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February 1, 1961

Robert A. Kehoe, M.D.
University of Cincinnati
The Kettering Laboratory
College of Medicine-Eden Avenue
Cincinnati 19, Ohio

Dear Dr. Kehoe:

Thank you for your very informative letter of January 21. I am extremely sorry that you did not write to me sooner, as the studies are essentially completed in Yugoslavia for this phase of our investigation.

Although, as you know, I am not an expert in the field of lead intoxication, I am well aware that the disease as it exists in Yugoslavia is certainly not classical lead intoxication, for indeed, none of the individuals in that area as far as I can determine, give a history of acute lead intoxication. As you mentioned, however, the press never tells the entire story and the problem over there is difficult. Briefly, there are at least 30,000 people dying of uremia and they are all located on one side of the Sava River. The other side, as far as we can determine, is essentially free of the disease. My original interest in this was derived from the historical fact that this is the area where much trench nephritis has occurred in 2 World Wars and also, this is the area where Fabry's Disease is known to occur. Preliminary studies before I went to Yugoslavia with a member of the Rockefeller Institute showed that the type 12 streptococcus known to cause kidney disease was also prevalent in the area. To confuse matters even more, Dr. Danilovic at the University of Belgrade had already published an article of which you are undoubtedly aware in the British Medical Journal concerning the origin of these cases of kidney disease, indicating that it was lead poisoning. Thus, a large group of people at the University of Belgrade feel that this is the cause of the disease. In contrast, in going over the data with Dr. Radosevic in Zagreb, we found that his studies already published in the Yugoslavian medical literature showed that of 45 cases, the majority had high normal or only slightly elevated lead values. In his experience, these were much lower than those observed in acute lead poisoning. He feels that these cases are not due to lead poisoning. To confuse matters even more, the professor at the University of Sarajevo obtained some specimens, split them in half, and sent one set to the toxicologist

in Belgrade who did the determinations for Dr. Dr. Danilovic, and the other half to a well-recognized toxicology laboratory in London. The results from London were normal and the results from Belgrade were elevated. Thus he feels there is no evidence for lead. I myself spent only two weeks in the field examining patients and briefly looking at some of the epidemiological evidence. From this preliminary survey it seemed highly unlikely that the kidney disease was due to an infectious agent. Dr. Gustave Dammin of Harvard University saw some of the specimens and agrees with this opinion. Unfortunately, outside of the studies in Zagreb, there have been very few pathological studies attempted. In those that have been done, the definition of the source of the material has not been clear. Thus the entire situation is quite hazy. In view of the confusion concerning lead intoxication, we decided that a quick survey should be made concerning lead before a larger and more thorough epidemiological study including possible infectious agents was undertaken. Thus we decided to institute a rapid survey of a group of 45 patients early in January. This study will be completed this week. The study is being conducted by Dr. Robert Griggs with the assistance of Dr. I. Sunshine, toxicologist from the Coroner's Office in Cleveland. To ease your mind, this survey is very inexpensive and will cost less than $5,000. It should yield information of value to the Yugoslavs and also will more clearly delineate our problems of the future.

The renal lesions are peritubular and not glomerular, develop slowly and primarily attack the older age group. I would hope that when Dr. Griggs returns next week and if there is any new information, he might have the opportunity to go to Cincinnati and discuss any suggestions you might have.

I hope this note will relieve your mind concerning the concept in relation to the disease that exists there and also to assure you that we feel the small investment of the National Heart Institute is not being wasted. We certainly would appreciate any suggestions you might have.

Very sincerely yours,

Charles H. Rammelkamp

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