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A NEW HYPOTHESIS TO EXPLAIN THE UNIQUE SPATIAL DISTRIBUTION OF BALKAN ENDEMIC NEPHROPATHY

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Abstract. Balkan Endemic Nephropathy (BEN) is a disease which appears in the Balkan Peninsula. The starting point for this research is an observation of an overlap of the area where BEN occurs and a geological formation known as the ex-alluvial cone of the Danube of the Sarmatia Sea. Based on the chrome in the water of this geological structure, a direct relationship between the content in heavy metals (especially Cr) of the water used in the current supply of some families is hypothesized to explain the prevalence of BEN. A database containing the nephropathy cases registered from 1958 until present per localities was created and cases were mapped. By questionnaires and interviews with the affected persons, the water sources used for a long period of time (over 10 years) were localised. Water samples were gathered from 15 localities where people have been affected by BEN and who are presently on dialysis. Two probes were sampled from each water source (the first after a long rainy period and the second after a long dry period) and the concentration of heavy metals analysed. In three localities, more detailed studies were done focusing on the people affected by BEN against the potable water sources used over 30 years. The analysis of water samples supports the hypothesis that heavy metals with a higher concentration than the accepted limit (in 41 of 42 sampling points, Cr values exceeded the maximum permissible concentration) have an important role in the appearance and development of BEN. The indepth study of three localities and the water sources used for long periods of time also supported the hypothesis.The results obtained support the idea of reconsidering the causes which contribute to BEN's appearance and development. The overlapping of localities of sick and deceased people with the extension of the ex- alluvial cone of the Danube of the Sarmatia Sea cannot be considered coincidental.

Key words: nephropathy, endemism, Pliocene coal, heavy metals, Chrome

1. INTRODUCTION

A series of studies done to consider some strategies to increase quality of life and local development identified the direct and indirect effects which the extension of Balkan Endemic Nephropathy (BEN) might have in the studied area. This is a severe disease which has a clinical evolution resulting in irreversible chronic renal failure. The major effects of the propagation of this disease are depopulation of the villages where it is prevalent and the *fear of place*, which affects territorial development.

This disease was analysed in numerous specialised studies, several hypotheses being suggested, but they were only partially confirmed. For example, in a study done in 1998, it was stated that BEN is determined by mico-toxin, especially ocratoxin A, which is fat-soluble and it is excreted with difficulty (Grollman et al., 2007; Shibutani et al., 2005; Clark & Snedeker, 2006; Grollman & Jelakovic, 2007; Tatu et al., 1998). In other studies some have suggested that geological structure has an essential role in the etiology of the disease (Mustaţă et al., 1968). The geological causes of BEN appear more frequently as a factor in the specialised studies done by the U.S. Geological Survey (Tatu et al., 1999).

Some researchers have advanced a hypothesis according to which BEN is caused by the deposits of Pliocene coal, these deposits having the most reduced degree of carbonization and containing a series of toxic organic compounds (Feder, 1975; 1979). The overlapping of the areas where BEN is prevalent with the regions with important reserves of Pliocene lignite suggest that the water which washes these deposits results in strong contamination with organic compounds (Tatu et al., 2000). The relationship between the deposits of Pliocene coal and BEN is underlined by Orem as well in studies done after 1999. The water which washes the deposits and then infiltrates into the soil is considered the source of BEN (Orem & Feder, 1999; Goldberg et al., 1994). This relationship is also underlined by other authors who brought to the public's attention the risks of settlements in areas with coal deposits from the Pliocene age (Finkelman, 1991). A serie of studies done in the 1990s show the areas of BEN spreading in the Balkans. This has raised new questions about the causes of BEN (Hall, 1992; Modalca et al., 2010).

In Romania, the disease was discovered in 1958, when doctors from the CFR Hospital in Drobeta Turnu Severin noticed 52 cases of uremia from the 162 households in the village of Ergheviţa. Further research showed that the number of affected people was much larger, out of which 70 percent women were aged between 30 and 40. The deaths recorded during the interval 1950-1953 due to BEN included only women. Another interesting observation was the concentration of sick people in certain families (Gluhovschi et al., 1966). The results of the research regarding the causes of BEN in Romania were synthesised in a monogram which came out in 1994. Environmental hypotheses regarding the determinants of BEN were presented as determinants in its appearance (Gluhovschi et al., 1994).

The first research done in Bulgaria, in the settlements with a large number of people affected by BEN advanced the hypothesis of intoxication with heavy metals, as the villages were provided with water coming from the nearby carst. The studies done previously developed this hypothesis, namely the high concentration of titanium, aluminium, chrome, copper, plumb, zinc, tin, cadmium, bismuth, molybdenum, nickel, cobalt, vanadium, wolfram, uranium (Nikiforov, 1960). Consequent research from other settlements better underlined this theory (Bachev, 1966; Angelieva & Mladenova, 1979) and, even if results are inconsistent, this is a plausible research direction. In Serbia, significant results in identifying the causes of BEN were obtained, where over 360 settlements were affected (Radovanovic, 1979).

2. MATERIALS AND METHODS

The starting point of this study was the use of statistical records of the number of people suffering from BEN at the local level. Spatial projection of the distribution of this endemic disease was done and the evolution of the number of patients on dialysis and the number of deaths resulting from BEN estimated.

Local households where people with BEN were registered, and water samples from the sources used for a long period of time were gathered. In the localities of Ciochiuţa, Boceni and Poroiniţa questionnaires were distributed, and on this basis the households with BEN cases were identified. All necessary permits were obtained for the described field research in South Western Romania (Oltenia). Collection of water samples and interviews of local villagers were conducted after the informed consent of the villagers was obtained. Due to the non-clinical and non medical nature of our research, and keeping in mind cultural consideration, verbal consent was obtained rather than written consent. The villagers consent it was necessary for collecting of water samples from their households, and to apply surveys and interviews. We asked, in three cases, to villagers to give us a written consent, but they totally refused it. It was, clearly, the existence of a strong fear root against written declaration, may-be, coming from the former totalitarian regime. The taken measures during the documentation process were focused on: relevance of the statistical information, selection of the representative villages, discussions with local authority and the citizens, identifying of the affected families, definition of the main steps for a honest results of interviews and the surveys, crossing of the information to identify the households using the same water sources, obtaining of the permission to collect the water samples, verifying of the water sample recipients, transportation conditions of the collected samples, choosing the laboratory for analysis, interpretation of the all obtained data.

The interdisciplinary analysis also examined the geological basins in the areas affected in order to identify the eventual determinants in the Quaternary deposits from these areas related to BEN.

3. RESULTS

3.1. The Spatial and Temporal Analysis of BEN

At present, in Romania the disease is spread in over 100 villages grouped in 4 areas: Ergheviţa-Bistriţa-Hinova; Vânju Mare; Strehaia; and Oraviţa-Reşiţa. In this study, research was concentrated in the areas Ergheviţa-Bistriţa-Hinova, Vânju Mare,

and Strehaia, areas in which the number of sick people increased (Fig. 1).

Research done after 1958 identified other localities affected by BEN: Ciochiuţa, Poroiniţa, Erghevita, Bistriţa, Poroina, Izvorul Aneştilor, Severineşti, Şimian, Cerneţi, Dedoviţa Veche, Fântana Domnească, Ghelmegioaia, Corcova, Jirov, Stângăceaua, Bârlogeni, Bărzuica; Tâmna, Brezniţa-Motru, Deleni, Ruptura, Buiceşti, Ţânţăreni, Văgiuleşti, Vânjul Mare, Batoţi, Livezile, Husnicioara, Hinova.

Analysis of statistical data regarding BEN from the dialysis centre of Drobeta Turnu Severin shows a continuous increase in the number of people on dialysis and of the affected localities. It should be noted that the low numbers at the beginning of the data are an artifact of the development of the medical assistance system in the region and do not reflect the prevalence of BEN prior to the time period analysed or the early stages of the trend lines (Fig. 2).

Water samples were collected from the affected localities. The establishment of sampling points was done on the basis of the questionnaires distributed to identify water sources used by the affected households. Out of the 42 water sources selected, two samples were gathered from each (2010), the first after a long rainy period, and the second in September, after a dry period. The samples were analysed for their content of heavy metals to verify the hypothesis of geological and paleo-geographical determination of BEN.

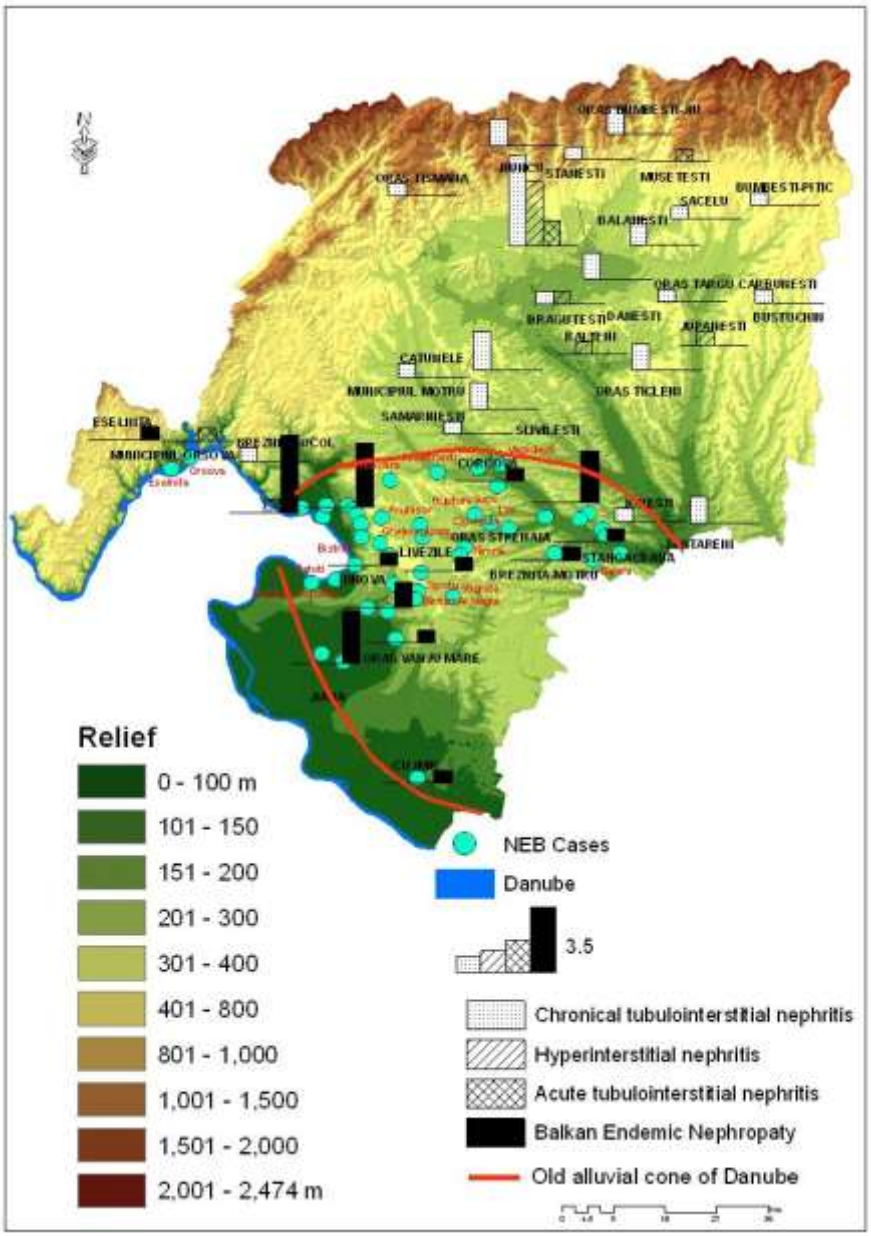
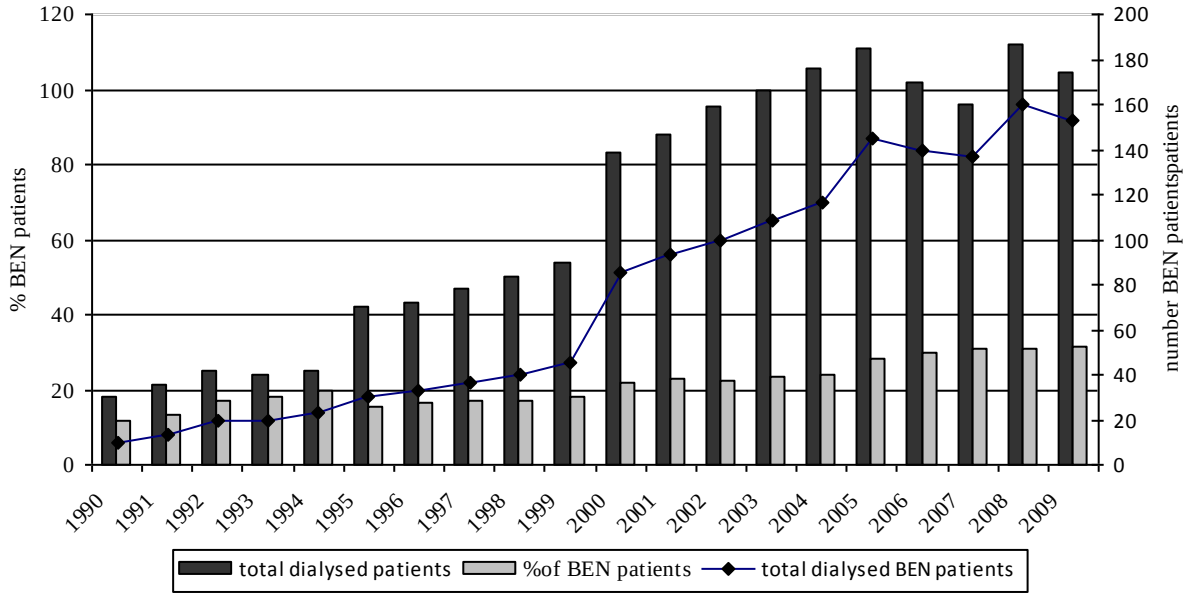


Figure 1. Territorial distribution of the BEN Cases



Source: Modalca et al., 2010, with adjustments

Figure 2. The evolution of the number of patients recorded at the dyalisis centres from Drobeta Turnu Severin

The very high concentrations of the heavy metals from the analysed wells and rivers (Table 1) show the important role of heavy metals in the determination of BEN. The results of the analysis shows unusually high values of chrome, plumb, cadmium, iron and copper, exceeding by far the allowed maximum concentrations in Romania.

3.2. The Geological Context of BEN Analysis.

Within the crystalline schists from the Danube Autochton from the Danube corridor, massifs of ultrabasic rocks and gabbros appear, at Iuţi and Plavişeviţa. Ultrabasic rocks are serpentinized and they separate the massif of gabbros in two parts. The massif of serpentinites consists of dunites, harzburgites, serpentinized wehrlites and they were studied in detail by (Codarcea & Krautner, 1935), (Bercia & Bercia, 1962). In the serpentinites' mass there are small rock bodies represented by troctolites and pyroxenites.

Within the serpentinized ultrabasic from Tişoviţa and Eibenthal there is chrome ore (Petrulian, 1935). The chrome ore contain crystals and nodules of picotite which have chromite inside, reaching up to 50 percent of the rock. In addition to disseminate the ore, bands and compact chromite ore lens appear. Chromite ore lenses have tens of meters in size and reach a content of up to 40 % Cr_2O_3.

Another possible source of chrome is represented by the ophiolites from the Severin nappe, ophiolites representing oceanic crust fragments. Within the Severin nappe, the ophiolites constitute a magmatic basic and ultrabasic formation. The sequence of ophiolites formation is (Ilie et al., 2010) the following: ultramaphic rocks, mafic cumulates, differentiated intrusive complex, and pilow lava. Its composition also consists of serpentinized ultramafic rocks and basalts. Within the serpentinites from the Severin nappe, lences of magnetite were emphasized (Popescu et al., 1998) that might also contain chrome. Ultramafites have an inhomogeneous distribution and they are represented by dunits, harzburgites, wehrlites and lherzolites. The presence of chromites was noticed (Ilie et al., 2010) in harzburgites as granules with sub-millimeter size. Basaltes are mostly chloritized having a greenish-olive colour. In basaltes, olivines frequently appear and it is possible to have chrome as trace element.

Fragments from these rocks are found in the Quaternary deposits of the old alluvial cone from the area of the Mehedinţi district and whose source-area is represented by the formations previously described. The rocks with chromite having a high density are concentrated nearby the source-area. Trivalent chrome, as it is found in the chromite, is less toxic. In exogenous conditions, under the action of external agents, it transforms into hexavalent chrome, having a high toxicity and being considered a human carcinogen (Zhitkovich 2011). In natural aquatic environments trivalent Cr is oxidized to hexavalent Cr by manganese dioxide, (Callender 2005). Chrome is re-mobilised in this form from fragments of rocks from Quaternary sands and gravels and carried along in the studied springs from the studied area.

An interesting observation is the localising of

water sources from the areas affected by BEN in large torrential basins, where accentuated erosion led to the interception of some aquifer beds. The lenticular structure of the deposits in an alluvial cone explains the possibility of the relative isolation of some underground waters (with high concentration of heavy metals) and their interception, either naturally (the apparition of springs), or anthropogentically (wells).

The research above emphasizes the concentration of sick people in certain areas of the localities and the high values of the concentration of heavy metals.

Table 1. The concentration of heavy metals in the sources of potable water and in rivers

Nr. Crt.	**Localising**	**Lat N**	**Long E**	**Cr [ppm] [mg/l]**
1	Barlogeni	44.56.885	23.45.141	0,310
2	Barlogeni	44.56.885	23.45.141	0,400
3	Stangacea	44.61.342	23.30.262	0,421
4	Stangacea	44.61.098	23.30.744	0,468
5	Motru River	44.59.972	23.29.227	0,421
6	Stancesti	44.61.674	23.26.513	0,452
7	Stancesti	44.61.736	23.26.511	0,412
8	Strehaia	44.62.088	23.21.234	0,395
9	Comanda	44.63.231	23.18.666	0,458
10	Ciochiuta	44.60.300	23.11.646	0,403
11	Ciochiuta	44.60.230	23.11.429	0,412
12	Ciochiuta	44.60.306	23.11.509	0,356
13	Valea Ursului	44.58.970	23.06.331	0,395
14	Prunisor	44.60.784	22.88.859	0,299
15	Dunare	44.62.088	22.65.270	0,329
16	Erghevita	44.60.478	22.78.342	0,484
17	Erghevita	44.60.608	22.78.289	0,375
19	Erghevita	44.60.874	22.78.071	0,403
20	Hinova Brook	44.53.719	22.77.535	0,468
21	Hinova	44.53.720	22.77.536	0,375
22	Hinova	44.53.721	22.77.539	0,458
23	Hinova	44.53.726	22.77.535	0,551
24	Oravita Brook	44.28.26.86	22.48.36.22	0,477
25	Poroinita	44.28.09.55	22.50.48.95	0,028
26	Poroinita	44.28.24.67	22.51.04.32	0,110
27	Poroinita	44.28.21.74	22.50.50.26	0,146
28	Poroinita	44.28.01.91	22.51.03.13	0,082
29	Poroinita	44.28.11.14	22.50.50.92	0,132
30	Poroinita	44.28.21.74	22.50.50.26	0,069
31	Livezi	44.30.40.46	22.51.52.30	0,071
32	Livezi	44.30.38.70	22.51.52.57	0,188
33	Livezi	44.30.42.91	22.52.05.08	0,143
34	Boceni	44.33.28.95	22.59.36.53	0,229
35	Boceni	44.33.43.12	23.00.10.00	0,111
36	Barzuica	44.34.13.74	23.00.58.33	0,161
37	Barzuica	44.34.20.28	23.00.56.12	0,118
38	Barzuica	44.33.54.87	23.01.16.62	0,176
39	Barzuica	44.33.43.42	23.01.22.99	0,196
40	Barzuica	44.34.06.41	23.01.09.33	0,082
41	Barzuica	44.35.46.58	23.19.20.99	0,085
42	Barzuica	44.37.35.86	23.17.29.74	0,165
CMA				**0,05**
	The concentration of heavy metals in the areas represented in figures 3,4,5			
	Values over the maximum admitted concentration			

An important argument supporting this theory which states that heavy metals (probably Cr) generate BEN is the analysis of the exposure of households in the perimeter of the settlement. In Ciochiuţa the people affected by BEN are localised around the same water source which has been used for a long period of time as potable water (Fig. 3).

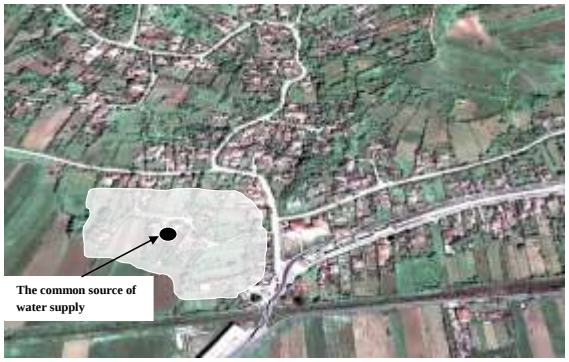


Figure 3. The concentration of the households affected by BEN in the locality Ciochiuţa

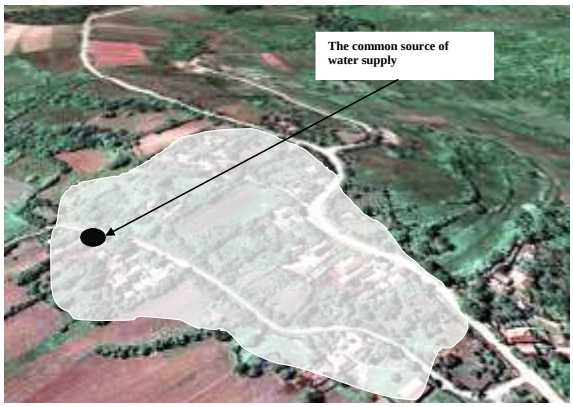


Figure 4. The concentration of the households affected by BEN in the locality Bărzuica

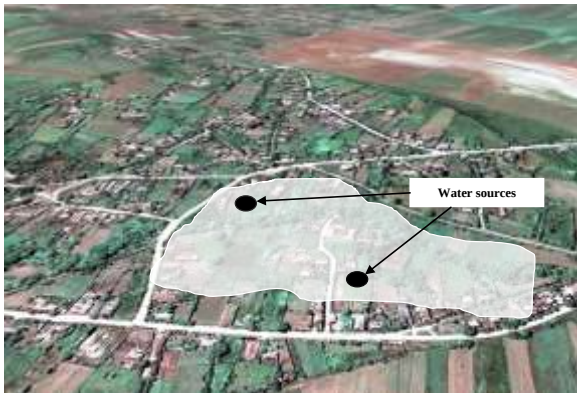


Figure 5. The concentration of the households affected by BEN in the locality Poroinița

In the locality of Bărzuica, known for the large number of affected people, seven water samples were gathered from the wells used for more than 10 years. The values recorded exceeded many of the maximum allowed concentrations. Based on interviews, the area around a water source used for more than 30 years was analysed. Over 90 percent of the people interviewed declared they have or had renal problems (Fig. 4).

The analysis of the water samples taken from Poroinița underlined the same issues of maximum allowed concentrations for heavy metals exceeded, as well as the similar percentages of people affected around some water sources used for long periods of time (Fig. 5).

4. CONCLUSIONS

The results obtained confirm the hypothesis that the concentration of the cases of deaths and sicknesses show a strong correlation with the sources of the local water supply in the various communities. These sources are relatively isolated, consisting of both natural springs and wells where it is possible to intercept beds with pseudo-fossil underground waters (waters which stayed for long period of time in contact with deposits containing heavy metals). Only a substantial supply from the same water source over a long period of time explains the clustering of deaths and sicknesses in the areas identified.

The majority of the studies considered suggest there might be a direct connection between the frequency of BEN and the existence of the beds of Pliocene coal. The comparative analysis of the spatial distribution of all types of nephrites from the north west of Oltenia shows that the presence of BEN in a very exact area. Compared to the other types of nephrites, it can be determined that certain geological deposits result following the deposition in lens structures of the sediments brought by the Danube, after the river crosses mountainous space. The areas crossed are known for the important content of heavy metals and especially Cr, which can also explain the high weight of the concentrations from the hilly area from the east-south-east. In contrast, the localities known for their exploitation of Pliocene lignite, inclusively at the surface (Braghină et al., 2009), from Gorj County (situated to the North of the limit of the alluvial cone) did not record cases of BEN during the interval 2002-2009.

The limits of the study might be demonstrated if research done in other areas from the Balkans confirmed that most of the cases concentrated around some sources of potable water in the rural environment and their existence was outside some Pliocene or Quaternary geological deposits, situated at the base of some mountainous areas rich in

serpentinites. The interviews of the affected households met numerous difficulties, due to the refusal of some inhabitants to admit that someone in the family is suffering from BEN, for the fear of social exclusion (problems related to marriage, especially the children's marriage). Numerous persons underlined this fear because young people which come from the families affected by BEN are considered certain victims of this disease.

The main conclusions are: the relationship between the spatial clustering of BEN and coal exploitation does not confirm that coal mininig is responsible for the production of some of the heavy metals, especially chrome. Research must be continued with concrete determinations of the relationship between the mechanisms of the disease appearance and influence of chrome, as well as extensions of the analysed area to some wider geographical area in the Balkans, and characterized by the incidence of this disease.

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