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ARTICLE

The Paleopathology of specific infectious diseases from Southeastern Hungary: a brief overview

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ABSTRACT The purpose of this study is to review the evidence for the presence of specific infectious diseases in past Hungarian populations. As for treponemal diseases, only few paleopathological cases had been published until relatively recently. New discoveries from the medieval Szeged furnished evidences for the Pre-Columbian occurrence of the disease in this area. Among mycobacterial infections, paleopathological analyses of thousands of skeletons provided a relatively high number of observations of 'classical' skeletal tuberculosis (TB) cases, and some cases of leprosy until the end of the 1990's. The use of DNA assays and the study of early stage traces of mycobacterial skeletal infections highly increased the number of observations during the last ten years. Unfortunately, these results present several biases of the classical osteoarcheological studies, such as the differentiation between the taphonomic and paleodemographic conditions of the series. The evolution of the paleopathological diagnostical methods necessitates the complete re-evaluation of the previously studied materials in order that we can obtain a more realistic paleoepidemiological picture of these diseases
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In Hungary, two important and several smaller physical anthropological collections can be used for paleopathological studies. The biggest and best-equipped collection belongs to the Department of Anthropology of the National Museum of Natural History (about 40 thousand skeletons), in Budapest. Another big collection of more then 30 thousand skeletons is disposable for the anthropological and paleopathological research at the University of Szeged.

The Szeged human skeletal material comes from archeological excavations in Southern and Eastern Hungary and represents a large chronological period from the Neolithic Period to Modern Ages. The richest part of this collection is from the Avar Age (6-8th centuries), the Hungarian Conquest Period (10-11th centuries) and the Arpadian Age (11-13th centuries). Actually, our material is stored in 9 premises of 4 distant buildings – we are working in cooperation with the National Museum of Natural History and the Museum of Szeged, to develop a common osteological centre in order to improve storage and research conditions.

Paleopathological research of specific infectious diseases has been one of the main activities of the Szeged team of anthropologists since the 1970's. This activity became more intensive in the 90's when among a large number of ancient TB cases some cases of leprous and treponemal infections were also identified (e.g. Maczel 2004; Marcsik 1972, 1994; Marcsik et al. 1994, 2007; Molnár and Pálfi 1994; Molnár et al. 1998, 2005; Pálfi 1991, 2002; Pálfi et al. 1997, 1999, 2002). In the field of paleomicrobiology, publications represent very successful interdisciplinary cooperation (e.g. Haas et al. 1999, 2000a-b; Donoghue et al. 2005, 2009; Zink et al. 2007).

This interest in specific infectious diseases led us to co-organize 3 parts of the ICEPID series (International Congresses on the Evolution and Paleoepidemiology of Infectious Diseases). We certainly do not want to forget the importance of the ICEPID series, thus we are to organize a second international TB conference in Hungary in 2011 (Szeged and Budapest).

New cases of infectious paleopathology

The recent expansion of the archaeological activity in the Szeged region (new highway excavations, excavations among the ruins of the medieval castle of Szeged, etc.) furnished a lot of new paleopathological cases during the past couple of years. At the same time, the development of the diagnostical methods and the results of the latest cooperation called forth new observations in infectious paleopathology.

The paleopathological evidences of treponemal infections have already been proven from Post-Columbian South-eastern Hungarian archaeological context (e.g. Marcsik 1994; Pálfi et al. 1997; Molnár et al. 1998). Several new treponemal cases have been discovered recently in the anthropological

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Figure 1. Early stage rhinomaxillary changes in leprosy: left maxilla showing periostitis on the nasal surface (Püspökladány, 10-11th centuries AD, Grave No 503, Adult Female).

Figure 2. Facies leprosa: erosion of nasal margins and loss of anterior nasal spine (Szeged-Kiskundorozsma, 7th century AD, Grave No 271, Mature Male).

material from the medieval Szeged Castle excavations (Ősz et al. 2006, 2009a). In these cases, the macro-morphological diagnosis was backed up by paleoradiological and paleohistological analyses; furthermore, the Pre-Columbian origin was suggested both by archaeological and radiocarbon dating (see more details in the present volume of Acta Biologica Szegediensis, Ősz et al. 2009b).

The paleopathological study of mycobacterial diseases (tuberculosis and leprosy) has furnished several important new results from the Szeged Collection. Among others, we have to mention the 2005-2006 results by Donoghue and collaborators: two of the examined Hungarian cases from the Püspökladány series (10th-11th centuries AD) with typical 'early stage' manifestations of *facies leprosa*, included in a larger paleomicrobiological study, were positive both for *Mycobacterium leprae* and *Mycobacterium tuberculosis*. We are presenting here one of these two cases with nasal periostitis (Fig. 1) – as early manifestations of leprous rhinomaxillary changes. Both cases were co-infected by leprosy and tuberculosis (Donoghue et al. 2005, 2009). These cases have been included recently to a phylogeographic analysis of *Mycobacterium leprae* (Monot et al. 2009).

Figure 3. Rhinomaxillary changes in leprosy (Szeged-Kiskundorozsma, 7th century AD, Grave No 517, Adult Male).

The 7th century Avar-Age series of Kiskundorozsma (Szeged) represents a remarkable material for the study of past mycobacterial infections (Molnár et al., 2006). In this small osteoarchaeological sample, 8 of the 94 skeletons revealed traces of the different stages of leprous infection (Fig. 2,3). Paleomicrobiological studies confirmed the *Mycobacterium leprae* infection (Donoghue et al. 2009). These cases permitted to 'move back' in the history of leprosy in the given geographical area: before these finds, the previously discovered earliest Hungarian leprosy cases had been dated to the 10th century (Pálfi et al. 2002; Marcsik et al. 2007, 2009).

Hereinafter, we would like to mention a case of probable leprosy, discovered recently in the Szeged Anthropological Collections. The isolated skull of an adult female specimen

Figure 4. Facies leprosa: rhinomaxillary changes (Szentes-Kistőke, 4-7th century AD, Grave No 11, Adult Female).

Figure 5. Multifocal spinal TB: lytic lesions, new bone formations, vertebral fusions, traces of cold abscess (Szeged-Kiskundorozsma, 7th century AD, Grave No 176, Senium Male).

(Fig. 4) comes from an archaeological excavation from the first half of the 20th century and has been dated to the relatively large 'Migration Period' (Szentes-Kistőke series, around 4th-7th centuries AD). The morphological aspects of the rhinomaxillary changes are characteristic of a *facies leprosa*. Unfortunately, we do not possess any postcranial bones. Complementary studies and a more precise dating should be necessary. At this moment, we can only conclude that this is a potential early-medieval leprosy case, which may be anterior to the oldest Avar Age cases in Hungary.

Compared to the dozen of new leprosy cases and to the half a dozen of treponemal cases, the number of new TB cases is much higher, especially if we consider both the chronic and the early forms of its manifestations. The above mentioned 7th century Kiskundorozsma series, very rich in leprous cases, furnished a very interesting multifocal spinal TB case too (Fig. 5, 6).

Following the chronology of the archaeological excavations, the paleopathological study of the 16-17th century Bácsalmás-Óalmás anthropological series was carried out in several steps. The first part of the series have already presented a high prevalence of early stage TB cases (e.g. Molnár and Pálfi 1994; Pálfi and Ardagna 2002; Maczel 2003; Fig. 7, 8). Ancient DNA analysis by Haas and co-workers had proved the relationship between the frequent early stage alterations and the TB infection (Haas et al 1999, 2000a). The study of the second part of the series – which was excavated later - is still in progress. The low number of the chronic forms and the high prevalence of early stage cases are to be mentioned. The morphological diagnosis of the Bácsalmás early stage TB cases was partially based on our previous research work, which is still going on, in the Terry Anatomical Collection in Washington DC.

The paleopathological study, still in progress, of the Late Neolithic series of Hódmezővásárhely-Gorzsa (4970 to 4594 BC) furnished several cases of infectious diseases, among them traces of possible TB infections. These cases might be the oldest known TB cases from Hungary – however, complementary biomolecular studies should be necessary (Masson et al 2009).

Some paleoepidemiological conclusions

The intensive study of the paleopathology of specific infectious diseases increased the number of the diagnosed ancient

Figure 6. Vertebral fusion in spinal TB (Szeged-Kiskundorozsma, 7th century AD, Grave No 176, Senium Male).

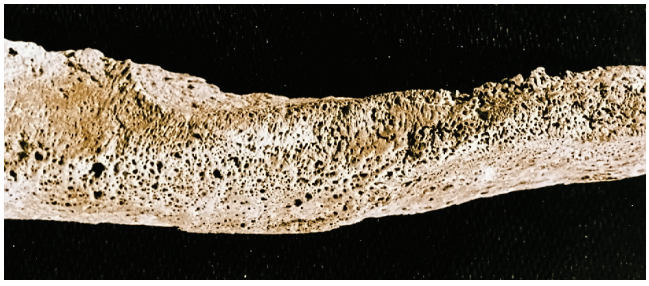

Figure 7. Early stage TB: periosteal lesions on the visceral surface on the 9th right rib (Bácsalmás-Óalmás, Grave No 61, Juvenile Male).

cases in our collections. As for treponematosis, due to the new discoveries from Szeged, its Pre-Columbian presence in Central Europe is not a question any more. Unfortunately, the low number of cases excludes all attempts of epidemiological reconstruction.

Figure 8. Early stage TB: hypervascularisation and resorptive lesions on the ventral bodies of thoracic vertebrae periosteal (Bácsalmás-Óalmás, Grave No 115, Juvenile Male).

The Hungarian part of the history of leprosy is partially redrawn – or rewritten – based on the new discoveries of the past few years. Leprosy co-existed with tuberculosis in our ancient populations and must have reached the Carpathian Basin before the Ancient Hungarians. This chronic disease was present among the Avars of the 7th century, or may even have been present among other peoples before the Avars during the Migration Period. However, in spite of the higher number of proven cases, this quantity is still insufficient for a serious paleoepidemiological reconstruction.

As for skeletal tuberculosis, the past few years have furnished a great number of data, and a lot of cases have been confirmed by paleomicrobiology. A new tendency is about to emerge: the so-called early stage forms are more frequent in the more recent periods. However, the limits of the osteoarcheological analysis do not allow us to formulate more precise hypotheses. We presented our first attempt at TB paleoepidemiology at the 1994 Copenhagen meeting of the European Anthropological Association (Marcsik et al 1994). In this work, only 11 classical cases were reported from the great number of 3.400 examined skeletons. In 1999, we tried to complete and re-summarize these results (Pálfi and Marc-

sik 1999). More than 5 thousand skeletons were considered from a period of a thousand years between the 7th and 17th centuries. As the evolution of the methodology permitted to recognize more and more cases – a total of 31 TB cases were identified -, the 'virtual prevalence' became higher than in 1994. Finally, Marcsik and co-workers tried to complete this table by another one containing more than 5 thousand skeletons studied between 1999 and 2006 (Marcsik et al 2007). Classical cases and DNA-confirmed early stage cases were considered during that period. Today, we have a lot of data about TB paleopathology in Hungary. However, we need to be extremely critical about our own results. The development of the methodology has continuously been modifying the results about the evolution of the disease.

Some biases

Our results about ancient TB-prevalence have presented certain problems related to the changes of diagnostic criteria, but also to other biases of paleopathological studies. Several of the examined series come from cemeteries of very long periods of occupation. For this reason, if the dating cannot be made more precise, we had better drop some series from the comparative studies. Excavation-related differences in the demographical structures of the series can also be problematic, as in all types of comparative osteoarcheological studies.

As for the biases related to paleoepidemiological studies of specific infectious diseases, solving the problems of 'methodological changes' should be the first task.

We need to establish specific temporary diagnostical packages for each specific infectious disease in order to find out which cases can and which cases cannot be kept in our statistics. Afterwards, we will always have to use the same criteria. When the evolution of the methods reaches an important new step, we must stop and make the necessary changes. And when we start using a new method, unfortunately, we also have to re-evaluate our previous studies.

The last and perhaps also the most problematic element of our comparative studies is the question of taphonomical differences, which is neglected by most of the comparative studies. The establishment of the 'specific diagnostical packages' mentioned above should be completed by the creation of the disease-specific criteria of 'observability'. If we use taphonomy-related correction factors corresponding to the observability of the disease-specific lesions, we can obtain much more realistic prevalence values.

The reconstruction of the infectious diseases of the past is a very complicated task – but one of the most beautiful tasks of human paleopathology.

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