Pangamic Acid

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Vitamin B15 (pangamic acid) was discovered, isolated, identified, and synthesized in the laboratory of E.T. Krebs, Sr., and E.T. Krebs, Jr., in San Francisco, California, in 1951.

Pangamic acid was first isolated from aqueous extracts of kernels from apricot stones, and later it was crystallized from rice shoots, rice bran, brewers yeast, bull blood, and horse liver. Subsequently it was identified with vitamin B15. It is still not known whether pangamic acid is synthesized in the body, or is taken in with food and then enters the circulation and tissues (Garkina, 1962). It has been demonstrated to be a remarkably safe substance for which no undesirable side effects have been recorded. Its toxic dose for man is 100,000 times the therapeutic dose (Krebs, 1971).

Experiments were conducted on 350 rats weighing 140-250 g. Vitamins C and B6 were injected one at a time in a 5 percent solution; B15 was used in a 40 percent solution. The lethal dose of B6 consisted of 1,200-2,500 mg/kg. Calcium pangamate in a dose of 2,000 mg/kg did not have any toxic effect. This corresponds to data in the literature that vitamin B15 is practically nontoxic. The lethal dose of vitamin C was 3,000 mg/kg (Alpatov et al., 1971).

It has been well established experimentally that vitamin B15 increases the rate of phosphorylation of creatinine to phosphocreatinine. The latter is a high-energy compound that upon hydrolysis back to creatine and phosphoric acid yields a high level of energy for the mediation of muscle contraction, nerve conductivity, and membrane permeability.

It has been listed in the Merck Index (7th Edition), Dorland's Illustrated Medical Dictionary (23rd and 24th Editions), and Tabors Cyclopedic Medical Dictionary (10th Edition, 1965). While its discovery has received little notice, as has been the fate of other vitamin discoveries made in this country, it has been accorded much attention abroad. In recent years many countries have contributed a substantial literature on B15 in French, German, Italian, Japanese, Portuguese, Russian, and Spanish. Many of these studies were done in prominent universities and in the medical institutions and hospitals associated with the USSR Academy of Sciences. The Russian papers published by the Mc-Naughton Foundation (Garkina, 1967) report clinical trials conducted on more than 1,000 patients suffering from cardiovascular diseases. A positive effect of B15 was observed in 80-90 percent of all patients treated. The calcium salt of pangamic acid was administered by intramuscular injections in daily doses of 15-20 mg for 20-30 days, or in daily intra-abdominal injections of 40-50 mg, or in daily doses of 50-100 mgm taken orally.

Experimental and clinical studies by a number of workers have revealed that the physiological role of pangamic acid in the organism is based on its lipotropic activity, on its stimulation of oxidative metabolism in cell tissues, and on its detoxifying activity (Udalov, 1965). Udalov (1965) found an increased excretion of 17-ketosteroids in the urine of patients and a concomitant decrease in the content of ascorbic acid and cholesterol in the blood. Bertelli et al. (1957) injected vitamin B15 into mice and noted a decrease in serum ascorbic acid content.

These workers assumed that the decrease in the content of ascorbic acid and cholesterol was due to their utilization for the synthesis of corticosteroids. They also point out the significance of pangamic acid as a new methyl donor in the biosynthesis of many biologically important compounds. Udalov and Sokolova (1962, 1965) performed experiments with rats kept on a protein-deficient diet in which pangamic acid served as the sole source of methyl groups. In these experiments it was shown that the administration of pangamic acid almost completely prevented fatty infiltration of the liver. Udalov (1965) has shown that pangamic acid can serve as a methyl donor in the methylation of amide groups of nicotinic acid with the formation of N-methyl-nicotinamide in men kept on a protein-deficient diet. The conclusion is drawn that the apparent universality of action of pangamic acid is due to its methylating activity and its activity in the respiratory processes taking place in the cells and tissues of living organisms (Udalov and Sokolova, 1962, 1965).

In recent years numerous works had appeared on drug treatment for children suffering from severe disorders of behavior and communication. The search for new drugs affecting the activity of the central nervous system is mainly directed toward finding drugs with a general stimulatory activity. During the first year of life almost one half of the O_2 taken up by the child in the resting state is utilized by the brain. Numerous clinical and experimental data have shown that lowered respiration in the brain or in some of its segments may lead to various disturbances in mental activity (Himwich, 1951). The reports of Garkina (1962) and Dokukin (1967) draw attention to the antihypoxic properties of calcium pangamate (B15) in oxygen starvation in the brain.

Two Russian investigators, MG. Blumena and T.K. Belyakova of the Moscow City Psychoneurological Clinic for Children and Adolescents, found improvement in speech in 12 of a group of 15 children diagnosed retarded after the oral administration of 20 mg of vitamin B15 three times daily. All children in this group displayed little interest in their environment, "lacked initiative and were rather passive." Four children in the group hardly verbalized, and none used language as a means of communication. Included in the experiment was a second group of six children whose mental state was characterized by "increased excitability, motor de-inhibition and tendency to affective outbursts." Both groups were treated for one month during a period free of schooling. The use of drugs was suspended four to five days prior to the treatment with vitamin B15. The efficacy of the treatment was controlled by constant clinical observation, and psychological tests were performed every 10 days.

After one month 12 of the first group of 15 children showed considerable improvement in speech development. The vocabulary of the four children who were virtually nonverbal prior to treatment was "considerably enriched." Some of them began to form disyllabic sentences. The general mental state and intellectual activity of the majority of the children in the group improved. Concentration improved and interest in toys and games developed.

The effect of vitamin B15 on the children in the second group was considerably less pronounced. Little improvement in their mental state was noted (Blumena and Belyakova, 1965).

The following case histories are presented in the form of reports from parents. The first group of reports described the reaction of children who have been diagnosed as autistic types, or rather children who suffer from severe disorders of learning, behavior, and communication.

Case #1, Jimmy, Age 7

His mother writes: *"You know that jimmy is emotionally disturbed and has a vocabulary of five or six words. I started giving Jimmy 200 mg of vitamin B15 for the past three weeks. I have noted a change in two areas. He has increased his vocabulary using words like candy, banana, chicken, dinner, couplets like 'get that,' 'get this.' He is constantly making sounds like he is trying to communicate. He has begun playing games with his brothers and sisters. He seems to want to be in their company now. Previously he never acknowledged his siblings' presence and never cared to be in their company, jimmy is on no other medication at the present time."*

Another letter three months later describes the following progress.

"jimmy tries to dress himself and with my guidance can dress himself completely. He communicates a feeling of hunger to me by saying 'dinner'. Recently when one of his toys broke he handed it to me and said the word 'broke'. Today he said 'mom' for the first time, jimmy's teacher visited him at home and was telling me that jimmy had a different look in his face and that he seemed to be looking almost like a 'normal kid,' because some of his strange expressions and behavior are disappearing."

Case #2, Jimmy, Age 4

"jimmy had a reaction almost immediately to the introduction of B15. We *became downright noisy. He still constantly is making sounds even in his sleep, at times you could hear a humming sound. He seems very pleased at his new noisiness also. He likes to hear himself, and he enjoys hearing himself played back on the tape recorder. He is saying a few more words, but now each word he tries is a different one. He says daddy quite clearly now and has said mommy once or twice."*

One month later, Jimmy's mother wrote that her supply of vitamin B15 was exhausted, and eight days later the change in Jimmy was drastic. She described that:

"jimmy can no longer sit still, his arms are going constantly, he can't even sit long enough to eat. He seems terribly distressed, almost as though he were in pain. He has lost eye contact and has become impatient and at times destructive. He punched the baby quite hard at least four times today. All this is completely unlike the Jimmy of a few weeks ago. It is a terrifying thing to see him go through this. He had come to be a peaceful, happy, easy child and generally a cooperative pleasant one. He had excellent eye to eye contact, but now he looks frightened and runs to us for assurance frequently. I know the B75 *was administered originally to stimulate speech and in that area he has improved, but obviously it has been doing a lot for him which we did not realize fully until this recent relapse. His old symptoms of headbanging have recently returned also."*

A letter dated 30 days later described how in 24 hours his crying had stopped and in 48 hours most of the bizarre behavior which had returned began to vanish.

"Within three days after he was back on the B15 he *was again happy, his mood was pleasant and he slept well at night. This was absolutely the best Christmas we ever had with jimmy. He enjoyed every minute of it. He enjoyed Santa instead of crying. None of his gifts caused him to become totally obsessed as in past years. He just seemed to enjoy everything as a normal child would. It feels good for me to use those words to describe our jimmy."*

The next letter from Jimmy's parents came seven months later. His mother wrote that:

"jimmy is really starting to use words.
Every day he has been saying words without the apparent effort it used to take. All the words are appropriate and relevant to what he is trying to express. He is just enjoying life so much now. He has a pleasant disposition and loves going out places. He is very patient and when he does get upset he is easily

calmed down."

Two months later Jimmy's mother wrote again to say that he is doing better every day.

"It's the most exciting thing I have every experienced. He was repeating words and he answers questions now. He asks what's this and he names many things. There is no strange look when he tries to talk anymore, instead he has a big proud smile. He said something very special for me, 'I love mommy.' Frequently when I walk into his room I hear him talking to himself."

Case #3, Janet, Age 4

Janet's mother wrote that she had been. vomiting daily after starting the vitamins, so she withheld everything but the vitamin B15 of which Janet would take 1 1/2 tablets daily without nausea or vomiting. Within several days she said two sentences. When she reported this to me by telephone, I told her to increase the B15 to 3 tablets daily.

"The following three days were the most exciting I have ever known. She spoke only in sentences, was eager to try everything and was quick to respond. Neighbors and other children commented on the remarkable difference. However, her teacher reported no change whatever in Janet's behavior or verbalizing at school and was slightly incredulous when I described Janet's improvement at home. Last Sunday when Janet was unaware of my presence I saw her cover her naked doll with her coat as she said 'that's all right baby, I know you are cold. I will cover you with my coat and make you warm."

The Russian literature on vitamin B15 reported its value in the treatment of a variety of forms of asthma. In taking case histories of my patients, I frequently came across the history of siblings who suffered from asthma and suggested that the child might benefit from the use of the vitamin B15 for treatment of the asthma. The following series of cases indicate that vitamin B15 is indeed a valuable treatment of asthma and other allergic conditions.

Case #4, Ellen, Age 12

Ellen's mother wrote:

"In 7959*, when Ellen was two and a half, she began to wheeze. Asthma was diagnosed, and she was started on antihistamines. Soon her attacks became more severe and occurred about once every two weeks lasting two to three days. The attacks continued on and off over the next year and a half during which time her pediatrician prescribed steam tents, antihistamines, ipecac to make her vomit, and adrenalin when necessary. She improved steadily, but in the spring of* 7965 *she was wheezing again and she began to have attacks of asthma severe enough to sometimes require adrenalin. She was also taking Tedral and antihistamines. Her pediatrician advised us to take Ellen to an allergist which we did. He treated her for a year at which time she did not improve. She had a series of desensitization injections, Tedral, antihistamines, and prednisone.*

"During the summer of 7966 *while riding her bike she had such a severe attack that she was taken to the emergency room of the local hospital. There she was given oxygen and an injection of adrenalin, and again prednisone was prescribed. In* 7966 *skin testing found her to be allergic to trees, grasses, molds, ragweed, and dust. A series of desensitization injections were begun. She continued taking antihistamines for a runny nose and eyes, Tedral for wheezing, and was put on prednisone whenever she had a severe attack. During the year of* 7966 *she was out of school for at least half of the school year due to her recurring attacks of asthma. She was unable to take gymnasium classes and had to be driven back and forth to school since any physical exertion would make her breathing even more labored. In January, 1971, vitamin* 675 *was begun.* We *were very willing to try. We waited for spring and early summer for any results and this was always one of the times of the year when Ellen became very asthmatic. However, that spring and early summer we had seen a great improvement. She had taken Tedral for a slight wheeze only about six times, has not needed prednisone or adrenalin, has been very active riding on her bike, swimming, and going on long hikes. We consider this a miracle medication for Ellen."*

The , follow-up report written six months later states that:

"Ellen has been taking the vitamin and

continues to be virtually free of asthmatic attacks. During the summer when there was a great amount of mold, she did have watery eyes and a runny nose on occasion. This has been a great improvement for her. She continues to be able to walk long distances, ride her bike, and the past year has been taking modern dancing courses. As you know, these were activities which at one time Ellen was never able to do without getting short of breath or wheezing. As long as she takes her vitamin she has been free of asthmatic attacks."

Case #5, Johnny, Age 9

At age nine, Johnny was an accomplished performer on the stage and in the movies. His mother wrote to confess that when she started him on the vitamin B15 she had very little hope "since she and her husband had given up all hope of ever curing Johnny's croaking," as they called it. Her letter stated:

"*I was always afraid to send him out on cold or damp days. Now he is out in every weather and without a hat or all muffled up as he always was. Best of all, when he runs up the stairs now or plays basketball, etc., he breathes quite normally. Up to the time he started on the vitamins he had great trouble sometimes recording, as they always seemed to pick up his wheezing on tape. Now he tapes without the slightest difficulty. Singing was always impaired by the wheezing. Now he has a fine voice. If possible I would like you to take another look at Johnny sometime next week to see for yourself the amazing recovery."*

Case #6, Paula, Age 18

Paula, age 18, wrote the following report about her improvement.

"*/ first took the B15 in the winter of 1970. I took one pill when I had an asthma attack and it usually cleared the congestion, but the frequency of the attacks has not changed. In May, 1971, I went to California and discontinued the B15 because I had only two asthma attacks. When I returned to New York, I started wheezing again because I was allergic to the dog and the cat after being out of the house for three months. In December I started taking the B15 four times daily. Within three or four days the wheezing stopped.*

"Before the B15 / used *to have coughing and/or wheezing attacks which lasted from one to two and a half hours. I usually use my Medi-Haler, cough medicine, and hot tea to relieve it. These attacks used to occur two or three times a week. Since resuming the B15, / have had only one such attack and it has lasted for half an hour.*

"To get to my house I have to walk up a steep hill. I always become short of breath, but in winter and fall I wheeze heavily. I use the inhaler and it clears up within the hour.

"With the B15 I still have shortness of breath, but I rarely wheeze heavily. If I do wheeze it clears within 15 minutes. I have been attending an exercise group for two years. Last year I started wheezing after half an hour and could not always finish the 80-minute class. Since taking the B15 I have not wheezed once this year while exercising. For me the 675 *seems to have a preventative effect. The inhaler and cough medicine can only be taken when the coughing and wheezing actually start, but the B15 when taken regularly controls the asthma. Another advantage of the* 675 *for me is that it does not cause an allergic reaction which occurred when I took other pills for asthma such as Tedral. This has been the first fall season since I had asthma that it has been under control. I attribute this control to the use of B15.*

Case #7, Scott, Age 10

Scott's mother writes that:

"Scott *has shown little problems with allergies since being started on vitamin* 675. *Previously he had problems breathing, especially when exposed to grasses, molds, ragweed, and other inhalants. Sometimes his eyes would water and itch."*

She continued that: *"Scott has been having injections for desensitization once every three weeks for the past year. In May the supply of B15 was exhausted and Scott did have several attacks and had to take Allerest. He also had a reaction to his injections and the doctor decided that he needed to come every two weeks instead of every three."*

She concluded the letter by adding Scott had started taking the B15 again

and has not had any problems since.

Case #8, Lisa, Age 11
Lisa's mother writes:

"Lisa has been on vitamin 875 *since last February. This was the first summer in three years that she did not have any hay fever. If she is without B15 for more than a few days her behavior changes and she is constantly angry. Whenever she does have the B15 she is much more cooperative and appears to be alert."*

Case #9, Tony, Age 9
Tony's mother wrote:

"Tony has become a very cooperative, agreeable, pleasant, and willing child. He has also become inventive and shows a great deal of initiative. I have no inkling as to the concentration span, and small muscle control appears no better. I don't know if this picture is because of lack of school pressures or participation in sports, the addition of vitamin 875*, or an accumulation of all of these things, but I am very thankful. At last he is a happy child. M.J. (Tony's brother) came home from* a *camping trip that very weekend with a cold and a slight trace of asthma. I did not take him to the doctor which I would normally have done. In one week he was completely without symptoms and has been so ever since. He took vitamin B1*5 *twice a day."*

The following patient has been diagnosed Cerebral Palsy. She is 16 years of age. The mother writes:

"It is difficult to measure a day-by-day improvement, but as I look back over the last year and a half I can truly say that I have noted great improvement. She seems to have much more assurance, better organization of thought, and expression in her excessive movements are better controlled. More concrete evidence is the fact that she is earning more money at the workshop because her production is better. Comparing hand samples, one sees a dramatic change. Since the addition of 875 *to the megavitamins, the whole picture seems to be even more improved."*

Pangamic acid is a classical example of a vitamin because it is almost impossible to escape the self-limiting mechanisms that prevent any toxic manifestations. A true drug is, by contrast, the exact opposite of a vitamin. It is toxic or at least irritative, stimulative, or depressive in any dose. Thus, it is really impossible to have a vitamin that is toxic or a drug that is nontoxic when each is used within the parameters of its optimal therapeutic response (Krebs, 1971).

The scientific and clinical progress of vitamin B15 has been characteristic of that of most important vitamins whose value becomes increasingly apparent as research and clinical application widen. This is in contrast to the history of all but a few drugs. Their lack of value becomes increasingly apparent as they are studied over the years. No vitamin has ever come into clinical application without the scope of its utility becoming more and more apparent with continuing studies (Krebs, 1971). While it appears that the potential therapeutic spectrum of pangamic acid is impressive, it becomes more so when one keeps in mind that it is a vitamin and not a drug. For this reason, it is most rationally handled as a physiological tool to be utilized for achieving specific physiological ends directed toward the prevention or amelioration of deficiencies grounded in the failure of the relevant metabolic pathways.

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