makkay J (2004) Vésztő-Mágor. Ásatás a szülőföldön. Békés Megyei Múzeumok Igazgatósága, Békéscsaba.
Masson M, Molnár E, Donoghue HD, Minnikin D, Lee OY, Pálfi Gy (2012) 7000-year-old tuberculosis cases from Hungary osteological and biomolecular evidence. ICEPT-2 The Past and Present of tuberculosis: a multidisciplinary overview on the origin and evolution of TB. Program and Abstract of the 2012 TB Evolution Meeting, University of Szeged, Szeged, p. 54.
Matos V, Santos AL (2006) On the trail of pulmonary tuberculosis based on rib lesions: results from the human identified skeletal collection from the Museu Bocage (Lisbon, Portugal). Am J Phys Anthropol 130:190-200.
Ménard V (1888) Tuberculose vertébrale. Asselin et Houzeau, Párizs.
Mostowy S, Cousins D, Brinkman J, Aranaz A, Behr MA (2002) Genomic deletions suggest a phylogeny for Mycobacterium tuberculosis complex. The Journal of Infectious Diseases 186:74-80.
MRE (2003) Visy Zs, Nagy M, B Kiss Zs (eds.) Hungarian Archeology at the turn of the Millennium. Ministry of National Cultural Heritage, Budapest.
Neparáczki E, Török T, Pósa A, Molnár E, Lovász G, Maixner F, Zink AR, Dutour O, Pálfi Gy (2011) Preliminary resultes from the paleomicrobiological studies of Mycobacterium tuberculosis infection in the Bác-

salmás-Óalmás anthropological series. Acta Biol Szeged55(1):41-45.
Nicklisch N, Maixner F, Ganslmeier R, Friederich S, Dresely V, Meller H, Zink AR, Alt KW (2012) Rib lesions in skeletons from early Neolithic sites in central Germany: on the trail of tuberculosis at the onset of agriculture. Am J Phys Anthropol 149:391-404.
Nuorala E, Götherström A, Ahlström T, Donoghue HD, Spigelman M, Lidén K (2004) MTB complex DNA in a Scandinavian Neolithic passage grave. In: Thesis and Papers in Scientific Archaeology 6., Paper I, Molecular Palaeopathology. Ancient DNA analysis of the bacterial diseases tuberculosis and leprosy. Archaeological Research Laboratory, Stockholm University, Stockholm.
Ortner DJ (2003) Identification of paleopathological conditions in human skeletal remains. Academic Press, San Diego.
Pálfi Gy, Dutour O, Deák J, Hutás I, eds. (1999) Tuberculosis: past and present. TB Foundation, Szeged & Golden Book Publisher, Budapest.
Pálfi Gy (2002) Paleoepidemiological reconstruction of tuberculosis with particular attention to Europe. In Bennike P, Bodzsár E, Susanne C, eds. Biennial Books of EAA 2:193-210.
Pálfi Gy, Bereczki Zs, Ortner DJ, Dutour O (2012) Juvenile cases of skeletal tuberculosis from the Terry Anatomical Collection (Smithsonian Institution, Washington, D.C., USA). Acta Biol Szeged 56(1):1-12.
Parsons LM, Brosch R, Cole ST, Somoskövi Á, Loder A, Bretzel G, Soolingen van D, Hale YM, Salfinger M (2002) Rapid and simple approach for identification of Mycobacterium tuberculosis complex isolates by PCR-based genomic deletion analysis. J Clin Microbiol 40(7):2339-2345.
Raff J, Cook DC, Kaestle F (2006) Tuberculosis in the New World: a study of ribs from the Schild Mississippian population, West-Central Illinois. Memórias do Instituto Oswaldo Cruz, Rio de Janeiro 101(Suppl. II.):25-27.
Roberts CA, Lucy D, Manchester K (1994) Inflammatory lesions of ribs: an analysis of the Terry Collection. Am J Phys Anthropol 95(2):169-182.
Sager PL, Schalimtzek M, Möller-Christensen V (1972) A case of spondylitis tuberculosa in the Danish Neolithic age. Danish Medical Bulletin 19:176-180.
Sahin A, Pepeler MS, Ergene E, Kucuksahin O, Sahin M (2012) Is hypertrophic osteoarthropathy associated with smoking? 2:145.doi:10.4172/2165-7920.1000145.
Santos AL, Roberts CA (2001) A picture of tuberculosis in young Portuguese people in the early 20th century: a multidisciplinary study of the skeletal and historical evidence. Am J Phys Anthropol 115(1):38-49.
Santos AL, Roberts CA (2006) Anatomy of a serial killer: differential diagnosis of tuberculosis based on rib lesions of adult individuals from the Coimbra Identified Skeletal Collection, Portugal. Am J Phys Anthropol 130(1):38-49.
Schultz M (1999) The role of tuberculosis in infancy and childhood in prehistoric and historic populations. In Pálfi Gy, Dutour O, Deák J, Hutás I, eds., Tuberculosis: past and present. TB Foundation, Szeged & Golden Book Publisher, Budapest, pp. 503-507.
Schultz M (2001) Paleohistopathology of bone: a new approach to the study of ancient diseases. Yearbook of Physical Anthropology 44:106-147.
Schour I, Massler M (1941) The development of the human dentition. The Journal of the American Dental Association 28:1153-1160.
Siklósi Zs (2010) A társadalmi egyenlőtlenség nyomai a késő neolitikumban a Kárpát-medence keleti felén. Doktori disszertáció, Eötvös Loránd Tudományegyetem, Bölcsészettudományi Kar, Budapest.
Steinbock RT (1976) Paleopathological diagnosis and interpretation: bone disease in ancient human populations. Charles C. Thomas Publisher, Springfield, Illinois.
Stloukal M, Hanâkovâ H (1978) Die Länge der Längsknochen altslawischer Bevölkerungen unter besonderer Berücksichtigung von Wachstumsfragen. HOMO - Journal of Comparative Human Biology 29(1):53-69.
Stuart-Macadam PL (1989) Nutritional deficiency diseases: a survey of scurvy, rickets and iron deficiency anemia. In Isçan MY, Kennedy KAR, eds., Reconstruction of life from the skeleton. Alan R. Liss Publisher, New York, pp. 201-222.
Ubelaker DH (1989) Human skeletal remains: excavation, analysis, interpretation. Taraxacum, Washington, 2nd edition.
Vlček E (1974) Anwendung von Zwei Methoden der forensischen Medizin zur Altersbestimmung in der Paläoanthropologie. Anthropologiai Közlemények 18:199-209.
Weisdorf JL (2005) From foraging to farming: explaining the Neolithic Revolution. Journal of Economic Surveys 19(4):561-586.
World Health Organization (2011) Global tuberculosis controll: surveillance, planning, financing. WHO Report, Geneva.
Zink AR, Molnár E, Motamedi N, Pálfi Gy, Marcsik A, Nerlich AG (2007) Molecular history of tuberculosis from ancient mummies and skeletons. Int J Osteoarchaeol 17:380-391.