

Editorial

Niacin and Cholesterol: The History of a Discovery

Research discoveries do not follow a simple path from A to B although this may appear to be the case to those not familiar with the history of a discovery. A simple observation made by one person eventually led to the development of the modern paradigm, the vitamins-as-treatment paradigm but the pathway was tortuous and difficult and depended upon events that were unpredictable. This then is a brief look at how an observation I made on myself opened up the whole field of nutritional medicine and paved the way for the use of vitamins and other nutrients in optimum doses in spite of intense opposition led by followers of the old paradigm, the vitamin-as-prevention paradigm. Dr. William B. Parsons, Jr., plays a major role in this development. I am delighted with his report which appears in this issue of the *Journal*.

Dr. H. Osmond and I had started our double-blind prospective placebo controlled studies of niacin as a treatment for schizophrenia. We were the first psychiatrists to conduct this type of therapeutic trial. It is now the gold standard for clinical research. But one of the problems with niacin is that it is a vasodilator, it opens the capillaries and this causes the flush that almost everyone has to go through when they start to use this vitamin. The flush can be very unpleasant and patients have to be motivated before they will undergo it. This was the reason why in our double-blind studies we included a hidden control using niacinamide which does not cause any flush. Luckily patients who need it the most i.e. patients with schizophrenia, and elderly patients flush the least. I wanted to experience the flush myself so that I could discuss it more intelligently with my patients. In 1954 I began to take 1 gram three times daily. I did not like the flush but carried on. It gradually decreased in intensity and the discomfort decreased substantially. At that time I had a minor problem with my

gums which bled when I brushed my teeth. Even with the help of my dentist and vitamin C in gram doses I could not solve this problem. I concluded I would not worry about it and would eventually have to lose my teeth. Two weeks after I started taking niacin while I was brushing my teeth and not quite fully awake I suddenly awakened in surprise. My tooth brush was clean, I had stopped bleeding. So was my dentist when he examined me shortly after that. My gums were firm and healthy. I tried to understand what had happened and eventually concluded that the niacin had increased the ability of my tissues to repair themselves from the trauma induced by chewing, especially since I had some malocclusion and my teeth did not meet squarely. I have no doubt that niacin is a major healing nutrient and accelerates healing of many tissues and organs.

About the same time my former professor of Anatomy and Histology at the University of Saskatchewan, where I took my first two years of medicine, was examining the effect of ultraviolet radiation on cholesterol levels in rabbits. He asked me whether he could use ultraviolet radiation on some of our patients in the mental hospitals to see if their cholesterol would decrease exposure to ultraviolet radiation. I agreed, knowing that the treatment was no more harmful than being in the sun, and that the additional attention given to these chronic patients would be helpful to them. I drove Professor Altschul from Regina to Weyburn, about 70 miles, to meet Dr. Osmond and his clinical staff. On the way there and back to Regina we shared research experiences. Dr. Altschul told me about his rabbit research. He found that heated cholesterol rapidly increased cholesterol levels in his rabbits whereas unheated cholesterol did not. He used cakes containing a lot of egg yolk baked by his wife. The same composition not baked had no effect. He remarked that in his opinion the heated cholesterol decreased the rate

of repair of the intima, the inner lining of the arteries. As soon as he said that I remembered my response to niacin. It occurred to me that if niacin really did increase the rate of repair of tissue and if Dr. Altschul was correct in his hypothesis, then niacin might be valuable in preventing hardening of the arteries. Dr. Altschul did not know anything about niacin. I described it to him and sent him one pound of pure niacin.

A few months later I received a call from Dr. Altschul. He was very excited and he kept repeating over and over "It works, it works!" I had forgotten about my niacin suggestion and asked him "Rudl, what works?" He then told me that he had given his rabbits niacin and it promptly brought their cholesterol levels back to normal. It had not occurred to me that niacin would do so. Then he added that we now needed to examine its effect in human subjects. I replied that I would look after that.

I was consultant to the pathologist of General Hospital Regina, Saskatchewan. I asked Dr. James Stephen whether we might do such a study. He replied that there would be no difficulty, that he would select a number of patients on the wards, would order cholesterol tests and after 48 hours on niacin would repeat the blood tests. I asked him whether we should contact their physicians first. He said that there was no need, that most of the doctors did not know what was happening to their patients and that he would look after it. Modern Ethics Committees would have heart attacks at this procedure. A few days later I received about 70 patients reports. Immediately it was clear that the niacin had lowered cholesterol levels significantly in this series. I called Dr. Altschul and we agreed to report this to the literature. Our paper appeared in *Archives of Biochemistry and Biophysics*, 54: 558-559, 1955, by Altschul R, Hoffer A & Stephen JD: "Influence of nicotinic acid on serum cholesterol in man." This paper is credited with being the beginning of the new paradigm.

The vitamin-as-prevention paradigm was based on two main assumptions: (1) That vitamins were only useful to prevent the classic vitamin deficiency diseases such as beri beri and pellagra and (2) that only very small doses were needed. These became the RDAs of modern nutrition. But niacin, a vitamin, lowered cholesterol levels, not a deficiency disease and was needed in very large doses, 3 to 6 grams daily. A few years later the FDA approved the use of niacin in large doses for the control of cholesterol levels. In view of the FDA's major campaign against vitamins I must conclude that they were not aware that niacin was a vitamin and looked upon it as a drug. The initial response to our report was an attack by an author written for *Nutrition Reviews*. He was so incensed that he misread our table where we showed the data and according to him we had proven that niacin had not lowered cholesterol levels. I promptly wrote to the journal and asked that he retract his comments and if he would not I wanted my letter published. He refused to correct his mistake and my letter was published.

The following year I was invited by the Mayo Research Foundation in Rochester, Minnesota, to spend a few days with them to report on my research into schizophrenia. I lectured to them on the adrenochrome hypothesis of schizophrenia and on our double blind controlled experiments which showed that niacin was therapeutic. In return they wine and dined me with a final banquet the evening before departure. At that dinner I sat beside Dr. Howard Rome, Chief of Psychiatry. I was tired of talking about schizophrenia so began instead to talk about niacin and its properties. I told Dr. Rome that it lowered cholesterol and gave him the reference. Then I returned to Regina. Ten months later Dr. W.B. Parsons, Jr., and his colleagues reported their excellent study that corroborated our observations.¹

Our study did not create any great re-

sponse from the medical literature. At that time authors who liked a paper they read asked for reprints. The number of reprints distributed was one measure of the level of interest. But the report by Dr. Parsons, followed by a second one, had the desired effect. The medical world and a few drug companies sat up and took notice. Our report was published in an obscure scientific journal not read by doctors and it came from a strange place called Saskatchewan which did not even have a medical school. Bill Parsons' report was in a very popular journal and came from one of the most highly respected medical institutions in the world. A few years earlier one of their scientists had been awarded the Nobel Prize for his work with the corticosteroid hormones. Ever since I have been grateful to Bill for the major role he played in developing niacin as one of the most useful treatments for the treatment of hypercholesterolemia, for saving many people from coronary occlusion and for making it possible for physicians everywhere to use niacin once it was approved by the FDA.

I did not know that my brief after dinner discussions with Dr. Rome had played any role until Bill told me about it many years later.

Here was that tortuous pathway from my bleeding gums to cholesterol levels in Dr. Altschul's rabbits, to a chance meeting with the Mayo Clinic staff, especially Dr. H. Rome to Dr. W. Parsons, Jr., Chief Resident, Mayo Clinic, to the FDA, and finally to general acceptance that niacin is the world's gold standard for lowering cholesterol levels. It not only lowers total cholesterol, it elevates HDL as well and restores the HDL/ LDL ratio to below five and it does so with safety and continuing efficacy. According to Bill Parsons,² it is the only way of really effectively dealing with hypercholesterolemia. The Coronary Drug Study,³ finally established the major role played by niacin. The development of the modern paradigm followed inevitably from this finding.

Bill Parsons writes at the end of his paper "Dr. Hoffer has correctly said that while pioneers in many fields argue about precedence, we are friends who readily acknowledge each other's roles in starting niacin research." Bill's role was unique. I wish I had found someone equivalent in schizophrenia research coming from an equally impressive establishment. If there had been such a person niacin would be the standard treatment for the schizophrenias today. Thanks Bill. Your role was of the utmost importance. Not a single psychiatrist from any of the major universities in Canada and the United States, including the National Institute of Mental Health, Bethesda, Maryland, showed the same curiosity and interest that you did.

—A. Hoffer, M.D., Ph.D.

References

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