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Correlation of Lead and Cadmium in Human Urine

Beginning in May 1973 the analysis of urine for the presence of cadmium has been performed in this laboratory on a routine basis. During the following months, the subjective impression emerged that when elevated urinary concentrations of lead were found, urinary cadmium concentrations were often elevated also. The present study was undertaken to evaluate the possible statistical relationship between the elevated concentrations of these two elements.

During the 15 months between May 1973 and August 1974, 1013 urine samples were submitted to this laboratory for analysis for heavy metal element concentrations. All samples of adequate volume to permit multiple analyses were assayed for cadmium, as well as for lead, mercury, and arsenic. The samples for this study were collected from inpatients at seven Marion County, Ind. hospitals, in addition to those from the Indiana University Medical Center, Indianapolis, Ind.

The lower convenient concentration limit for cadmium by the method employed in this study is 1 μg/l of urine, and the vast majority of all samples were found to contain concentrations of cadmium at or below this value. Since an arbitrary lower limit for inclusion in the body of data for the statistical analysis had to be established, only cases in which the urinary cadmium concentration exceeded 1 μg/l were reviewed. From this laboratory, only lead concentrations in excess of 50 μg/l of urine are reported to exceed the maximum normally occurring value. Therefore, only cases in which the urinary lead concentrations exceeded this value were reviewed for the statistical study.

Methods

All analyses were performed by atomic absorption spectrometry, using a Perkin-Elmer Atomic Absorption Spectrometer, Model 305. Both elements were analyzed by essentially the same technique, employing an appropriate volume of once-diluted urine [*1*]. The tantalum boat was used to contain the sample for analysis. Lead determinations were performed at 284 nm, and cadmium determinations were performed at 229 nm. Aqueous standard solutions were assayed simultaneously, and quantitation was done from a standard curve.

All statistical data reductions were performed by standard computer procedures [*2*].

Results

Figure 1 shows that 788 of the total of 1013 samples were of adequate volume to permit analysis for cadmium as well as the other requested metal elements. Of these 788, 426, or

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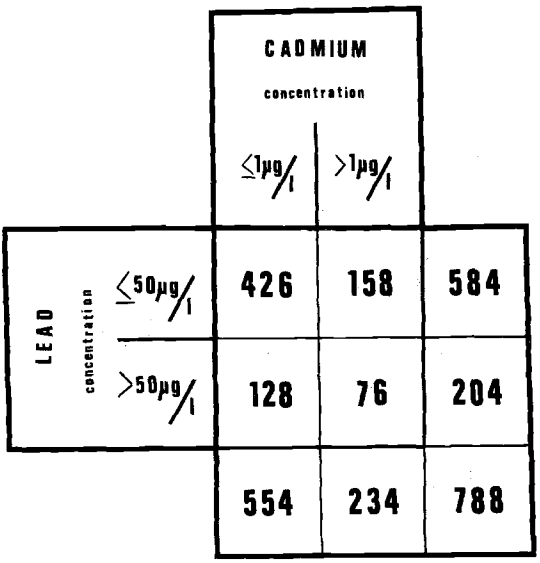

FIG. 1—*Number of cases and urinary concentrations of lead and cadmium.*

54%, were below the critical concentration of both elements arbitrarily set for inclusion in the statistical study and were considered toxicologically nonsignificant. One hundred twenty-eight, or 16%, had lead concentrations in excess of 50 μg/l but had cadmium concentrations of 1 μg/l or less. Another 158, or 20%, were found to have cadmium concentrations greater than 1 μg/l but to contain 50 μg/l or less of lead. Of the 788 analyzed, 76, or 10% of the total, were found to have concentrations of both cadmium and lead which exceeded the minimum criteria for review.

Of the 204 samples which contained more than 50 μg lead/l, 76, or nearly 40%, contained more than 1 μg/l of cadmium, also. These 76 cases were reviewed for further evaluation. The question under consideration was "When the concentrations of lead and cadmium simultaneously exceed 50 μg and 1 μg/l of urine, respectively, are the two concentrations further elevated in a related fashion?"

For the statistical evaluation, 21 cases were deleted from these 76. Five were rejected on the basis of their having been collected from patients who had previously been administered pharmacotherapy for lead intoxication, known to produce inappropriately high urinary lead concentrations [*3*]. An additional 16 individual cases were rejected because the urine samples were known to have been randomly collected; that is, the samples were known not to have been collected continuously over a 24-hour period. It has been shown that urinary lead excretion is continuous, but highly variable, throughout a diurnal period [*4*].

Figure 2 shows the mean lead and cadmium concentrations from randomly collected and 24-hour continuously collected urine samples compared by Student's *t* test. Comparison of the mean lead concentrations from the two sample groups revealed no significant difference between them. However, a substantially lowered mean cadium concentration was found in the randomly collected urine samples when compared to that from the samples collected continuously over a 24-hour period. It was felt, therefore, that the randomly collected urine samples less reliably reflected the total body cadmium content and should be rejected. For these reasons, only data from patients who had presumably received no metal-directed therapy prior to collection of the urine sample for analysis

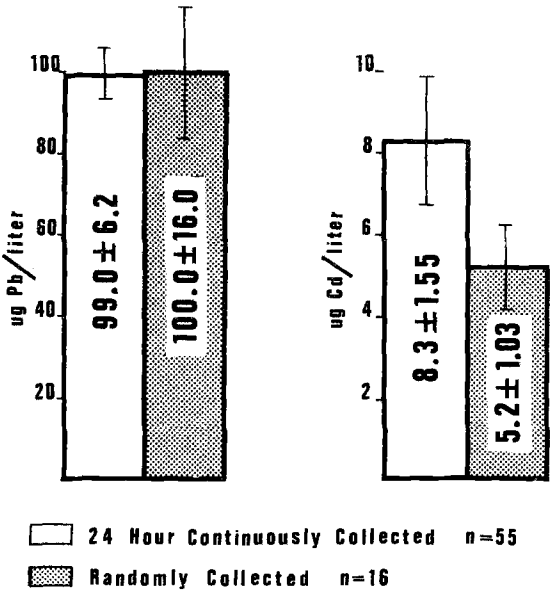

FIG. 2—*Mean (± standard error) urinary concentrations of lead and cadmium.*

and whose urine had been collected continuously over a 24-hour period were included for analysis.

Although the correlation was modest (correlation coefficient = 0.42) due to the small sample size and very high inherent variability, regression analysis revealed that when the urinary lead concentration was greater than 50 μg/l and the urinary cadmium concentration was greater than 1 μg/l, a highly significant positive linear relationship existed between the two. The mean apparent increase in cadmium concentration as a function of increasing lead concentration is shown, with the standard error of that change, in Fig. 3. There is an approximately 1 to 10 ratio of cadmium to lead concentration throughout the range of values encountered in this study.

Discussion

These studies have shown that intoxication by more than one metal element at the same time may well be more common than might be naively suspected. The particular combination of cadmium and lead is strongly suggested. Two of every five samples tested which contained toxicologically significant concentrations of lead also contained elevated concentrations of cadmium. Above the nontoxic urinary concentrations as defined in these studies, a linear relationship exists between the concentrations of these two elements. These studies have, also, reinforced the importance of continuously collecting urine samples over a 24-hour period for analysis of metal elements.

Multiple element intoxication should be entertained in the determination of diagnosis and treatment of any possible heavy metal intoxication.

Summary

A statistical evaluation of the relationship between elevated concentrations of lead and cadmium in human urine is presented. The importance of the 24-hour continuously collected urine sample is confirmed.

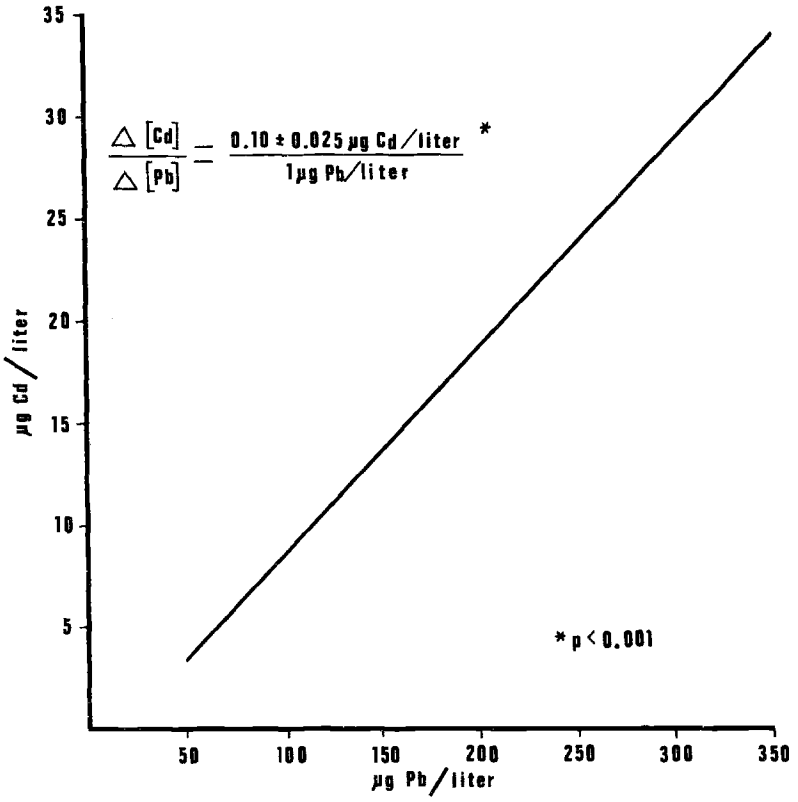

FIG. 3— *Linear relationship between urinary concentrations of lead and cadmium.*

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