

# Elevated Blood Copper/Zinc Ratios in Assaultive Young Males<sup>1</sup>

WILLIAM J. WALSH, H. RONALD ISAACSON,<sup>2</sup> FATIMA REHMAN AND ANMARIE HALL

*Health Research Institute, 1804 Centre Point Drive, Suite 102, Naperville, IL 60563.*

Received 23 October 1996; Accepted 10 December 1996

WALSH, W.J., H.R. ISAACSON, F. REHMAN AND A. HALL. *Elevated blood copper/zinc ratios in assaultive young males.* *PHYSIOL BEHAV* 62(2) 327–329, 1997.—In research conducted over the past 20 years, we have observed abnormal trace-metal concentrations, including elevated serum copper and depressed plasma zinc, in blood samples collected from violence-prone individuals. The purpose of the study reported here was to test the validity of our observation that assaultive young males have elevated blood copper/zinc (Cu/Zn) ratios when compared to a control group of young males with no history of assaultive behavior. All male patients between the ages of 3 years and 20 years who made a first visit to the outpatient Pfeiffer Treatment Center in Naperville, Ill., during a two-month period were evaluated. Based on interviews with patients and their families and application of a standardized behavior scale, 135 assaultive young males and 18 controls with no history of assaultive behavior were identified. Blood samples were collected from test subjects and controls and analyzed for serum copper and plasma zinc concentrations by an independent laboratory using atomic absorption methods. The median Cu/Zn ratio for the assaultive subjects was 1.40 compared to 1.02 for controls, a statistically significant difference ( $t = 5.94$ ;  $p < 0.01$ ). © 1997 Elsevier Science Inc.

Copper/zinc ratios  
imbalance

Zinc deficiency

Elevated copper

Behavior disorders

Assaultive behavior

Biochemical

IN recent years, research into understanding the relationship between human body chemistry and human behavior has increased. Preliminary evidence suggests that chemical imbalances in the body may be as important an influence on behavior as are poverty, abuse, and other environmental factors that have traditionally been accepted as the root causes of aberrant behavior (21).

We have studied the relationship between biochemical imbalances, including abnormal trace-metal concentrations, in behavior disordered children and criminals for the past 20 years (23). Recently, our research has focused specifically on the effects of abnormal concentrations of copper and zinc.

## *Zinc Deficiency, Metal Metabolism and Behavior Disorders*

Zinc is an essential trace metal which is a component of more than 80 enzymes, and zinc deficiency has long been recognized as playing a role in a number of physiological disorders, including dermatologic conditions such as eczema, acne, and psoriasis; poor wound healing; growth retardation; delayed sexual maturity; hypogeusia and chronic immunodeficiency (1,3,6–9,11,12,14–18,20,22,24). In most cases, abnormally low levels of zinc appear to involve a malfunction of the metal-binding protein metallothionein (10,13).

Zinc has been found in high concentrations in brain hippocampus, and it has been postulated that it may modulate neuro-

transmitter and synapse functioning (5). Although its precise role is not fully understood, low zinc levels at these sites could alter neuron activity, thus affecting behavior. Further, zinc deficiency often results in elevated levels of copper in the blood due to the dynamic competition of these metals in the body (2). Elevated copper has been associated with hyperactivity (23) and schizophrenia (19).

## *Observations of Abnormal Trace-Metal Concentrations in Violence-Prone Individuals*

At the Pfeiffer Treatment Center, a not-for-profit outpatient clinic operated by Health Research Institute (HRI), we have collected blood samples and tested them for trace-metal concentrations in a population of approximately 5,000 patients evaluated for a variety of behavior disorders since 1989. We have observed that many of these patients have symptoms of zinc deficiency along with depressed levels of zinc in their blood plasma. We have further observed a strong relationship between patients exhibiting violent behavior and abnormal levels of copper and zinc in the blood. These observations corroborate ongoing HRI research, conducted over the past 20 years, during which we have collected and tested blood and hair samples for trace-metal concentrations in a population of adult criminals (23).

<sup>1</sup> First presented as a poster at the 24th annual meeting of the Society of Neuroscience in Miami Beach, Fla., November 18, 1994.

<sup>2</sup> Correspondence and reprint requests should be directed to H. Ronald Isaacson, Health Research Institute, 1804 Centre Point Drive, Suite 102, Naperville, IL 60563.

### Study Objective

In a preliminary retrospective test of 49 behavior-disordered young males and 17 normals, the test group exhibited a median Cu/Zn ratio of about 1.5 compared to 1.0 for the normals (23). Based on these results, we designed an experiment to test the hypothesis that Cu/Zn ratios in the blood of violent young males are elevated compared to Cu/Zn ratios in non-violent young males.

### METHODS

#### Patients

All male patients between the ages of 3 years and 20 years making a first visit to the outpatient center for evaluation of behavior disorders between January 15, 1994, and March 15, 1994, were enrolled in the study. Patients with a history of mental retardation, autism, head injuries or schizophrenia were excluded from the study. The patients were divided into two groups: A test group of individuals who had a history of frequent assaultive behavior, and a control group of individuals who had no history of assaultive behavior.

#### Screening for Violent Behavior

Test subjects and controls were interviewed by a trained interviewer during an intake session. The evaluations included in-depth medical histories and interviews of 35 to 45 min in length conducted with patients and/or their families, coupled with application of the Walsh-Isaacson Behavior Scale [Figure 1].

The interviewer probed for information about the types and frequency of violent or assaultive behavior exhibited by the patients. The Walsh-Isaacson Behavior Scale was used to assign numerical values to violent behavior by ranking it on a scale that measures both the intensity and the frequency of the behavior.

Using information gathered during the intake interview, behavior disorders exhibited by the patients were assigned numerical values ranging from 1 to 5 based on the type, or intensity, of the behavior. The interviewer also probed for information on the frequency of assaultive behavior, which was categorized according to Figure 1, with no occurrence of assaultive behavior receiving a score of 0.0.

A total of 153 subjects—135 assaultive young males and 18 controls—were identified using this protocol.

#### Profile of Subjects

Patients in the study were males from 27 states throughout the United States ranging in age from 3 years to 20 years. Subjects in the test group ranged from 3 years to 20 years in age,

| <u>Behavior Intensity</u> | <u>Behavior Frequency</u> |
|---------------------------|---------------------------|
| 1. Normal Behavior        | 1. Yearly                 |
| 2. Verbal Assaults        | 2. Monthly                |
| 3. Destructive Rages      | 3. Weekly                 |
| 4. Physical Assaults      | 4. Daily                  |
| 5. Aggravated Assaults    | 5. Many Times Daily       |

**Test Subjects:** Behavior Intensity 2,3,4, or 5

**Controls:** Behavior Intensity 1 (Normal Behavior)

FIG 1. Walsh-Isaacson Behavior Scale.

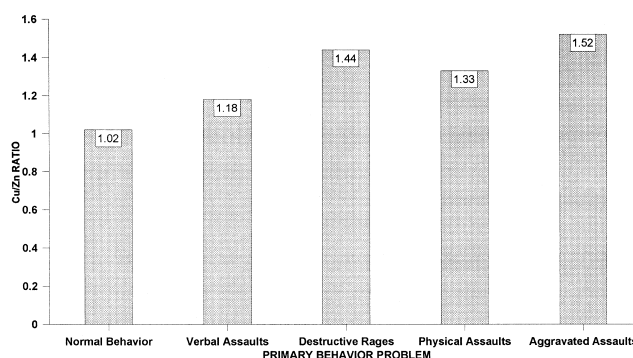


FIG 2. Copper/Zinc Ratio for various types of assaultive behavior.

with a median age of 9.5 years. Controls ranged in age from 5 years to 18 years with a median age of 10 years.

**Test subjects.** The primary behavior problems for the 135 subjects were verbal assaults/rages (18 percent); destructive rages (21 percent); physical assaults (42 percent) and aggravated assaults (19 percent).

The frequency of these behaviors was several times daily for 53 percent of the test subjects, at least once daily for 69 percent of the subjects, at least once weekly for 93 percent and at least once monthly for 99 percent.

**Controls.** The 18 young males in the control group had no history of verbal or physical assault, temper tantrums or other evidence of violence-prone behavior.

#### Measuring Cu/Zn Ratios

To obtain measurements of zinc and copper concentrations and ratios, two 2.5 ml samples of blood were drawn from each individual in both the test and control groups according to established protocols for blood collection and handling (19,4) and serum and plasma fractions forwarded for independent analysis by the SmithKline Beecham Clinical Laboratories (SKBL), which is accredited by the College of American Pathologists. Serum copper and plasma zinc concentrations were obtained using atomic absorption analysis. Plasma zinc has been reported to be a better indicator of zinc status than serum zinc (2). According to SKBL, normal values for plasma zinc and serum copper are: Plasma Zn (mcg/dl) Range 60–130; serum Cu (mcg/dl) 70–155 (4).

### RESULTS

The results and statistical analysis were as follows:

|  | <u>Mean Cu/Zn Ratio</u> | <u>Standard Deviation</u> |
|--|-------------------------|---------------------------|
| Assaultive subjects<br>( <i>n</i> = 135)   | 1.40                    | 0.54                      |
| Controls<br>( <i>n</i> = 18)   | 1.02                    | 0.18                      |
| <i>t</i> = 5.94 (one-tailed “ <i>t</i> ” test for unequal standard deviations) <i>p</i> < 0.01 |                         |                           |

The results were further categorized according to the intensities of behavior exhibited by the subjects, with the Cu/Zn ratio being highest in subjects with a history of aggravated assaults followed, in descending order, by subjects who exhibited destructive rages, physical assaults, verbal assaults and normal behavior [Figure 2].

## DISCUSSION

*Conclusion*

The hypothesis that assaultive young males have elevated blood Cu/Zn ratios compared to non-assaultive controls was supported by our experiment. These preliminary findings bear out our general observations that suggest a correlation be-

tween behavior disorders and abnormal metal metabolism or other irregularities in body chemistry, and our specific observation that elevated Cu/Zn ratios may play a role in violence-prone behavior. In addition, four separate outcomes studies have indicated significantly improved behavior after normalizing Cu/Zn ratios and other biochemical factors, using zinc and other nutrients (25).

## REFERENCES

1. Collipp, P. J.; et al. Zinc deficiency: Improvement in growth and growth hormone levels with oral zinc therapy. *Ann Nutr Metab* 26:287-291; 1982.
2. Cunnane, S. C. Zinc: Clinical and Biochemical Significance. Boca Raton FL: CRC Press, Inc.; 1988.
3. Cunningham-Rundles, C.; et al. Zinc deficiency, depressed thymic hormones and T-lymphocyte dysfunction in patients with hypogammaglobulinemia. *Clin Immunol Immunopathol* 21:387-394; 1981.
4. Directory of Services, SmithKline Beecham Clinical Laboratories; 1993.
5. Ebadi, M.; Murrius, L. C.; Pfeiffer, R. F. Hippocampal zinc thioneine and pyridoxal phosphate modulated synaptic function. In: Vitamin B-6. *Annals of the New York Academic of Sciences*, Vol. 585. New York: New York Academy of Sciences; 1990.
6. Ecker, R. J.; Schroeder, A. L. Acrodermatitis and acquired zinc deficiency. *Arch Dermatol* 114:937-943; 1978.
7. Golden, B. E.; Golden, M. H. N. Effect of zinc supplementation on the dietary intake, rate of weight gain and energy cost of tissue deposition in children recovering from severe malnutrition. *Am J Clin Nutr* 34:900-908; 1981.
8. Good, R. A., et al. Zinc and immunity. In: Prasad, A.S., ed. *Clinical, Biochemical, and Nutritional Aspects of Trace Elements*. New York: Alan R Liss; 1982.
9. Hambridge, K. M.; Walravens, P. A. Zinc deficiency in infants and preadolescent children. In: Prasad, A.S.; Oberleas, D., eds. *Trace Elements in Human Health and Disease*. Vol. 1. New York: Academic Press; 1976.
10. Hamer, D. H. Metallothionein. *Ann Rev Biochem* 55:913-951, 1986.
11. Heinkin, R. I.; Bradley, D. F. Hypogeusia corrected by nickel and zinc. *Life Sci* 9:701-706; 1970.
12. Henzel, J. H.; et al. Zinc concentrations within healing wounds: significance of post-operative zincuria or availability and requirements during tissue repair. *Arch Surg* 349:357-362; 1970.
13. Kagi, J. H. R.; Schaffer, A. Biochemistry of metallothionein. *Biochemistry* 27:8509-8515; 1988.
14. Laditan, A. O.; Ette, S. I. Plasma zinc and copper during the acute phase of protein-energy malnutrition (PEM) and after recovery. *Trop Geogr Med* 34:77-83; 1982.
15. McMillan, E. M.; Rowe, D. Plasma zinc in psoriasis. Relation to surface area involvement. *Br J Dermatol* 108:301-306; 1983.
16. Molokhia, M. M.; Portnoy, B. Zinc and copper in dermatology. In: *Zinc and Copper in Medicine*. Springfield, IL: Charles C. Thomas; 1980.
17. Sandstead, H. H.; Prasad, A. S.; et al. Human zinc deficiency, endocrine manifestations, and response to treatment. *Amer J Clin Nutr* 20:422-427; 1967.
18. Schmidt, K.; et al: Determination of trace element concentrations in psoriatic and non-psoriatic scales with special attention to zinc. In: *Trace Element Analytical Chemistry in Medicine and Biology*. Vol. 1. New York: Walter de Gruyter; 1980.
19. Smith, J. C.; Holbrook, J. T.; Danford, D. E. Analysis and evaluation of zinc and copper in human plasma and serum. *J Amer Coll Nutr* 4:627-638; 1985.
20. Sprenger, K. B. G.; et al. Improvement of uremic neuropathy and hypogeusia by dialysate zinc supplementation: a double-blind study. *Kidney Int Suppl* 16:5315-5319; 1983.
21. Understanding and Preventing Violence, Volume 2: Biobehavioral Influences. Resiss, A.; Miczek, K.; Roth, J., eds. Washington, D.C.: National Academy Press; 1994.
22. Van Rij, A. M. Zinc supplements in surgery. In: *Zinc and Copper in Medicine*. Karcioğlu, Z. A. and Sarper, R. M., Eds. Springfield, IL: Charles C Thomas; 1982.
23. Walsh, W. J.; Isaacson, H. R. Pfeiffer Treatment Center and Health Research Institute, Naperville, Ill.; unpublished data.
24. Withers, A. F.; Baker, H.; Musa, M. Plasma zinc in psoriasis. *Lancet* 2:278-282; 1968.
25. Walsh, W. J.; Isaacson, H. R.; Blab., L. B. Biochemical Treatment of Behavior Disorders. 149th Annual Meeting, American Psychiatric Association, New York, 1996.