

CRITICAL EVALUATION OF ENVIRONMENTAL EXPOSURE AGENTS IMPLICATED IN THE ETIOLOGY OF BALKAN ENDEMIC NEPHROPATHY

**Thomas C. VOICE¹, David T. LONG², Zoran RADOVANOVIC³,
James L. ATKINS⁴, Shawn P. MCELMURRY¹, Nedialka D. NIAGOLOVA⁵,
Evangelos A. PETROPOULOS⁶, AND Varban S. GANEV⁷**

¹Civil & Environmental Engineering, Michigan State University, USA; ²Geological Sciences, Michigan State University, USA; ³Epidemiology, Kuwait University, Kuwait; ⁴Walter Reed Army Institute of Research, USA; ⁵National Centre of Radiobiology & Radiation Protection, Bulgaria; ⁶Institute of International Health, Michigan State University, USA; ⁷Medical University of Sofia, Bulgaria;
E-mail: voice@msu.edu

EXTENDED ABSTRACT

Balkan Endemic Nephropathy (BEN) is a kidney disease that has been reported in only certain rural villages in Bosnia, Bulgaria, Croatia, Romania and Serbia. The cause of BEN remains a mystery, but researchers seem to agree that exposure to one or more environmental agents is at least partially responsible. In this study we 1) tested three previously identified hypotheses for exposure that may occur through drinking water, soil or food: nitrogen compounds, organic compounds that leach from lignite deposits, and heavy metals, 2) integrated these findings with the existing body of literature on proposed environmental exposure agents and 3) proposed criteria for testing hypotheses on environmental agents and used these criteria to critically evaluate the evidence on those hypotheses that have been suggested to date.

Data collected in the Vratza endemic region of Bulgaria indicate that nitrate levels exceed drinking water guidelines in the majority of wells, and in springs in endemic villages. This suggests a pathway by which water supplies may become contaminated from surface sources. The presence of dissolved organic matter was clearly indicated in many of the drinking water samples, but no significant differences were found between BEN and non-BEN villages and elevated levels of PAHs were not found, as has been suggested previously. Differences in the concentrations of some heavy metals were found, and uranium exceeds drinking water guidelines in both types of villages.

On the basis of this investigation and a thorough review of the existing literature on other hypothesized agents, six criteria were developed for evaluating environmental hypotheses in the etiology of BEN. All of the previously hypothesized agents were evaluated by a panel of BEN researchers and a consensus statement on each was produced. The panel concluded that the strongest case is found for mycotoxins, but the specific compound may be unidentified, and may include ochratoxin A. Other agents which should be considered in future studies include inorganic agents that have not been adequately studied, perhaps a heavy metal, and viruses.

Key words: Balkan endemic nephropathy, environmental exposure agents, nitrate, nitrite, ammonia, polycyclic aromatic hydrocarbons, heavy metals