# PhD THESIS

# EVALUATION OF ENDOCRANIAL BONY CHANGES IN RELATION TO TUBERCULOSIS IN THE ROBERT J. TERRY ANATOMICAL SKELETAL COLLECTION (WASHINGTON, DC, USA)

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SZEGED 2018

#### INTRODUCTION

Tuberculosis (TB) is one of the oldest known infectious diseases that has been plaguing humans and animals for thousands of years. It is caused by a number of pathogenic mycobacterial species belonging to the *Mycobacterium tuberculosis* complex (MTBC) that usually spread by airborne transmission. Thus, tuberculosis primarily affects the lungs (*i.e.*, pulmonary TB); however, the haematogenous or lymphogenous dissemination of TB bacteria from the respiratory tract into other parts of the body, including the central nervous system (CNS) or the skeleton, results in the development of different types of extra-pulmonary tuberculosis, such as tuberculous meningitis (TBM) and osteoarticular TB.

In 1993, tuberculosis has been declared a global health threat by the World Health Organization (WHO). Despite significant advances in the global fight against TB in the last few decades, it still presents a health emergency, especially in developing countries. According to estimates of the WHO, in 2016, there were approximately 10.4 million new incident cases of active TB disease globally, and tuberculosis remained one of the top 10 causes of death and the leading cause of death from a single infectious agent, with accounting for about 1.7 million deaths worldwide. Therefore, a renewed interest and funding to the research of the disease and of its aetiological agents (*e.g.*, science projects concerning the origin and evolutionary history of the MTBC or the palaeopathological diagnostics for TB) has sparked since the late 20<sup>th</sup> century in order to eliminate or at least control TB in the future. The palaeopathological research of tuberculosis, essentially based upon the macromorphological diagnosis of the disease in ancient human bone remains, may provide invaluable data on the different manifestations of TB and on the effects of the disease upon human mortality and morbidity around the world throughout prehistoric and historic times.

Using modern medical knowledge, palaeopathologists attempt to establish a retrospective diagnosis of prehistoric and historic cases with tuberculosis by macroscopically identifying pathological conditions (*e.g.*, bony lesions suggestive of osteoarticular TB, such as signs of spinal TB or TB arthritis of the large, weight-bearing joints) in skeletons of people lived in the past that may be related to different forms of the disease. However, utilisation of modern diagnostic criteria for tuberculosis in the palaeopathological practice may not be appropriate, since on the one hand, probable TB-related bony changes observed in recent cases may differ from those of detectable in ancient human bone remains, due in part to the introduction of antibiotics in the treatment of tuberculosis. On the other hand, in modern clinical TB cases, bony changes cannot be surveyed with macromorphological methods but with medical imaging techniques (*e.g.*, X-ray radiography, computed tomography, and magnetic resonance imaging)

only; nevertheless, subtle bony alterations may be impossible to be visualised by the latter ones. Therefore, they are not relevant to the diagnosis of tuberculosis in recent cases and are not described as diagnostic criteria for the disease by physicians in the modern medical literature, even if they can be potentially important elements of TB identification for palaeopathologists. Furthermore, the assessment of TB prevalence in past human populations has traditionally relied upon the palaeopathological diagnosis of spinal TB and/or TB arthritis of the large, weight-bearing joints only. Since osteoarticular TB occurs in less than 2% of all patients with active tuberculosis and according to estimates, accounted for approximately 3 to 5% of all TB cases in prehistoric and historic times, it is difficult to assess the true prevalence of the disease in human osteoarchaeological series from the pre-antibiotic era based only on the abovementioned diagnostic criteria.

In order to contribute to facilitating the establishment of a more reliable and accurate palaeopathological diagnosis of TB and the assessment of a more relevant disease prevalence in past human populations, a number of palaeopathological and palaeomicrobiological studies were performed on human osteoarchaeological material and documented skeletal collections since the late 20<sup>th</sup> century that have revealed a positive correlation between different types of tuberculosis (*e.g.*, skeletal TB, pulmonary TB and/or TB pleurisy, and tuberculous meningitis (TBM)) and subtle bony alterations, including non-endocranial lesions (*e.g.*, vertebral hypervascularisation and periosteal new bone formation on the visceral surface of ribs) and endocranial alterations (*i.e.*, abnormally pronounced digital impressions (APDIs), periosteal appositions (PAs), abnormal blood vessel impressions (ABVIs), and granular impressions (GIs)). However, the diagnostic value of the different endocranial alteration types possibly associated with TBM has more recently been questioned, as their precise aetiology is still a matter of controversy, and additionally, similar or even the same morphological features can be found in non-TB-related cases, such as in non-specific inflammatory (*e.g.*, bacterial meningitis) and haemorrhagic (*e.g.*, epidural haematoma) processes.

Nevertheless, detailed analysis of well-documented collections of pre-antibiotic era skeletons of known cause of death (e.g., Hamann–Todd Human Osteological Collection, Robert J. Terry Anatomical Skeletal Collection, and Coimbra Identified Skeletal Collection) can serve as a unique and important basis for determining the appropriate palaeopathological diagnostic criteria for TB in past human populations, since bone remains of specimens identified to have died of tuberculosis and not treated with antibiotics may exhibit similar TB-related bony changes to those of observable in skeletons of people lived in the past; in contrast to recent cases with tuberculosis, they can be surveyed not only with medical imaging techniques but

also directly with macromorphological methods; and even subtle bony changes can be recognised in them. Since the last three decades, the *Terry Collection* has been used to define and refine palaeopathological diagnostic criteria for tuberculosis in several studies; nonetheless, the four likely TBM-related endocranial alteration types (*i.e.*, APDIs, PAs, ABVIs, and GIs) were beyond the scope of the aforementioned research projects.

# AIMS & OBJECTIVES OF THE DISSERTATION

The main aim of the PhD dissertation is to expand knowledge and understanding about the development of the four possible TBM-associated endocranial alteration types (*i.e.*, abnormally pronounced digital impressions (APDIs), periosteal appositions (PAs), abnormal blood vessel impressions (ABVIs), and granular impressions (GIs)), to improve their palaeopathological interpretation, and to contribute to strengthening their diagnostic value in the identification of TB in human osteoarchaeological material from the pre-antibiotic era. Thus, review of the modern medical and palaeopathological literature regarding TB was conducted, with special attention to bony changes probably related to the disease.

Furthermore, for the first time, a detailed investigation focusing on the macromorphological characteristics and frequencies of the above-mentioned lesions affecting the inner surface of the skull (*i.e.*, APDIs, PAs, ABVIs, and GIs), and of their co-occurrence with each other and with non-endocranial bony changes likely associated with TB was performed on all individuals recorded to have died of different types of TB (*e.g.*, pulmonary TB, miliary TB, peritoneal TB, and osteoarticular TB) in the *Robert J. Terry Anatomical Skeletal Collection*, and on a control group consisting of randomly selected specimens from the remaining skeletons of the *Collection* who were identified to have died of causes other than TB (*e.g.*, other infectious diseases, cardiovascular problems, cancer, and external causes, such as suicide and homicide). Nonetheless, it must be noted that the disease registered as the cause of death on the morgue record and/or death certificate of individuals selected from the *Terry Collection* may not have been the only medical condition present in the specimens that could contribute to the development of bony changes in the skeleton.

# The objectives of the PhD dissertation are the following:

- 1) To macroscopically evaluate the selected skeletons from the *Terry Collection* for the presence of APDIs, PAs, ABVIs, and GIs, and for their co-occurrence with each other and with non-endocranial bony changes possibly related to TB;
- 2) To compare the frequencies of APDIs, PAs, ABVIs, and GIs, and of their co-occurrence with each other and with non-endocranial bony changes probably associated with TB,

- between individuals with TB as the cause of death and specimens with non-tuberculous (NTB) causes of death, considering the sex and age at death of individuals;
- 3) To macromorphologically characterise APDIs, PAs, ABVIs, and GIs regarding the prominence (APDIs), as well as the localisation, extent, and number (PAs, ABVIs, and GIs) of the detected lesions in the affected cranial bone(s);
- 4) To provide example cases from the *Terry Collection* showing the most important macromorphological characteristics of APDIs, PAs, ABVIs, and GIs; and
- 5) To evaluate the diagnostic value of APDIs, PAs, ABVIs, and GIs concerning the palaeopathological identification of TB.

#### **MATERIALS & METHODS**

The detailed macromorphological investigation focusing on the detection of the four likely TBM-related endocranial alteration types (i.e., abnormally pronounced digital impressions (APDIs), periosteal appositions (PAs), abnormal blood vessel impressions (ABVIs), and granular impressions (GIs)) and of possible TB-associated non-endocranial bony changes (e.g., rib lesions, vertebral changes, and joint alterations) in the skeleton was performed on 302 specimens with TB as the cause of death and on 302 randomly selected individuals with NTB causes of death from the Terry Collection. From the 604 surveyed skeletons, 177 were excluded from the examination considering the four endocranial alteration types probably related to tuberculous meningitis (TBM): the skullcap was missing in two cases and the skull was not sectioned in a further 173 cases; therefore, precluding the accurate observation of the inner surface of the skull; whereas the age at death was uncertain in two additional cases; thus, compromising the statistical analysis of data. The remaining 427 specimens with skulls sectioned in the transverse plane and occasionally also in the mid-sagittal plane were divided into two groups on the basis of their causes of death: one composed of 234 individuals with TB as the cause of death (TB group) and the other consisting of 193 specimens with NTB causes of death (NTB group).

During the macromorphological investigation, for each selected individual, detailed written and pictorial descriptions of all observed bony changes likely associated with TB were made on a data collection sheet. With respect to the APDIs, their prominence was registered (3-level scale: 1) very slight, 2) slight, and 3) pronounced); whereas concerning the PAs, ABVIs, and GIs, the affected cranial bone(s); the number of detected lesions in the affected cranial bone(s) (unifocal or multifocal); and the extent of the endocranial surface area the observed lesion(s) covered in the affected cranial bone(s) (4-level scale: 1) less than one-fourth, 2) less

than one-half, 3) less than three-fourths, and 4) at least three-fourth) were recorded. Besides the four endocranial alteration types, the presence of non-endocranial bony lesions possibly related to TB was also recorded in the 427 examined specimens.

After the detailed macromorphological evaluation of the selected skeletons, subsequent statistical analysis of data was performed: absolute and percentage frequencies of the four types of endocranial alterations probably associated with TBM, and of their co-occurrence with each other and with non-endocranial bony changes likely related to TB were calculated in both the TB group ( $\Sigma$ =234) and NTB group ( $\Sigma$ =193), considering the sex and age at death of individuals; and  $\chi^2$  testing of data to determine the significance of differences (if any) in frequencies of the four examined lesion types affecting the inner surface of the skull and of their co-occurrence with each other and with possible TB-associated non-endocranial bony changes between the two groups was undertaken.

# **RESULTS & DISCUSSION**

- 1) As for the presence of abnormally pronounced digital impressions (APDIs), periosteal appositions (PAs), abnormal blood vessel impressions (ABVIs), and granular impressions (GIs), at least one of them was registered in approximately two-thirds of the evaluated skeletons from the *Terry Collection*, with APDIs representing the most frequently detected lesion type and with PAs, ABVIs, and GIs occurring in smaller but similar proportions of specimens. In addition, the co-occurrence of APDIs, PAs, ABVIs, and GIs with each other and/or with probable TB-related non-endocranial bony changes was noted in about one-third of the surveyed individuals.
- 2) APDIs, PAs, ABVIs, and GIs were registered in both the TB group and NTB group; nonetheless, all of them were recorded more commonly in specimens with TB as the cause of death than in individuals with NTB causes of death. Whereas APDIs and PAs occurred in the TB group about twice as often as in the NTB group, ABVIs and GIs were approximately three and a half times and ten times more frequent in specimens with TB as the cause of death than in individuals with NTB causes of death, respectively. Moreover, the co-occurrence of APDIs, PAs, ABVIs, and GIs with each other was about five times more common in the TB group than in the NTB group; whereas their association with likely TB-related non-endocranial bony changes occurred approximately three times more often in specimens with TB as the cause of death than in individuals with NTB causes of death. The  $\chi^2$  comparison of the frequencies of APDIs, PAs, ABVIs, and GIs, and of their co-occurrence with each other and with possible TB-associated non-endocranial bony changes revealed a statistically significant difference between

the TB group and NTB group; therefore, similar to the results of previous studies, constituting evidence that there may be a positive correlation between APDIs, PAs, ABVIs, and GIs and tuberculous meningitis (TBM). Thus, they can be used as diagnostic criteria for TBM in the palaeopathological practice. Although not all of them may be considered as specific vestiges of the disease – since pathological conditions other than tuberculosis (*e.g.*, bacterial meningitis, trauma, scurvy, and epidural haematoma) may also result in the development of similar or even the same morphological features –, palaeopathologists could still use them to identify TB in human osteoarchaeological material from the pre-antibiotic era, especially when they simultaneously occur with each other and/or with non-endocranial bony changes probably related to TB.

- 3) With respect to the macromorphological characteristics of abnormally pronounced digital impressions (APDIs), periosteal appositions (PAs), abnormal blood vessel impressions (ABVIs), and granular impressions (GIs), in more than two-thirds of the selected skeletons from the *Terry Collection* that showed APDIs, the very slight stage of the aforementioned lesion type was detected. As for the localisation of PAs, ABVIs, and GIs, the findings of the PhD dissertation were similar to those of previous studies: PAs and ABVIs were situated particularly in the frontal and parietal bones; whereas GIs were localised predominantly in the occipital and temporal bones, with the pattern and distribution of GIs resembling that of most frequently observed in the affected meninges during the pathogenesis of TBM. Regarding the extent of lesions, whereas the majority of the detected PAs and ABVIs covered less than one-half of the inner surfaces in all cranial bones examined, the extent of the endocranial surface area the observed GIs covered in the affected cranial bones only occasionally exceeded one-fourth of the inner surfaces. Concerning the number of lesions, PAs, ABVIs, and GIs were registered most commonly as multifocal alterations in all cranial bones evaluated.
- 4) In the PhD dissertation, a number of example cases were provided that showed the most important macromorphological characteristics of APDIs, PAs, ABVIs, and GIs (*i.e.*, APDIs: prominence; PAs, ABVIs, and GIs: localisation, extent, and number of lesions in the affected cranial bone(s)), as well as of their co-occurrence with each other and/or with likely TB-associated non-endocranial bony changes. Therefore, they may give a better insight into the macromorphological characteristics of the above-mentioned lesions and may provide palaeopathologists with a stronger basis for establishing a more reliable and accurate diagnosis of tuberculous meningitis (TBM) in ancient human bone remains that exhibit bony changes resembling those of the example cases presented in the PhD dissertation.

5) On the basis of the results of the PhD dissertation, the diagnostic value of abnormally pronounced digital impressions (APDIs), periosteal appositions (PAs), abnormal blood vessel impressions (ABVIs), and granular impressions (GIs) in the palaeopathological identification of TBM is not equal. PAs may have the weakest diagnostic value. Even if they were detected in the TB group about twice as often as in the NTB group, the  $\chi^2$  comparison of the frequencies of PAs revealed a statistically only significant difference between the two groups; thus, suggesting a weaker correlation between PAs and TBM in comparison with APDIs, ABVIs or GIs. APDIs may have a stronger diagnostic value than PAs, since – similar to the PAs – they were registered in the TB group approximately twice as frequently as in the NTB group; but – in contrast to the PAs – the  $\chi^2$  comparison of the frequencies of APDIs revealed a statistically not only significant but extremely significant difference between the two groups; therefore, indicating a stronger correlation between APDIs and TBM than between PAs and TBM. In comparison with PAs and APDIs, ABVIs may have a stronger diagnostic value, as they were about three and a half times more common in the TB group than in the NTB group; and – similar to the APDIs – the  $\chi^2$  comparison of the frequencies of ABVIs revealed a statistically extremely significant difference between the two groups; thus, suggesting a stronger correlation between ABVIs and TBM than between PAs or APDIs and TBM.

Nevertheless, the findings of the PhD dissertation fit in with those of previous studies concerning the specificity of PAs, APDIs, and ABVIs for TBM, as more than 10%, 30%, and 6% of the skeletons in the NTB group exhibited them on the inner surface of the skull, respectively; therefore, indicating that PAs, APDIs, and ABVIs cannot be considered as specific vestiges of TBM. Nonetheless, in about one-half of the specimens with PAs, APDIs or ABVIs in the NTB group, other probable TBM-related endocranial alterations and/or likely TBassociated non-endocranial bony changes were also noted. Since the disease registered as the cause of death on the morgue record and/or death certificate may not have been the only medical condition present in the surveyed individuals from the Terry Collection, specimens identified to have died of causes other than TB could still have suffered from TB at death. Thus, in the aforementioned cases with PAs, APDIs or ABVIs in the NTB group, the tuberculous origin of the recorded endocranial and non-endocranial lesions cannot be excluded. However, it is also possible that in these cases – similar to the other one-half of individuals with PAs, APDIs or ABVIs in the NTB group, where no signs of other probable TBM-related endocranial alterations or of likely TB-associated non-endocranial bony changes were observed –, medical conditions other than TB might result in the development of the detected lesions.

Among the four evaluated endocranial alteration types, GIs may have the strongest diagnostic value, as they occurred about ten times more often in the TB group than in the NTB group; and – similar to the APDIs and ABVIs – the  $\chi^2$  comparison of the frequencies of GIs revealed a statistically extremely significant difference between the two groups; therefore, suggesting a strong correlation between GIs and tuberculous meningitis (TBM). Furthermore, the results of the PhD dissertation may support those of previous studies regarding the specificity of GIs for TBM, as – in contrast to the APDIs, PAs, and ABVIs – GIs affected only the minority of the skeletons composing the NTB group, and in the vast majority of the abovementioned cases, possible TBM-related endocranial alterations other than GIs and/or probable TB-associated non-endocranial bony changes were also recorded. It must be noted that even if the registered cause of death of the evaluated individuals may not have been TB, specimens could still have suffered from the disease but their death was attributed to another medical condition; thus, it is very likely that in the above-mentioned cases, the observed endocranial and non-endocranial bony changes might result from TB.

In summary, even if the periosteal appositions (PAs), abnormally pronounced digital impressions (APDIs), and abnormal blood vessel impressions (ABVIs) cannot be considered as pathognomonic features of TBM, palaeopathologists could still use them – with necessary circumspection – to identify the disease in human osteoarchaeological series from the preantibiotic era, especially when they simultaneously occur with each other and/or with possible TB-related non-endocranial bony changes. Moreover, the findings of the PhD dissertation may confirm that the granular impressions (GIs) can be considered as specific vestiges of TBM; and therefore, the palaeopathological diagnosis of TBM can be established with a high certainty when GIs are present in ancient human bone remains.

# RESEARCH SIGNIFICANCE & PERSPECTIVES

In the last few decades, palaeomicrobiological analyses of biological remains (e.g., DNA, proteins, and lipid biomarkers) of TB bacteria extracted from skeletons and mummies of people lived in the past have provided invaluable data not only on the evolution of TB but also on its palaeoepidemiology. Nevertheless, the findings of recent palaeoepidemiological studies on the osteoarchaeological have confirmed complementarity human series of palaeomicrobiological and traditional, macromorphology-based palaeopathological analyses, as their combined application may contribute to facilitating the establishment of a more reliable and accurate palaeopathological diagnosis of TB in ancient human bone remains and the assessment of a more relevant prevalence of the disease in past human populations.

The above-mentioned examinations require excessive scientific knowledge on the macromorphological diagnostics of tuberculosis that underlines the importance of the research project conducted on skeletons of known cause of death from the *Terry Collection*, since its results may provide palaeopathologists with a stronger basis for identifying TB and with a more sensitive means of assessing the prevalence of the disease in human osteoarchaeological series. Nonetheless, further investigations on human skeletons of known cause of death from documented collections other than the *Terry Collection* are necessary to confirm the trends noted in the PhD dissertation. Refinement of macromorphological diagnostic criteria and their application in the palaeopathological practice may open new perspectives in the palaeoepidemiological and evolutionary research of tuberculosis.

Finally, findings of the PhD dissertation may draw physicians' attention to the rather high prevalence of meningeal involvement in TB patients; and thus, may contribute to further improving the modern medical practice regarding the identification of tuberculous meningitis (TBM). According to the modern medical literature, TBM – the most common form of central nervous system (CNS) TB (~70–80%) – occurs in less than 1% of all active TB cases, with children under the age of 5 years representing the most vulnerable group affected by the disease. Although – because of the particular composition of the *Terry Collection* – there were no children among the surveyed skeletons, the four probable TBM-related endocranial alteration types (*i.e.*, APDIs, PAs, ABVIs, and GIs) and their co-occurrence with each other and/or with likely TB-associated non-endocranial bony changes were observed in a number of adolescent and adult individuals with TB as the cause of death from the *Terry Collection*. It must be noted that the vast majority of the aforementioned specimens were identified to have died of pulmonary TB and only two of them were recorded to have died of TBM.

Nevertheless, the results of the PhD dissertation fit in with those of recent studies revealing that at autopsy, a large number of individuals died of pulmonary TB without developing neurological signs and symptoms exhibited tubercles in the CNS; and therefore, indicating that involvement of the CNS in pulmonary TB is quite common. The abovementioned findings may incite physicians to check pulmonary TB patients for involvement of the CNS even if they do not display neurological signs and symptoms suggestive of the disease, since early, accurate diagnosis and prompt, adequate treatment are crucial in determining the clinical outcome of TBM that carries a high short-term mortality and a substantial excess morbidity among survivors: approximately one-third of the affected patients die of TBM and up to one-half of the survivors remain with serious neurological sequels, despite the initiation of anti-tuberculosis therapy.

# LIST OF PUBLICATIONS (MTMT ID: 10043233)

# 1) THE 2 PAPERS PROVIDING BASIS FOR THE THESIS-

**Spekker O**, Hunt DR, Váradi OA, Berthon W, Molnár E, Pálfi Gy. 2018. Rare manifestations of spinal tuberculosis in the Robert J. Terry Anatomical Skeletal Collection (National Museum of Natural History, Smithsonian Institution, Washington, DC, USA). *International Journal of Osteoarchaeology*, accepted. **IF**<sub>2017</sub>: **1.038** 

Molnár E, Donoghue HD, Lee OY-C, Wu HHT, Besra GS, Minnikin DE, Bull ID, Llewellyn G, Williams CM, **Spekker O**, Pálfi Gy. 2015. Morphological and biomolecular evidence for tuberculosis in 8<sup>th</sup> century AD skeletons from Bélmegyer-Csömöki domb, Hungary. *Tuberculosis* **95**(Suppl. 1): S35–S41. DOI: 10.1016/j.tube.2015.02.032 **IF**<sub>2015</sub>: **2.711** 

# 2) PEER-REVIEWED JOURNAL ARTICLES-

**Spekker O**, Pálfi Gy, Kozocsay G, Pósa A, Bereczki Zs, Molnár E. 2012. New cases of probable skeletal tuberculosis from the Neolithic period of Hungary – A morphological study. *Acta Biologica Szegediensis* **56**(2): 115–123.

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**Spekker O**, Hunt DR, Váradi OA, Berthon W, Molnár E, Pálfi Gy. 2018. Rare manifestations of spinal tuberculosis in the Robert J. Terry Anatomical Skeletal Collection (National Museum of Natural History, Smithsonian Institution, Washington, DC, USA). *International Journal of Osteoarchaeology*, accepted. **IF**<sub>2017</sub>: **1.038** 

# **TOTAL IF: 6.46**

# 3) PAPERS PUBLISHED IN CONFERENCE PROCEEDINGS-

**Spekker O**, Kozocsay G, Bereczki Zs, Pálfi Gy, Molnár E. 2012. *Csonttuberkulózis nyomai Vésztő Mágori-halom neolit kori temetőben*. In Mesterházy B (ed.): 11<sup>th</sup> International

Conference on Applications of Natural, Technological and Economic Sciences (Szombathely, Hungary, 19 May 2012). Presentations. Nyugat-magyarországi Egyetem: Szombathely, Hungary; 208–213.

**Spekker O**, Pálfi Gy, Molnár E. 2014. Csont-ízületi tuberkulózis nyomai Vésztő Mágori-halom neolit kori temetőben. In Vágvölgyi Cs, Szekeres A (eds.): *A biológia jövője, a jövő biológusai. Avagy szemelvények a magyarországi felsőoktatási intézményekben végzett tudományos munka eredményeiről. Válogatás a XXXI. Országos Tudományos Diákköri Konferencia Biológia szekciójának dolgozataiból. JATEPress: Szeged, Hungary; 69–80.* 

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Váradi OA, Kecskeméti A, **Spekker O**, Molnár E, Bereczki Zs, Szekeres A, Vágvölgyi Cs, Pálfi Gy. 2016. Cases of tuberculosis infection verified by lipid biomarker analysis in Hungarian archaeological samples. In Gál SzS (ed.): *The talking dead. New results from Central and Eastern European osteoarchaeology. Proceedings of the First International Conference of the Török Aurél Anthropological Association from Târgu Mureş.* Mega Publishing House: Cluj-Napoca, Romania; 129–142.

# 4) CONFERENCE PRESENTATIONS-

#### A) National conferences-

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**Spekker O**. 2013. Csont-ízületi tuberkulózis nyomai Vésztő Mágori-halom neolit kori temetőben. In 31<sup>st</sup> National Scientific Students' Association Conference (Szeged, Hungary, 2–4 April 2013). – 2<sup>nd</sup> place; JATEPress Publication Award

**Spekker O**, Pálfi Gy, Bereczki Zs, Paja L, Molnár E. 2013. Hendikeppel az avar korban – A mozgáskorlátozottság hatása a csontokra. In "Hadak útján". A Népvándorláskor Fiatal Kutatóinak XXIII. Konferenciája (Veszprém, Hungary, 2–4 October 2013). Abstract Book. Laczkó Dezső Múzeum: Veszprém, Hungary; 11.

**Spekker O**, Paja L, Hunt DR, Ortner DJ, Dutour O, Molnár E, Pálfi Gy. 2017. A tuberkulózissal összefüggésbe hozható endocranialis elváltozások makromorfológiai jellegzetességeinek, előfordulásának és együttes megjelenésének vizsgálata a washingtoni Terry Collection-ben. In A Magyar Biológiai Társaság Embertani Szakosztályának 389. ülése Dr. Farkas L. Gyula

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# B) International conferences-

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