Editor's Notebook: Bernard Rimland, Ph.D.

The most air-tight study in psychiatry? Vitamin B6 in autism

"Your psychiatric colleagues are a bunch of bigots!" I said. "They are not really interested in helping autistic children—all they want to do is downplay the value of vitamins and keep using those stupid toxic drugs!"

"No, you're wrong! Psychiatrists ignore your study because it was conducted by your small institute, which they've never heard of. Besides, you used your new computer-clustering design, rather than the usual double-blind, crossover design that psychiatrists like. If your study had been done at a major medical school, like this one, and had used conventional methodology, rather than the new design you invented, they would really pay attention to your work."

"I don't really believe that, Noch," I said to my friend Enoch (Noch) Callaway, M.D., who was then (in the 1970s) Professor of Psychiatry and Director of Psychiatric Research at the University of California Medical Center in San Francisco.

"Let's plan and carry out a really well-designed study, the best possible study, and do it from here, and you'll see—if the results are positive, they'll be accepted," he said.

"I don't believe that," I retorted.

"Let's try it," Noch insisted. "I'm sure we can get a grant to do it. I am very familiar with the grant procedures at NIMH, and I'll be glad to write the grant application. It will be the best-controlled, most air-tight study ever conducted in the field of psychiatry."

I was still skeptical, but I agreed, and we went to work on a grant proposal. Noch enlisted the assistance of Professor Pierre Dreyfus, the Chairman of the Department of Neurology at the University of California Medical School at Davis, near Sacramento.

I had recently completed a study of over 200 autistic children, using high doses of several vitamins, including vitamin B6, which turned out to be the most effective of the several vitamins in my study. About half of the children were found to have responded well to the vitamin B6, and I selected 16 of the responders for the new study. The sixteen were divided into two groups, matched on age, sex, weight, and severity.

Each of the 16 children was to be put through a 5-phase procedure as follows: Phase One—baseline; Phase Two—test period A (B6 or placebo); Phase Three—baseline two; Phase Four—test period B (B6 or placebo); and Phase Five—baseline three.

To measure changes, if any, in the children's behavior, a special "Target Symptom Behavior Checklist" was to be developed individually for each child after several visits, telephone calls, and mail contacts with the child's parents and teachers.

To help guard against the possibility of human error, urine specimens were to be collected at the ends of Phases Two and Four. Additionally, the remaining contents of the B6 and placebo bottles from Phases Two and Four were saved for laboratory analysis.

All three members of the research team, Callaway, Dreyfus and I, were experienced researchers with many publications. Despite that, we requested the Research Design section of the National Institutes of Mental Health to review our design and make any suggestions that might improve the study. The NIH research specialists made several minor suggestions, all of which we accepted. It would be the most air-tight, double-blind, placebo-crossover study ever conducted.

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>
> *Linus Pauling, two-time Nobel prize winner*

The study was conducted in the form of a giant triangle, with myself and our San Diego Institute being the anchor of the triangle, and Callaway and Dreyfus, each 500 miles north, being the other apexes.

After matching the 16 subjects into paired groups of 8, I sent the names and addresses to Dreyfus, who decided when each child would receive the vitamin B6. Only Dreyfus knew which child was given the B6 first.

The Target Symptom Checklists were completed by the parents, teachers, and local physicians, and sent to our Institute in San Diego. When all of the data had been collected, Callaway came to San Diego and he and I went through the complete data file for each child to determine, if we could, when the B6 had been given. We then telephoned Dreyfus with our decision for each child, except for Child 16, for whom we could find no difference between the placebo and the B6. Dreyfus compared our reports with his list, and informed us that we had correctly classified the B6 periods for 11 of the 15 children. In the case of the sixteenth child, the code said that bottle B had contained the B6. However, on analyzing the contents of the remaining capsules in the A and B bottles for Child 16, it was discovered that *both* bottles contained B6. Furthermore, the urine samples showed high levels of B6 in the urine for both phases. The source of this error is unknown, but Child 16 was removed from subsequent analysis.

Lab tests also showed a discrepancy in the case of Child 14. This was one of the 4 children whom we supposedly misclassified as being on placebo when according to the code he should have been on B6. However, the urine tests showed higher levels of B6 in the urine when he was supposed to have been on the placebo. The data for this child were left in the analysis, since they militated *against* the hypothesis.

Statistical comparison of the behavioral ratings for the 15 children while they were on the B6 versus the placebo showed a statistically significant difference: $P<.05$, thus confirming the value of the B6 and supporting the results of our previous study. The report appeared in the *American Journal of Psychiatry*, Vol. 135, April 1978, pp. 472-475.

Callaway was surprised by the positive results. He had felt that my previous experiment, involving some 200 children, in which I had used the new computer-clustering procedure, must have been in error. He was so impressed with the new results that the following summer, when he started his yearlong sabbatical at the Tours University Medical School in France, he brought with him a supply of vitamin B6 and magnesium and urged his colleagues in France to undertake follow-up studies in their population of hospitalized children. The French research group was extremely skeptical They argued that B6 was "so weak you couldn't kill someone with it if you wanted to"—so how could it do better than drugs powerful enough to kill? Callaway persisted, and the Tours researchers, under the direction of Dr. Gilbert LeLord, undertook a study on 42 hospitalized children, including some who were autistic. The results were so dramatic that even the skeptics changed their minds. They began a series of 12 studies, conducted over the next 10 years, during which the vitamin B6 was tried with children, with adults, with B6 alone, with B6 and magnesium, using behavioral, electrophysiological, biochemical, and conditioning criteria. *All* of the studies, including 11 double-blind, placebo-crossover studies, provided positive results—and did so safely. No adverse effects were reported.

Several subsequent studies, by researchers in Venezuela and Italy, also yielded positive results. Two-time Nobel prize-winner Linus Pauling stated, "My opinion, based on these Rimland studies and others, is that... treatment with vitamins and minerals should be tried for every autistic child..."

Despite positive results from (probably) the most air-tight study in psychiatry, and an unbroken series of 17 additional studies of B6 and magnesium in autism over a 30-year period, all yielding positive results, bigots continue to insist that there is no evidence that B6 and magnesium are effective in autism. A recent NIMH booklet on autism makes the blatantly false statement that "clinical studies of the vitamin (B6) have been inconclusive." Eighteen consecutive positive studies, including 11 double-blind, placebo cross-overs, are "inconclusive"!

Meanwhile, toxic drug use continues...