

Controversies in the Treatment of Autistic Children: Vitamin and Drug Therapy

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Abstract

A survey of approximately 4,000 questionnaires completed by parents of autistic children provided ratings on a variety of treatments and interventions. Among the biomedical treatments, the use of high-dosage vitamin B₆ and magnesium (n = 318) received the highest ratings, with 8.5 parents reporting behavioral improvement to every one reporting behavioral worsening. Deanol (n = 121) was next most highly rated, with 1.8 parents reporting improvement to each one reporting worsening. Fenfluramine (n = 104) was third, with a ratio of 1.5:1. Thioridazine hydrochloride (Mellaril), by far the most often used drug on the list (n = 724), was fourth with a helped-worsened ratio of 1.4:1. The research literature on the use of vitamin B₆-magnesium is briefly reviewed, and mention is made of recent findings regarding high-dosage folic acid in autism and biotin in Rett syndrome. (*J Child Neurol* 1988;3(Suppl):S68-S72).

The Institute for Child Behavior Research (ICBR) in San Diego was established in 1967 to serve as an international clearing house for information on autistic children. Since autism is a low-incidence disorder, it has been difficult for even the larger research centers to collect a substantial amount of case history data, inasmuch as the patients generally come from geographically limited area. ICBR currently holds in its data bank detailed case history information on over 9,600 autistic children from over 40 countries. Data are submitted for use in our research both by the parents of the children and by hundreds of professionals who cooperate in our research efforts.

A major function of ICBR is the collection of data which will permit us to evaluate the various forms of therapy—and there are many—which have been proposed as means of treating autistic children. By carefully monitoring the published literature, and by supplementing information gained from the literature with information acquired from the thousands of parents of autistic children with whom we correspond, we are able to provide parents and professionals with reasonably objective and up-to-date data for evaluating the treatment options available to them.

Although this paper concerns medical and nutritional treatments for autism, I would like to emphasize that the optimal treatment now available for autistic children is an intensive, carefully planned, highly structured educational program, preferably one based on the principles of behavior modification. Every other treatment that has been proposed for autism must be considered controversial.

Starting in 1967 and continuing to this day, ICBR has been collecting from parents their evaluations of a variety of drugs, and other treatments, using our questionnaire, Form E3. We now have approximately 3,500 completed E3 forms in our database. Additionally, as the result of a recent mailout to supplement the information on Form E3, we received returns on an updated drug treatment questionnaire, submitted by more than 1,000 parents. The complete data analysis will be made available at a later date in our newsletter, the *Autism Research Review International*, and in other publications available from our institute. The following may be considered a preview of those findings.

Form E3 asks the parents to evaluate the various treatments afforded the child, on a six-point scale, as follows: 1 = no effect, 2 = possibly helped a little, 3 = some improvement, 4 = definitely helped, 5 = made a little worse, 6 = made much worse.

The various treatments were then rank-ordered in terms of the ratio of number of autistic children helped to the number of autistic children made worse. At the

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top of the list, based on rankings by 318 parents, was treatment by vitamin B₆ and magnesium. Forty-three percent of the parents reported the child had been helped (ratings of 3 or 4), opposed to only about 5% of the children having been made worse (ratings of 5 or 6). This provided a helped-worsened ratio of 8.5:1, by far the best of any of the substances evaluated. Next on the list was the prescription drug deanol, which was rated by 121 parents. Twenty-nine percent of the children were said to have been helped, while 16% were said to have been made worse, thus providing a helped-worsened ratio of 1.8:1.

Third on the list was fenfluramine, rated by 104 parents. Twenty-nine percent of the parents reported favorable effects, whereas 19% reported adverse effects, thus giving a ratio of 1.5:1. Thioridazine hydrochloride (Mellaril), by far the most often used drug on the list (n = 724), came in fourth, with 34% of the parents reporting their children to have been helped, and 23% reporting adverse effects, thus yielding a ratio of 1.4:1.

Analyses of the data are still in progress, and will be reported more completely later. Let us take a closer look at the three substances at the top of the list, vitamin B₆-magnesium, deanol, and fenfluramine, starting with fenfluramine.

Fenfluramine, widely available as the appetite suppressant drug Pondimin, has received a great deal of publicity in the past few years as a treatment for autism. Since it dramatically lowers serotonin levels, and since about 40% of autistic children have high serotonin levels, the serotonin-lowering effect of fenfluramine was thought to be at the root of any benefits it might produce.¹ However, Ritvo et al, who initially introduced fenfluramine as a treatment for autism, have more recently reported that fenfluramine seems to have its best effects on patients with initially low serotonin levels.² Fenfluramine was given a great deal of media attention when it was introduced as a treatment for autism by means of a brief article in the *New England Journal of Medicine* describing an open clinical trial of the drug on only three autistic boys.¹ The publicity (national television, news magazines, etc), along with the wide availability of the drug as an appetite suppressant, led to many informal trials of fenfluramine on autistic children, with and without medical supervision. This has caused concern.^{3,4}

Concerns have also been expressed about the safety of fenfluramine,^{3,4} but the present data show fenfluramine to induce adverse side effects in only about 19% of the children—lower than most of the drugs considered. (It should be noted that the adverse effects mentioned in this paper are only those,

largely behavioral, reported by the parents. Most of the more serious, long-term side effects are not reflected in our parental ratings of the treatments.)

Deanol, rated second by the parents in our survey, is no longer sold as a prescription drug, although DMAE-H3, a close variant of it, is available on a nonprescription basis from the TwinLabs Co, which sells it as a nutritional supplement. Deanol, and its successor DMAE-H3, are natural substances, very much like vitamins, but are not classified as vitamins, inasmuch as the body is capable of producing them in limited amounts. These substances are precursors to acetylcholine. A case of an autistic child who improved on deanol is presented in my book, *Infantile Autism: The Syndrome and Its Implications for a Neural Theory of Behavior* (1964).⁵

It should come as no surprise that vitamin B₆ and magnesium received the highest ratings by parents in terms of safety and efficacy. The published reports in the scientific and medical literature also lead to the same conclusion. All 12 published reports in which vitamin B₆ has been evaluated as a treatment for autistic children have provided positive results.⁶ Despite these remarkably consistent findings, and despite vitamin B₆ being much safer than any of the drugs used for autistic children, there are at present very few practitioners who use it or advocate its use.

Research on the use of vitamin B₆ with autistic children began in the 1960s. In 1966 two British neurologists, A.F. Heeley and G.E. Roberts, reported that 11 of 19 autistic children excreted abnormal metabolites in their urine when given a tryptophan load test.⁷ Giving these children a single 30-mg tablet of vitamin B₆ normalized their urine; however, no behavioral studies were done. A German investigator, V.E. Bonisch, reported in 1968 that 12 of 16 autistic children had shown considerable behavioral improvement when given high-dosage levels (100–600 mg/d) of vitamin B₆.⁸ Three of Bonisch's patients spoke for the first time after the vitamin B₆ was administered in this open clinical trial.

My own research on the use of vitamin B₆ in the treatment of autism began in the 1960s, after my book *Infantile Autism*⁵ was published. Among the hundreds of letters I received from parents of autistic children, a number reported good results after their having tried various vitamins, at high-dosage levels, on their children. The first ICBR study of vitamins in autistic children was initiated in 1968 and completed in 1971, using rather large doses of four vitamins: C, niacinamide, B₆, and pantothenic acid.^{9,10} These were the vitamins that were most often mentioned favorably by

the parents in describing their own uncontrolled experiments. Since this study has been fully reported elsewhere, I will merely summarize it by saying that a 4-month trial, using over 200 autistic children in a highly sophisticated, computer-controlled experimental design, yielded significant positive results, with vitamin B₆ being clearly the best of the four vitamins investigated.

Our second study was a double-blind placebo-controlled crossover experiment using 16 children who had proved responsive to vitamin B₆ in the first study.¹¹ This study was conducted collaboratively with researchers from the University of California medical schools in San Francisco and Davis. The positive results of these two experiments led to the initiation of a series of studies on autistic children and adults by Gilbert Lelord and his colleagues at the Tours University medical school in France.¹²⁻¹⁸ Lelord and his colleagues experimented with vitamin B₆ alone, magnesium alone, and B₆ and magnesium together, and used not only behavioral criteria in their studies, but also evoked potentials and measures of the excretion of urinary metabolites. All of the studies conducted by Lelord and his group have provided positive results. Not only were the autistic children found to have improved behaviorally, but the vitamin B₆ and magnesium also improved the cortical reactions in evoked potential studies and normalized the excretion of urinary homovanillic acid (HVA), which tends to be quite high in autistic patients. In a recent conference report, Lelord et al¹⁹ summarized their results on 91 patients as follows: 13 (14%) improved markedly, 30 (33%) improved, 38 (42%) showed no improvement, and 10 (11%) worsened. The researchers noted, "In all of our studies, no side effects were observed. . . ."¹⁹

Several recent studies by two groups of United States researchers, Thomas Gualtieri et al of the University of North Carolina²⁰ and George Ellman et al at Sonoma State Hospital in California,²¹ have also shown positive results with autistic patients.

As yet, no patient has been reported as having been cured with the use of vitamin B₆ and magnesium; however, there have been many instances where remarkable improvement has been achieved. In one such case an 18-year-old autistic patient was about to be evicted from the third mental hospital in his city. Even massive amounts of drugs had little effect on him, and he was considered too violent and assaultive to be kept in the hospital. The psychiatrist tried the vitamin B₆-magnesium approach as a last resort. The young man calmed down very quickly. The psychiatrist reported at a meeting that she had recently

visited the family and had found the young man to now be a pleasant and easygoing young autistic person who sang and played his guitar for her.⁶

Another example: A mother in England reported to me that her 17-year-old severely autistic son, a husky 6-ft, 160-lb young man, was so violent and assaultive, against himself and others, that he had to be hospitalized. In the hospital he beat his head against the walls so hard that the nurses, who were familiar with such behavior, told the mother that they could not bear to watch. The mother wrote me that "Anthony. . . would smash 7 windows in three minutes, become exceedingly oversexed by grabbing, especially females, by their legs and attacking them, plus his peers, and masturbating like crazy." After some weeks on Super NuThera (a specially formulated mixture of vitamin B₆, magnesium, and other nutrients), "He is playing football, hockey, he goes swimming twice a week, he has PE lessons. . . he enjoys pottery and has recommenced general education in the classroom."

In a later letter this mother wrote, "The Super NuThera was missed out for one day in error whilst Anthony went on a long train trip to York; on the following day his behavior was that of a wild beast, self-mutilation and attacking others. His normal behaviour was restored on the day after his previous bad one and has remained good so far."

On a recent trip to England I visited this patient at his hospital, and the attendants strongly confirmed the mother's reports.

Although the two examples I have provided are of quite violent individuals, the majority of autistic persons are not violent. Improvement, while on vitamin B₆ and magnesium, shows in many ways, especially in improved eye contact and improved speech. There is much less self-stimulatory behavior reported, more interest in the world around them, fewer tantrums, and in general the patients are reported as being considerably more normal.

It is important to recognize that if vitamin B₆ helps, it helps only because the child *needs* a much greater than normal amount of the vitamin. This cannot be said for any drug. Vitamin B₆ is given to facilitate metabolism, not interfere (albeit selectively) with metabolism, as drugs do. Vitamin B₆ is implicated in more vitamin-dependent neurologic disorders than any other vitamin.²²

For many decades vitamin B₆, even in quite large amounts, was considered to be perfectly safe. A 1966 review published by the American Academy of Pediatrics concluded: "To date there has been no report of deleterious effect associated with daily ingestion of

large doses of vitamin B₆ (0.2 to 1.0 g per day).²³ Seventeen years later Schaumburg et al reopened the question of vitamin B₆ safety by publishing a paper in which were reported several instances of serious, though reversible, peripheral neuropathy due to "pyridoxine abuse."²⁴ Abuse of any substance is certainly to be avoided. The administration of vitamin B₆, along with magnesium and other nutrients, especially the B vitamins, to autistic patients who benefit from this treatment, can by no stretch of the imagination be considered abuse. The patients reported by Schaumburg et al were taking 2–6 g/d of vitamin B₆ without the magnesium and other B vitamins which nutritionally sophisticated people have known, since the 1950s, to be essential if relative deficiencies of other B vitamins are not to result from overdosing on B₆. The usual dosage of vitamin B₆ for autistic patients runs from about 350 to 1,000 mg/d—far less than the dosage levels used by the Schaumburg et al patients. Starting with our very first study in 1968, all the children were given a multiple vitamin tablet to guard against the kinds of problems experienced by Schaumburg et al patients, and no such symptoms have been reported in any of the many hundreds of autistic patients we are aware of who have taken vitamin B₆, magnesium, and other nutrients.

Vitamin B₆ is not the only vitamin that has been found useful in autism. I would like to mention briefly the work that has recently been done on the use of folic acid in the treatment of autism. Several researchers have reported favorable effects on patients whose autism is associated with fragile X syndrome.²⁵ Recently I had occasion to visit Dr Jerome LeJeune in his laboratories in Paris. LeJeune, who is a pioneer worker on the use of folic acid in the treatment of fragile X cases, told me about several cases of nonfragile X children who had shown remarkable improvement when given massive amounts (0.5–0.7 mg/kg/d) of folic acid, even though he had no specific rationale for trying the folic acid on these children. In both cases truly astonishing improvement was reported.²⁶ This requires further investigation.

One other B vitamin, biotin, has been reported to have brought about some improvement in a Rett case.²⁷ Since biotin, like folic acid and vitamin B₆–magnesium, is a natural, very safe substance, it is hoped that further work along these lines will be undertaken.

Readers interested in learning more about our work, and in joining our growing list of professional correspondents and collaborators, are welcome to write to us. Publication 39, which summarizes the work done to date on vitamin B₆ in autism, and

answers the questions most frequently asked, is available on request.²⁸

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