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Thalassemia Major and Malaria in the Republic of Macedonia in the Past Times

UDK 616.936(091)
616.155.194.125(091)

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Abstract: *The article concerns Mediterranean anemia (Thalassemia Mayor) in the territory of R.Macedonia. It elaborates the earliest cases, chronological span, and the geographic distribution of this rear type of anemia, which is associated with malaria. The earliest evidence regarding presence of this serious disease dates from the 4 century B.C. Disease was The most frequent in the Middle Ages, in The Strumica region, at necropolises in Vodoca, Holly Fifteen Martyrs of Tiveriopolis and the Orta Mosque.*

Key words: *bones, paleopathology, anemia, malaria*

Skeletal remains of people throughout history have concealed numerous data, not only about physical appearance, age and gender, but also regarding traces of diseases, injuries and anomalies.

The article deals with two serious diseases of different types, but closely connected, thalassemia and malaria. The first disease belongs to anemia types (hematologic diseases) and the second one is an infectious, parasitic disease.

I. Basic data on thalassemia and malaria[1]

Thalassemia is a congenital hemolytic anemia caused by a genetic defect in the hemoglobin (red cells pigment) structure. The blood of thalassemic patients is of light red color and watery (thalassemia means water/sea in blood).

The types of haemolytic anemia may have secondary effects on bone, because the greatly reduced red cell life span in these conditions provokes a great expansion of the haemopoietic bone marrow in the long bones, vertebrae and the skull.

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[1] According to: a. C. Aufderheide, c. Rodrigez - Martin, *The Cambridge Encyclopedia of Human Paleopathology, (Infectious diseases*, part 7, *Malaria*, pp. 228-237), (*Hematological disorders*, part 11, pp. 359-365), Cambridge University Press, 2006, pp.478

T. Waldon, *Palaeopathology*, Cambridge University Press, 2009, pp.136-137

D. J.Ortner, .W. G. J. Putschar, *Identification of Pathological Conditions in Human Skeletal Remains*, Washington 1985, pp. 251-263

T. 1 West Necropolis – Stobi, Gradsko, Skeleton No 846 Thalassemic changes of scull (a), and post-cranial skeleton (b)

It can occur in homozygote (thalassemia major) and heterozygote (thalassemia minor) form.

Only the first form, when an individual inherited thalassemic genes from both parents, has clinical symptoms and skeletal changes.

The most severe changes are in the scull. Bones of cranial vault is widened (especially frontal, and parietal), eroded, porous, with completely destroyed external table. Cross-section shows radial rearrangement of the bone with appearance described as "hair on end".

Similar changes show ribs, pelvis and other flat bones. In long bones cortex is thin, medullary cavity is wide.

Thalassemia major results in a very high mortality in childhood, and short lifespan, affected persons rarely surviving after puberty.

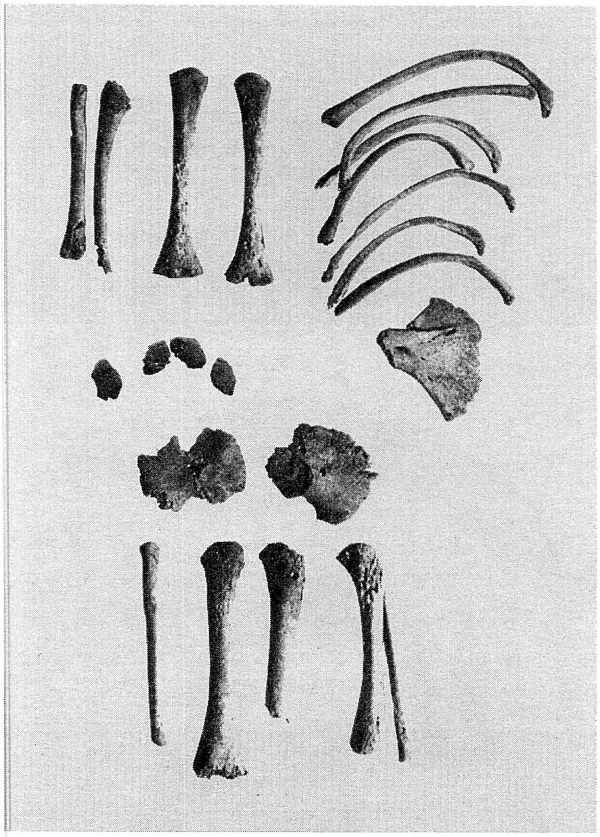
Thalassemia minor (heterozygote form) with no skeletal or clinical changes, has advantage in malaria-infested areas. Partly abnormal haemoglobin reduces the severity of the symptoms of malaria.

Thalassemia has affected mainly central and eastern Mediterranean populations. Due to this it is also known as Mediterranean anemia.

Researchers have shown that there is geographical concordance of malaria and thalassemia.

Malaria, which means "bad air", is an acute or chronic, recurrent, febrile parasitic human infection by protozoa (Plasmodium), transmitted by mosquitos.

In spite of efforts to control the disease, still 3000 people die of malaria every day.



T. 2 West Necropolis – Stobi, Gradsko, Skeleton No 2110 Thalassemic changes of post-cranial skeleton

The most vulnerable age group is children up to 5 years of age, but adults having survived the acute malaria bear the consequences for entire life, due to affected spline and liver.

II.Cases from R. Macedonia

In the researches I have carried out on over 20.000 individual skeletons, total number of 16 cases of thalassemia has been recorded.

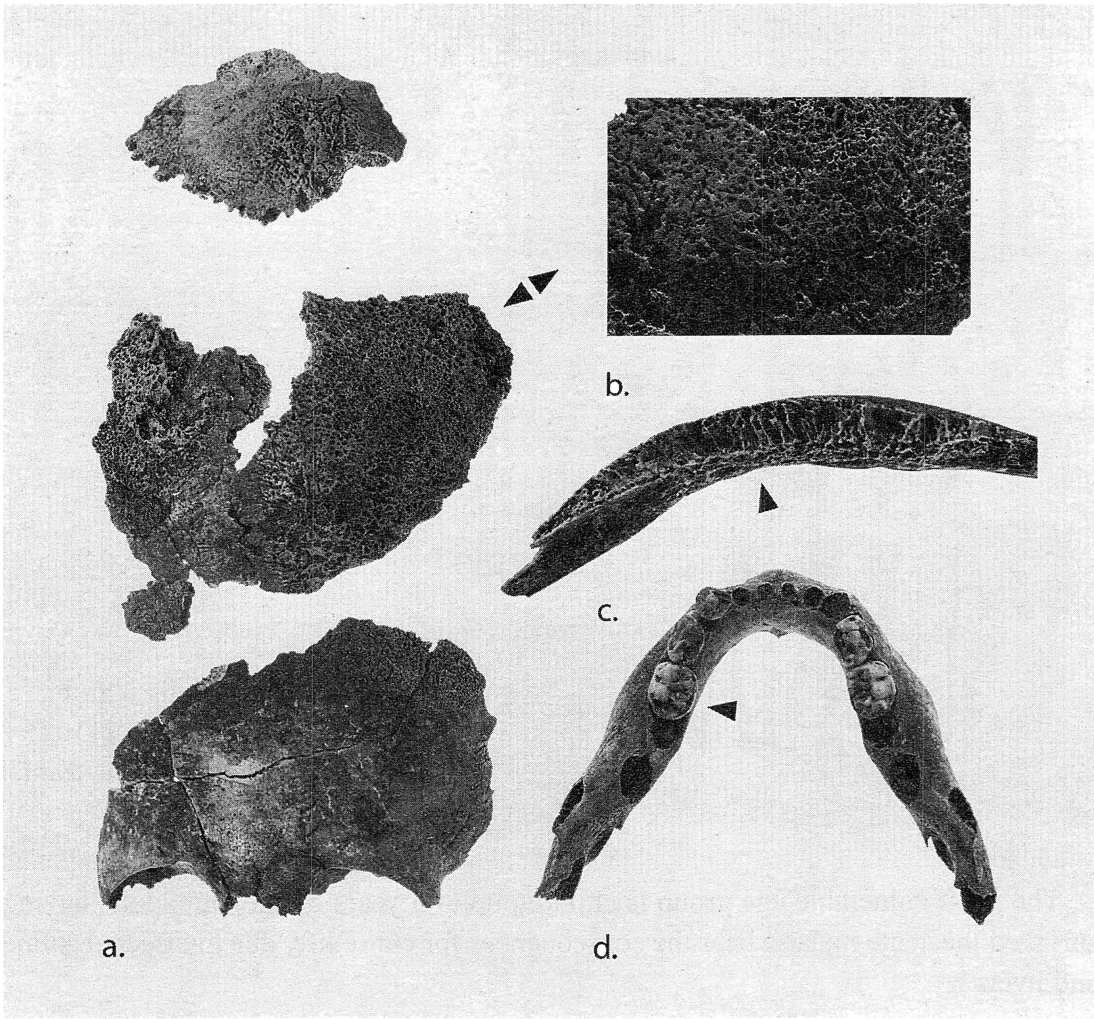
The most obvious changes have been observed in three skeletons, two from the Antiquity and one from the Middle Ages.

1. West Necropolis – Stobi, Gradsko (2nd century BC – 6th century AD)[2]

Skeleton No 846 belongs to a child at 1,5 to 2 years of age.

The entire skeleton was affected from the disease (T. 1). Fragments of the scull show typical "hair on end" changes. Long bones are bent, with thinner cortex, widened medullar cavity and irregular spongy tissue.

[2] The researches in 1992 were carried out by Republic Institute for Protection of Cultural Monuments – Skopje (RZZSK) and Museum of Macedonia-Skopje. The chronology was determined by Z.Vincic, M. Ivanovski and V. Sanev, the Heads of the research team. Unpublished. My gratitude for the information.



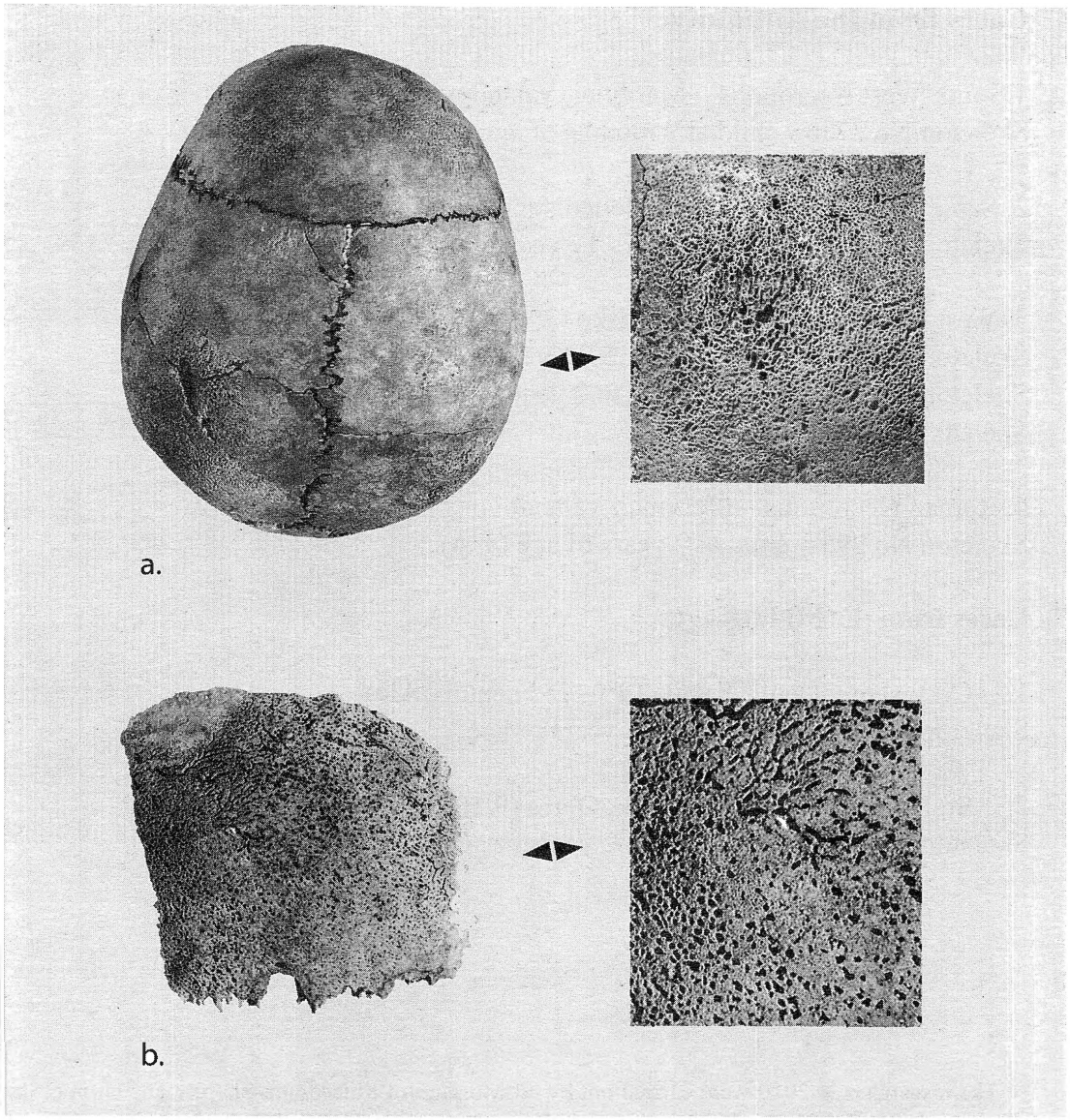
T. 3 Vardarski Rid – Gevgelija, Skeleton No 44
a. – b. severe porous changes of cranial vault
c. cross-section of right parietal bone
d. carious teeth in mandible

Similar changes on post-cranial skeleton have been observed on skeleton No 2110, newborn baby from the same necropolis (T. 2).

2. Vardarski Rid-Gevgelija (11th – 13th century AD)[3]

Skeleton 44, child at 7 years of age, shows especially severe changes on cranial vault with typical rectangular disposition of trabeculae in cross-section (T. 3, a-c). All teeth were affected by caries, which is sometimes associated with thalassemia (T. 3, d).

[3] The researches of the Medieval Necropolis in 2010 were carried out by NI Museum of Gevgelija. The chronology was determined by E. Slamkov, the Head of the research team. Unpublished. My gratitude for the information.



T. 4 Talassemia cases in the Antiquity
a. Marvinci – Valandovo, Skeleton No 295
b. West Necropolis – Stobi, Gradsko, Skeleton No 160/a

In other cases the changes consist of mainly widened cranial bones with very strong localized defects (honey-combed appearance) of cranial vault.

They have been briefly described in two chronological groups, from the Antiquity (early to late Antiquity) and from the Middle Ages (advanced to late medieval period) and shown on T. 4-5.

Cases from the Antiquity

1.South-West Necropolis – Marvinci, Valandovo (4th century BC)[4]
Skeleton No 2736 - child at 9 months of age.

2. Samuil's Fortress – Ohrid (Hellenistic Period)[5]
Skeleton No 197 - juvenile at 15 - 17 years of age.

3. West Necropolis – Stobi, Gradsko (2nd century BC – 6th century AD)
Skeleton No 160/b[6]- juvenile at 15-16 years of age (T. 4).
Skeleton No 852/c – child at 1,5 to 2 years of age.
Skeleton No 2123- newborn baby.

4. Roman Necropolis – Marvinci, Valandovo (Late Roman Period)[7]
Skeleton No 295 – child at 7 years of age (T. 4).

Cases from the Middle Ages

1. Crkvishte – Demir Kapija (9th – 15th century AD)[8]
Skeleton No 376/b – child at 3-4 years of age.[9]

2. St. Pantheleimon –Plaoshnik, Ohrid (9/10th -18th century AD)[10]
Skeleton No 54/08 – child, up to 2 years of age[11].

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[4] The researches in 2010 were carried out by NI Museum of Macedonia-Skopje. The chronology was determined by Z. Videski, MA, the Head of the research team. Unpublished. My gratitude for the information.

[5] The researches in 2008 were carried out by NI Museum of Ohrid. The chronology was determined by M-r R. Petkovski, the Head of the sector research team. Unpublished. My gratitude for the information.

[6] A.Wesalowsky, *Burial customs in the West Cemetery*, in *Studies in the antiquities of Stobi I* (1973), Beograd, pp. 97-137

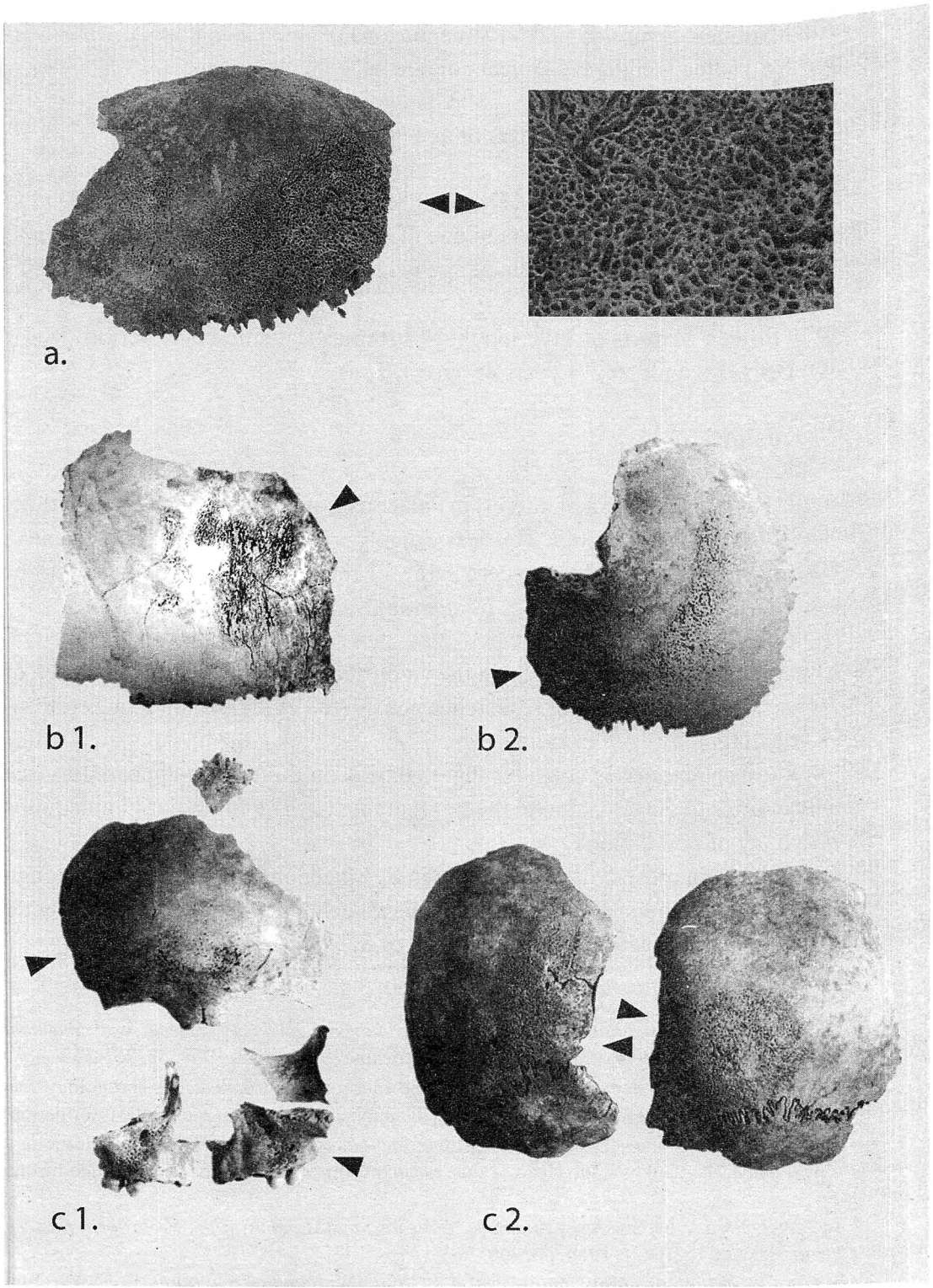
[7] C. Krestevski, Report on the archaeological excavations carried out at the site of Isar-Marvinci in 1997, submitted to RZZSK. Ф. Вељановска, *Античкото население од Марвинци-Валандово*, Скопје 2006, pp.57, pl.14

[8] Б. Алексова, *Просек-Демир Капија, Dissertationes I,* Скопје-Београд, 1966, pp. 102

[9] Ф. Вељановска, *Антрополошки карактеристики на средновековното население од Црквиште-Демир Капија*, Скопје 2001, pp.48, F.14

[10] The researches in 2008 were carried out by NI Institute and Museum of Ohrid. The chronology was determined by P. Kuzman, the Head of the research team. Unpublished. My gratitude for the information.

[11] According to the Report on the anthropological analyses of medieval finds from Plaoshnik, carried out in 2008 by M. Velova.



T. 5 Thalassemia cases in the Middle Ages, Strumica
a. Skeleton BB 1/7, Holly Fifteen Martyrs of Tiveriopolis,
b. 1 Skeleton No16/96a
b. 2 Skeleton No 150/01, Orta Mosque
c. 1 Skeleton No 776
c. 2 Skeleton No 552, St. Leontij, Vodocha

3. Orta Mosque – Strumica (12th -17th century AD)[12]
Skeleton No 16/96a – child at 2-3 years of age
(T. 5, b 1)
Skeleton No 150/01 – child at 2 years of age (T. 5, b 2)

4. St. Leontij, Vodocha, Strumica (14th -18th century AD)[13]
Skeleton No 522 – child at 8-9 years of age (T. 5, c 2)
Skeleton No 776 – child at 3-4 years of age (T. 5, c 1)

5. Holly Fifteen Martyrs of Tiveriopolis – Strumica (late medieval period)[14]
Skeleton BB 1/7 – child at 2-4 years of age (T. 5, a).

III. Disscusion

Talassemia has been a subject of interest in Palaeopathology for a long period of time. Unfortunately, except for the articles by J. L. Angel[15] referring to east Mediterranean and Greece, most of the analyses concern faraway regions (Africa and America) or deal with similar but not identical types of anemia (Sickle-cell anemia).

Angel identifies thalassemia already in the Neolithic on the grounds of presence of cranial cribras, which are by recent researches considered evidence for acquired Iron-deficiency anemia[16].

In addition other researches consider that malaria could not have appeared in east Mediterranean prior to 500 BC, due to the unfavorable climate for malarial mosquitos and slight density of population[17].

Thalassemia within present day population in R. Macedonia is well known through the researches of Academician G. Efremov and his associates from the Research Center for Genetic Engineering (Macedonian Academy of Sciences and Arts - Skopje).

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[12] М. Стаменкова, *Прелиминарен извештај од археолошкото истражување на локалитетот Орта Џамија во Струмица 1984-1987*, in Зборник на трудови Струмица, 1989, pp. 351-355

[13] The researches were carried out by NI Institute and Museum of Strumica. The chronology was determined by J. Ananiev, the Head of the research team. Unpublished. My gratitude for the information.

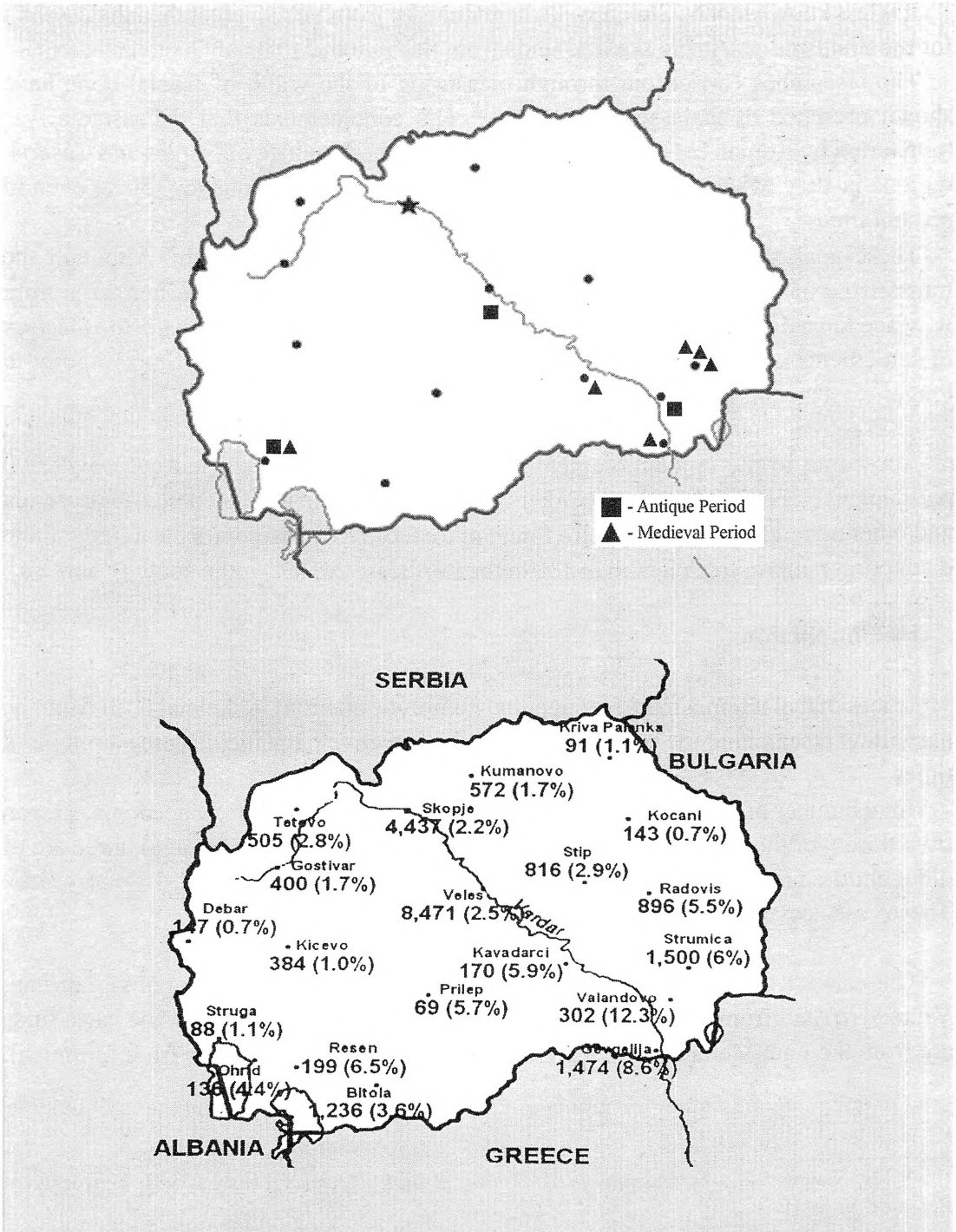
[14] The researches were carried out by NI Institute and Museum of Strumica. The chronology was determined by M. Stamenkova, the Head of the research team. Unpublished. My gratitude for the information.

[15] J. L. Angel, *Porotic hyperostosis, Anamias, Malarias, and Marshes in the Prehistoric Eastern Mediterranean*, Science 153,1977, 1966, pp. 760 -763

J. L. Angel, *The People of Lerna: Analysis of a Prehystoric Aegean Population*, Princeton and Washington, 1971, pp. 78 - 91

[16] P. L. Stuart – Macadam, *Nutritional Deficiency Diseases: A survey of Scurvy, Rickets, and Iron – Deficiency Anemia*, in M. Y. Iscan, K. A. R. Kennedy, *Reconstructio of Life from Skeleton*, New York, 1989, pp. 203 - 222

[17] A. C. Aufderheide, C. Rodrigez - Martin, *The Cambridge Encyclopedia of Human Paleopathology*, Cambridge University Press, 2006, pp 228-237, 359-365



T. 6 Chart 1 Geographic distribution of thalassemia in the Antiquity and the medieval period in R. Macedonia

Chart 2 Distribution of thalassemia and other hemoglobinoathies in R. Macedonia (G. Efremov, 2007)

It is less known that N. Stojanovski, hematologist from Veles, researched thalassemia for the first time analyzing skeletal finds from Stobi in the 1980`s.[18]

The researches carried out through measuring of the width of frontal bone have shown presence of thalassemia in Stobi[19]. His conclusion is that thalassemia was transferred by Roman legionaries from Campania, the province of Naples and Caserta, regions in Italy, where thalassemia shows exclusively high frequency (50%) even in present times.

These analyses also confirmed presence of thalassemia in Stobi. Although the transferring of this disease from other regions cannot be excluded, earlier cases from R. Macedonia dating from the early Antiquity, as well as favorable climate, the location of settlements near rivers, frequent floods (documented precisely in Stobi)[20] point to longer existence of thalassemia and malaria in Macedonian territories.

According to the epidemiological study of G. Efremov[21], carried out on 22.000 participants (school children and workers) from all regions in R. Macedonia, thalassemia and other hemoglobinopathies were found in total of 2.6% cases with clear geographic distinction ranging from less than 1% in the northeast to 10% in the south (Chart 2).

IV.Conclusions

Traces of thalassemia major (congenital hemolytic anemia) in skeletal finds from the past allow researching the presence of malaria (infective parasitic disease) throughout times.

Total number of 16 cases of Thalassemia has been recorded in R. Macedonia. Eleven (two thirds) of them belong to small children (Infans I, 0 – 6 years of age), three are of older children (Infans II, 7-14 years), and two are juveniles (Juvenilis, 15 – 21 years). These cases cover the short lifespan of thalassemia affected persons.

The earliest finds are from the 4th century BC (Southwest Necropolis-Marvinci, Valandovo) and from the Hellenistic Period (Samul`s Fortress-Ohrid). The latest finds are from the Late Medieval and the Ottoman Period (three necropolis from Strumica).

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[18] N. Stojanovski, *Thalassemias in Titov Veles Region. Doctoral Thessis*, 1983, University of Belgrade, Yugoslavia

[19] Widened bones of cranial vault is neither the only, nor a sufficient change for diagnosing specifically thalassemia, since it occurs in acquired Iron-deficiency anemia and also in some other diseases (Paget's disease, etc.).

D. J. ortner, W.G.J. Putschar, *Identification of Pathological Conditions in Human Skeletal Remains*, Washington 1985, pp. 251-263

[20] V. Sanev, S. Sarzovski, Excavations of the Inner City Wall at Stobi, 1972-1974, Studies of the Antiquities of Stobi III, Titiv Veles 1981, pp. 229-232

[21] G. Efremov, *Thalassemias and other hemoglobinopathies in the Republic of Macedonia*, in Hemoglobin 31 (1) (2007), pp.1681-1693

Equal number of cases has been discovered from the Antiquity (early – late Antiquity) and the Middle Age, eight in each group. Regionally, the biggest number of cases comes from the three necropolises in Strumica (five cases) and from Stobi (four cases).

In the span from the early Antiquity to the late medieval period Thalassemia and closely associated malaria were present in the south parts of R. Macedonia (Middle and Lower Vardar Valey, southeast and southwest Macedonia). Stobi is the northernmost point of recorded cases.

The population in R. Macedonia was affected by malaria till mid-20th century. The regulation of riverbeds, drainage of marches, and regular disinfection have fortunately resulted in perishing of this disease.

Nevertheless, the Thalassemic gen, which is still present within the modern Macedonian population, conceals the long history of this disease.

Translated by Nada Andonovska

Таласемија мајор и маларија на почвата на Р. Македонија во минатото

Резиме

Трагите на таласемија мајор (вродена хемолитичка анемија) на скелетните наоди од минатото, овозможуваат истражување на присуството на маларијата (инфективно, паразитско заболување) во минатото.

Откриени се вкупно 16 случаи на таласемија. Единаесет (две третини) припаѓаат на помали деца (Infans I, 0-6 години), три на повозрасни деца (Infans II, 7-14 години), и два се јувенили (Juvenilis, 15-21 година). Нашите случаи го покриваат распонот на краткиот животен век на заболените од таласемија.

Најстарите наоди се од IV век пред н.е. (југозападна некропола-Марвинци, Валандово) и хеленистички (Самуилова тврдина-Охрид). Најмладите наоди се од доцниот среден век и турското средновековие (струмичките некрополи: Орта Џамија, Св. Петнаесет маченици, Водоча).

Еднаков број на случаи е откриен во античката (рана-доцна антика) и средновековната група, по осум. Регионално, најбројни се наодите од трите струмички некрополи (пет), потоа од Стоби (четири).

Од раната антика до доцното средновековие, таласемијата е присутна во јужните делови на Р Македонија (средното и долно Повардарие, југоисточна и југозападна Македонија). Стоби е најсеверната географска точка на присуството на таласемијата.

Во Македонија маларијата била присутна до средината на минатиот век. Регулацијата на речните корита, исушувањето на мочуриштата и редовната дезинсекција придонесоа, за среќа, денес таа да е заборавена болест.

Сепак, таласемичниот ген, сè уште присутен кај современото население од нашата земја, ја крие долгата историја на оваа болест.