Childhood Schizophrenia: A Case Treated with Nicotinic Acid and Nicotinamide

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The classification of children into a group of slow learners and mental defectives, whether congenital or acquired, is not a satisfactory method of diagnosing and may not lead to useful treatment. This concept of mental retardation has been severely criticized by many workers.

For example, Toolan[1] stated, "We had advanced to the dubious point where many persons considered mentally deficient to be purely a psychological diagnosis." The idea is not new that any illness which occurred during the early developmental stages of growth could produce retardation. An examination of the annotated bibliography by Goldfarb and Dorsen[2] shows this idea was popular many years ago and has remained fashionable since.

It seems likely that the separation of hospitals for retarded patients from the general stream of psychiatry and even more from medicine, has had some undesirable effects. One of these is the great emphasis on teaching the patients to the detriment of proper diagnosis and treatment as if the learning defect in many cases was primary and not secondary to the main illness. Yet this was inevitable because the clinical criteria for diagnosis for a large proportion of cases are vague and the main emphasis had to remain with psychometric tests. Raub, Mercer and Hecker[3] found that out of 37 cases diagnosed mentally deficient by school progress and social adjustment, 8 were too disturbed to be re-tested, 9 had normal intelligence, 4 had defective verbal intelligence but performed well, 10 had borderline intelligence, and 6 were in the high grade defective range.

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Biochemical Treatment

In the twentieth century biochemists have found certain abnormalities in a small fraction of the total population of retarded children and for some of these biochemical treatment has shown great promise for overcoming the metabolic disorder. Some of the subgroups of mental deficiency are (a) phenyl pyruvic oligophrenia (Cowie;[4] Tischler, Gibson, McGeer and Nuttall;[5] Armstrong and Tyler;[6] Mitoma, Posner, Bogdanski and Udenfriend;[7] and Woolf, Griffiths, Moncrieff, Coates and Dilli-stone[8]), and (b) maple syrup urine disease (Mackenzie and Woolf[9]).

When the specific indications for treatment are not known, treatment results are not striking. For example, Albert, Hoch and

Waelsch[10] found that glutamic acid raised intelligence significantly but slightly. It is possible that glutamic acid might be extremely useful for some types of deficiency not yet characterized, if treatment were started early enough as with phenylketonuria.

Hormonal treatment following specific indications are more apt to yield valuable therapies. Thus Reiss, Berman, Pearse, Albert-Gasorek and Hillman[11] use certain hormones for treating defective children after they have determined the particular kind of deficiency; e.g., chorionic gonado-trophin has been successful in improving certain types.

Recognizable Syndromes

Many defective children have recognizable syndromes with a characteristic clinical and pathological pattern. Crome[12] examined 282 brains, which included 146 idiots and 93 imbeciles. Of this group, 91 had pathological changes, 191 brains were not classifiable. Crome concluded that the anatomical bases of milder grades of deficiency remains largely unknown. But children can also have functional psychosis including manic depressive disease (Campbell[13]) and schizophrenia. The bibliography of Goldfarb and Dorsen[2] lists 584 abstracts and a substantial number of these deal directly with childhood schizophrenia. Griesinger in his textbook *Mental Pathology and Therapeutics*, 1882, states that although insanity before puberty is rare, almost all forms do occur.

The Schizophrenic Syndrome

The schizophrenic syndrome must depend to some degree upon the substrate in which it arises. Age and life experience must be vital in determining the shape of the illness—the impact of a disease which can impair learning at a crucial period of growth can be terribly disruptive. There is, therefore, no way of knowing what proportion of defective children of unknown etiology are schizophrenic. The best estimates range around 15% to 30%. Toolan[1] found that 25 out of 103 defective children were schizophrenic.

Many of these children resembled youngsters with organic brain disease, particularly if the onset occurred before the age of five. Drubin and Singer[14] found that 17 out of 21 psychiatric patients classed as mentally deficient were not deficient on retest.

Benda[15] described two groups of emotionally disturbed children as either autistic or schizophrenic. They were usually physically normal in appearance and moved around rapidly and skillfully. Their early development was slower in certain areas such as interest in environment but the first two years were fairly normal. They appeared intelligent but seemed incapable of using language. They were often skillful in things which interested them such as toys, opening doors, etc., but seemed to have difficulty in locating the source of stimuli. They thus appeared to be deaf.

The line of dermarcation between the two syndromes; i.e., autism and schizophrenia, is unclear—perhaps they are manifestations of the same basic process, although Rimland's[16] excellent review makes this very unlikely.

Some of the best work on childhood schizophrenia comes from Bender[17-23] and her colleagues. Using criteria described by Bender, Fish[24] was able to select three babies at age one month who subsequently became schizophrenic. The criteria she used were (1) disturbance in the temporal organization of maturation, (2) disturbance in physical growth, (3) disturbances in vasovegetative functioning, (4) activity disturbances, (5) motor disturbances especially molluscous muscle tone, (6) plastic organization of perceptual impressions and disturbance of body image and orientation in space, (7) presence of anxiety.

Michael, Morris and Saroker[25] have laid to rest the old idea that introverted children

are more susceptible to schizophrenia. Out of 606 children seen in the Dallas Child Guidance Clinic and followed up 14 to 29 years (mean=26), 164 classed as introverted by the usual clinical ratings yielded one schizophrenic later on. From 174 ambiverts, 6 became schizophrenic, and from 268 extroverts, 3. It seems likely early clinicians confused the presence of schizophrenia with predisposition.

But the fact remains that few psychiatrists have the clinical skill and acumen of Bender and Fish and a substantial number of cases of childhood schizophrenia were probably misdiagnosed. A large number of papers dealing with pediatric schizophrenia are, therefore, papers describing how to recognize them. This kind of paper is now rare in journals dealing with adult schizophrenia.

In general, treatment of children with schizophrenia remains unsatisfactory. Many psychiatrists believe nothing can be done for them and if they don't believe so, act as if they did. This may explain the preoccupation of some with the mothers, fathers, families and other environmental factors as etiologies in a direct sense. Treatments which have been suggested are psychological (Eickhoff[26]) or physiological-psychological (Silver,[27] Fish,[28] Bender[19] and many others).

Adult Treatment With Nicotinic Acid

In 1952, I began to treat adult schizophrenics with nicotinic acid and/or nicotinamide, as adjuncts, and these treatment trials have been continued until now. The results have shown that when this vitamin, in doses of 3 gm. per day or more, is given for at least one month, the patients make a much better therapeutic response using objective criteria such as readmission rates, duration of stay in hospital, suicide rate in community, community adjustment, five-year cure rates, etc. Some patients have been continually on maintenance therapy for nearly 10 years with no evidence of any toxicity (Hoffer, Osmond, Callbeck and Kahan,[29] Hoffer and Osmond,[30] Hoffer,[31] Osmond and Hoffer[32] and Denson[33]).

In a recent review of all the schizophrenic patients treated with nicotinic acid in 1952, Hoffer and Osmond[34] found that 10 years later, 12 (75%) did not require any further treatment in hospital, 4 had required a total of 6 admissions, but none were in hospital 10 years later. From a comparable group of 27, only 10, or 37%, did not reappear in hospital. The remaining 17 were readmitted for a total of 63 admissions. That is, 75% of the treated group had achieved a 10-year-cure rate compared to 37% of the comparison group.

In a survey of all schizophrenic patients treated at another psychiatric ward by psychiatrists not associated with the research group, similar results were obtained. Out of 169 patients treated with nicotinic acid plus other treatments between 1956 and 1962, 70 patients were readmitted for 137 admissions totaling 12,452 days. The comparison group of 349 patients provided 166 patients who were admitted 380 times for a total of 44,823, days.

Treating Children With Nicotinic Acid

In 1954, I began some preliminary trials of nicotinic acid on a small series of children considered to be mentally retarded. All were students in a school for retarded children. This was a double blind experiment using placebo for treating the comparison group. The children were given 1 gm. of either nicotinic acid or placebo per 50 pounds of weight for 3 months. At the end of the treatment period parents and teachers were asked to report on the change they observed in these children. Out of 11 children who were given placebo, 3 were improved and 8 not improved. Out of eight who received nicotinic acid, seven were improved. Chi Square with Yates Correction was just over 4.0; i.e.,

this has less than *5%* chance of being due to chance alone. However, such a small series and the fact nicotinic acid produced a flush invalidated the *blindness* of the experiment and the results were not reported. Another flaw with this experiment was its hit-and-miss character. The group was heterogenious and included organic cases, mongoloids, schizophrenics, etc.

Recently it became possible to select homogenious groups using a chemical assay. Clinical criteria were discarded and the absence or presence of an abnormal chemical in urine was used. The biochemical test was described by Irvine,[35] and Hoffer and Osmond,[3637] and its relationship to clinical diseases in psychiatry by Hoffer and Osmond,[3034] and Hoffer.[31]

With the co-operation of the local school for retarded children, 24 children were examined, 1 per week, for the presence of mauve factor in their urine. The assays were made by Miss M. Mahon, Lab Scientist I (see Hoffer and Mahon[38]). All children, whether positive or negative, were then started on nicotinamide, 1 gm. per 50 pounds body weight. The parents were given the result of the test. Then they were told that many children, whether positive or negative, responded well to this simple vitamin medication and that the medication would be provided for them free, as long as they felt their child was improving. Parents of retarded children are desperate for some "cure" for their children, and it was logical to expect them to follow the regime faithfully. Those who found the vitamin really helped would continue to ask for it.

After one year the records were examined merely to see how many from each group were still taking medication. Parents who stopped getting nicotinamide did so in two ways. They either did not ask for it any more, or they would call and report no improvement. They were encouraged to continue a few more months and if there was no further change the vitamin was stopped.

Out of 16 children who were mauve[3538] negative, 5 continued to take the vitamin and 11 discontinued. One of the negatives who continued was an epileptic retarded child who was controlled better (Hoffer[31]). Out of eight mauve positive children none were discontinued and in all, the parents were optimistic and believed their children were better; i.e., quieter, less aggressive and starting to learn. Chi Square for this distribution is 7.5 ($p<0.01$).

In this report I will describe the result of treating one child from age 9 to age 17 with nicotinic acid and later nicotinamide. One case alone does not provide proof for any new treatment, but when it is one of a series of several hundred cases, it can be very informative. It does prove that this vitamin can be given safely for many years and does show how a total treatment program can help a severely sick child develop into a nearly normal young girl just about through adolescence.

The History of Miss M. G.

Problem: June, 1951

At age five this girl was referred to an outpatient psychiatric clinic for diagnosis and treatment for a marked delayed speech development. M.G. was the second child in a family of three girls. Birth was normal with no evidence for birth injury. She weighed $7^1/2$ pounds. Development appeared normal. She was breast fed with no difficulty for eight months. She sat at age 4 months, walked alone by age 11 months. Until age five she had had none of the usual childhood diseases.

Speech Development

M.G. was a very quiet and passive baby and did very little babbling. She began to use a few words by age 3 and at age 4 years knew about 20 words. Most of these were Spanish which she had learned from a Spanish maid. By age $4^1/2$ years she was constructing phrases and at age 5 had learned about 100 words. There were no behavioral problems at any time.

On examination the speech therapist found no abnormality in muscle development of tongue, jaw, lips nor pharynx. Her hearing was normal. She was able to make all the sounds. When interested, she talked freely, but if asked to repeat a word by her mother she blocked or mumbled. The speech therapist considered her speech was not bad for having spoken only one year. During testing M.G. was restless.

Psychological Testing

On the revised Stanford-Binet Intelligence test Form L she had an I.Q. of 78-plus. The psychologist believed this was an under-evaluation because there was a marked scatter in responses covering five year levels. She failed vocabulary at the age four level. At the six year level she discriminated well. She was able to reason and remember at this level but refused to complete the items.

The psychologist concluded M.G. was normally intelligent.

Clinical Evaluation

She was a child of average intelligence and with normal physical development. It was felt this speech difficulty was an emotional response to a mother-daughter relationship by which M.G. sought attention.

Progress: July, 1954

In the fall of 1951 she entered Grade 1. During her first year she learned to read and during her second year in Grade 1 she learned enough arithmetic to be promoted to Grade 2. In Grade 2 she was in the slow group but her test in May, 1954, with the California Mental Maturity Scale indicated she had achieved second grade, seventh month, i.e., one year's development, and she was promoted to Grade 3. No serious retardation was evident.

By July there had been some deterioration. She was restless during sleep and hyperactive during the day. She would talk in bursts, laughed loudly and excessively when in a group with other children. She tried to participate with groups but when rejected, very quickly withdrew and remained on the fringe. There she would talk to her doll or go to her room. Sometimes with adult encouragement she would return to the group. She did not sulk.

Her memory appeared good, but if pressed she would reply she did not remember. Her thinking was concrete and her grasp of arithmetic remained very poor. When talking to herself she did not make up imaginative stories but merely repeated real events using correct names and places. The chief recurrent theme in her stories was about animals. An experienced and skillful psychiatric nurse, who observed her carefully several weeks, expressed her opinion she was probably a juvenile schizophrenic. This was also my clinical impression. On July 20, 1954, she was started on nicotinic acid—1 gm. per 50 pounds body weight.

Progress: November 26, 1954

By September 5, 1954, both parents had noted an increase in curiosity. She asked more questions. She showed more imagination when playing with her parents and could make an occasional joke. She slept more restfully and did not awaken so early each morning and was more interested in playing with other children.

Two months later, November 26, there was little additional improvement. Her sentences were poorly formed, she remained in the bottom half of her class. But she was not a behavioral problem. She joined the family more frequently in conversation, helped with serving, setting the table, etc. She looked after herself well.

Her parents were disturbed at her slow progress and because there were no facilities for a program of special education and care decided to send her a well-known residential school for disturbed children.

Progress: June, 1955

She was evaluated at a well-known child psychiatric department. She was again found to be physically normal. The EEG was also normal.

Mentally she appeared retarded. Her severe dysarthria and some mild incoordination suggested organic brain damage.

She had excellent control over her impulses but was emotionally inhibited but cheerful and relaxed. On the Wechsler Intelligence Scale for children she listed 64, and on the Stanford Binet Form L she tested 62. She seemed emotionally well adjusted.

She was accepted in the school and continued to take her medication regularly.

Further Progress

By the fall of 1957 she had shown slight improvement but it was not certain whether nicotinic acid played any substantial role. For this reason all medication was stopped for a trial period of about three months without informing her teachers (except the director, who knew).

By the end of 1957 there had been a marked regression in her mental state. She had lost much of her spontaneity and exuberance. In February, 1958, she was started on nicotinamide, again without informing her teachers. The amide was given her because the nicotinic acid flush would have given away the fact she was on medication again.

On April 16, 1958, the director reported the consensual opinion that M.G. has shown a definite improvement. Since then she has continued to take nicotinamide regularly, 1 gm. per 50 pounds, and is still taking it.

Progress: July 25, 1960 (age $14^{1}/2$)

A psychiatric nurse who had been with her several weeks prepared the following report:

Memory: Excellent for places, names and events. She never forgets her pills and even if she is out for a meal she produces it from her purse to take. I do not believe she is a visualizer.

Reading: Reads words she recognizes, with ease. Seems unable to sound out other words even if they are quite simple. Recognizes numbers readily, but may say them backwards, ; e.g. speed limit sign 35, may say 53, and then correct herself. Can read typewritten or printed words more easily than handwriting.

Mathematics: Very poor.

Writing:

(a) Style—has improved but becomes large and scrawly if she rushes.

(b) Content—asks for help in composing. Feels she needs to see the address written in front of her—then she copies from it.

Spelling: Fair for the simple words she uses. If she hurries she makes mistakes.

Speech: Clearer than she used to be. When she is corrected for mispronouncing a word, she will usually try it again but is not always successful. The faster she speaks the more errors she makes. When she speaks quickly she sometimes says her words backwards; e.g., blue dress would become 'dress blue'. She uses correct sentence structure and grammar usually, but when she uses a plural she errs; e.g., foot—feets ; fish-fishes, etc.

Manner: She has the rather common adolescent giggle and strained type of laugh when she makes a mistake or does not know something specific. Seems a bit clumsy although she does not drop or spill things ; e.g. , will bump you or step on your foot without any apparent notice until you draw her attention to it, then she says she is sorry. Her behavior is quite childish at times in that she will sit on her father's lap any time she feels like it, no matter where she is or who else is present.

Interpersonal Relationships: She is usually happy, pleasant and co-operative, but does rebel verbally, quite emphatically on occasion. However this is dispelled quickly when an explanation is offered. When she received word that her family would be two days late in meeting her it was observed that she was near tears, although she didn't speak of it. Several times she spoke to me about when I would be leaving

and why I couldn't stay longer. The night before I left, she again mentioned that she had only seen me for ten days and wished it could be longer (I had a card from her a week after I returned home and she spoke of it again).

When we were at Disney Land she was eager to go on most of the rides; however there was one scary-looking ride on which she refused to go although her younger sister coaxed her. Her mother and father and D. went on it while M. stayed with us. She didn't say she was scared of it but just said she wouldn't go on it (To me this showed good judgment because I wouldn't go either). This is the first time I have seen her show normal fears. She apparently has some good friends at school and had four letters waiting for her when we got to -- City.

Appearance: Well developed, very pretty girl with a nice figure. She weighs about 125 pounds and is about 5 feet 3 inches in height, with quite a large frame. Her skin is clear and glowing and she has brown, wavy hair. Her right shoulder looks about $^{1}/2$-$^{3}/4$ of an inch higher than the left.

Appetite: Eats very heartily.

Sleep: Falls asleep quite promptly and does not waken abnormally early as she used to. Restless at times during sleep.

Summer, 1962: M. spent most of the summer with her parents and her younger sister D. ($1^{1}/2$ years younger). During this period M. was physically normal. Menses were normal and there was no evidence of premenstrual tension.

Her relationships with her family were very good. She got along well all summer and was reluctant in the fall to go back to school. She had several arguments, or quarrels with D. but held her own and did not yield merely to please D. However, she did cry after these battles. Over three years ago she would have given in early. She used to awaken early in order to be with her mother and would offer to help in the kitchen and other household work. But last summer she was more normal, more like D. and would avoid helping her mother by feigning sleep, etc. until the major portion of the work was done. She was more like other teen-agers. She kept her room clean, made her bed. But the mother had given both girls holiday privileges which meant they could sleep in and make up their rooms later. But they had to have their rooms made up before inviting in guests. D. would often delay doing her room until later in the morning. M. was disturbed by this and

complained to her mother. She could not, herself, adapt to the less routine manner during the summer.

With friends M. also got along well. They knew of her slowness but would discuss things with her. She loves to talk and is very able to carry on long conversations during which she describes her preference for various pieces of popular music, her life at her school, etc. She has a very good memory and can easily relate events and experiences she has had. She is not very good in abstract discussions.

With strangers she appears to be at ease and will listen to adult conversation without interrupting, or intruding. If an adult talks to her she responds easily ; but she could not carry on too well with teen-agers her age. She is then able to function at about a 14-year-old level. D. is much ahead of M. in her social relationships.

M. does very little reading unless directly urged to do so. But she is able to read simple stories and understands them. She refuses to read aloud.

She enjoys parties and seems to get along well. Her interest in boys seems to be intellectual in that having boy friends is a good thing but there is no emotional involvement.

She is happier with teen-age girls. In December, 1962, the school gave the following report:

In the classroom, M. is normally very quiet and attentive. However, she at times seems preoccupied and pressure is required to regain her attention. She is somewhat self-conscious and does not always react positively to correction. She completes all assignments, but does not initiate work independently.

M. participates eagerly in all phases of the recreational program. She requires leadership in organized activities, but she is always very cooperative and exhibits a sense of fair play. She seems to particularly enjoy the square dance classes in which she has done very well.

In the dormitory her dressing habits have improved. Her color coordination is better and her tendency to wear too much jewelry and other accessories has lessened. Her personal hygiene

habits are good. M. likes most foods and will eat those she doesn't particularly like, without comment. She shows willingness to accept responsibilities assigned in the dormitory and will often do other duties as well. In the preparation of breakfast and serving she does well.

M. conducts her self properly on trips off campus. She demonstrated good social graces on a visit to the State Fair, shopping trips to town and social functions at school. In summary, she has been happy this period and her work is good.

In October, 1965, I examined M. and found her nearly normal. The main problem remaining was some difficulty in grasping new concepts and in expressing herself. To accelerate the treatment she was started on thyroid 200 mg. per day. Within a few weeks her mood, which had been within a normal limit, became more even and she was able to relate more gently to a difficult and somewhat demanding grandmother.

November, 1966, she was in a rehabilitation school where she could relate to other young people and she is being educated in preparation for full employment. During the summer of 1966 she was very helpful on her parents' ranch.

A single case does not prove that a given treatment was responsible for a clinical result, whether therapeutic or toxic, for one cannot rule out spontaneous remissions or responses to other variables which are not under one's control. Single reports merely illustrate how a treatment is given. Series of cases do provide proof, for with every success the odds increase that the treatment given is, indeed, responsible. But there must be knowledge of the natural history of the illness. No treatment is really successful unless the remission rate is significantly better than the one which would result had no treatment been given.

This case was presented to illustrate what one might expect from a total treatment program, using whatever methods are considered advisable. In this instance a combination of interested and devoted

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parents, special training in a school skilled in dealing with these problems, plus the use of nicotinamide for more than 12 years, brought a sick girl to a state of adolescence which is within the range of normal, and it seems likely she will be nearly normal. No one now could find any evidence of psychosis or of organic deterioration in her, and on intelligence tests she would be within the normal range.

Other children with similar problems, especially if they have malvaria (see Hoffer and Osmond[30]) and if there is no definite organic illness to account for the difficulty, should be given a similar long term therapeutic trial with nicotinamide; for it can do no harm, does not interfere with any other treatment and may recover, or nearly recover, very sick children.

Note: As of December 31, 1969, this girl has steadily improved in all areas of personality and it is likely she will be independent in the future.

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