Nutrient Pioneers

A. R. Patton[1]

Third in Series **James Waddell William Rose**

Not long after Harry Steenbock at the University of Wisconsin had discovered that vitamin D activity can be produced by irradiating ergosterol with ultraviolet light, the DuPont Company found itself with a license to use the Steenbock patent to make vitamin D for poultry feed. It was known that egg production depended on either cod liver oil or outdoor sunshine, and the latter was seldom available in winter or in modern laying batteries.

A recent Ph.D. in biochemistry at Wisconsin was hired because he was familiar with the process. This was James Waddell, who came from Alberta. He had been primarily responsible for the discovery that copper is an essential element in nutrition. Of Scottish ancestry, he told me that his name was derived from "Tweed Dale," and that it really should be pronounced with the accent on the first syllable, although nobody did. This was of interest to me, because my grandparents came from the river Tweed (Galashiels and Kelso).

At the plant in New Brunswick, New Jersey, he irradiated some ergosterol, tried it on chicks, and they got rickets. It worked for the rats in the lab, but not for chickens. This was a matter of desperation, because jobs weren't to be had in the thirties due to the Depression, so he persevered.

Work by others eventually disclosed that the vitamin D made from ergosterol (called vitamin D-2) isn't the real, natural vitamin D, but a sort of imitation that works for some species. But chickens and turkeys could tell it wasn't the real thing, and would have none of it. The natural form of vitamin D, (called vitamin D-3) is the result of irradiating 7-dehydrocholesterol, normally from sunshine on the skin. This had eluded discovery because it has the same ultraviolet absorption spectrum as ergosterol.

About the time vitamin D-3 manufacture from 7-dehydro was well on the way, World War II broke out, Germany blockaded Norway and shut off all supply of cod liver oil to North America, and suddenly DuPont's production of vitamin D-3 became of paramount importance to the war effort. Without it there would be no commercial egg production.

1. 727 Franklin Street PortTownsend, Wa. 98368

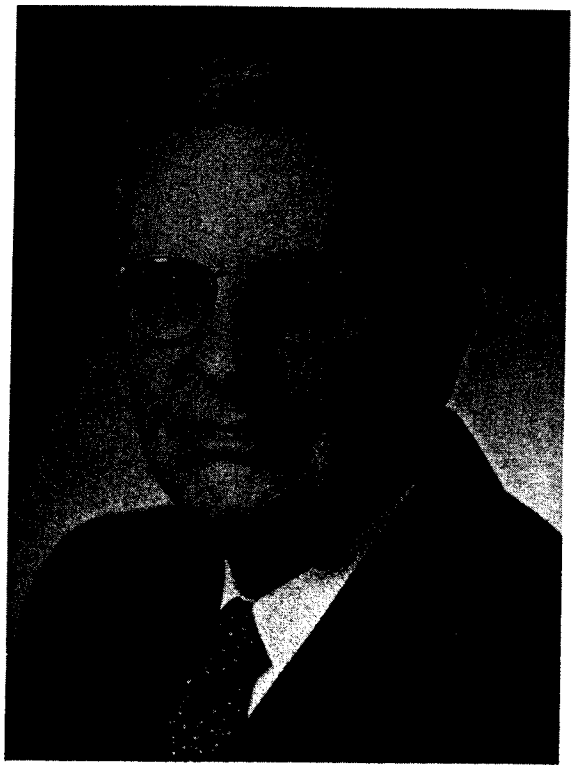
Kenneth King, the next administrative step above Waddell, was on the phone one day trying to find out where to buy more cholesterol to make into 7-dehydro. The only market source was the spinal columns of cattle. When he was asked how much cholesterol he needed, Ken replied, "I don't know — maybe we need all the cholesterol in the world!" In spite of the War Urgency, the next day the U.S. Dept. of Justice moved in and padlocked all the files, and DuPont was charged with trying to corner the cholesterol market (which didn't even exist).

We often went down to the Raritan to eat lunch at the Rutgers cafeteria, and there we frequently met one of the professors who was the third generation in shell fish research. The outcome was that DuPont established a mussel farm in Chesapeake Bay. The smelly mussels were trucked up to New Brunswick, the saponifiable gunk was got rid of (no doubt polluting some stream of water). The cholesterol was purified, twisted into 7-dehydro with a molecular monkey wrench, and irradiated at 2650 angstroms if I remember right.

The resulting vitamin D-3 was dissolved in corn oil, sprayed on special wheat flour (a fraction between two bolting cloths in a mill DuPont bought for the purpose) and sold to feed manufacturers for use in chick and laying formulas. If you ate any eggs in North America during World War II, chances are they contained synthetic D-3 which had been stored in the cold room where I kept my lunch.

With James Waddell as director of research, the group was expanded. I was employed by DuPont a dozen years or so, partly in the lab and partly as a nutrition consultant. I was supposed to be the amino acid authority. I suggested that they produce lysine (a major wheat deficiency), and methionine (a major soy bean deficiency). In one of the old powder mills on the bank of the Brandywine (where the U.S. Government had asked Mr. DuPont to make gunpowder close to the capital so it couldn't be cut off by the British), pilot production of DL-methionine was begun.

We had the only supply of methionine in any quantity. A call came from Grace Hospital in Detroit, pleading for some methionine



William Rose University of Illinois

at once. All efforts had failed, and a 14-year old girl was in a coma with a liver condition. I immediately air-mailed 150 grams. A few weeks later we received a remarkable letter from the Hospital. As soon as it arrived, they had injected it IV. Within a few minutes her eyelids had begun to flutter. Two weeks later she was dismissed from the hospital to return home.

It had been a long time from 1881 when phenylalanine was discovered, until 1922 when Mueller discovered methionine, the next to the last of ten dietary essential amino acids for rat growth. I recall a hot steamy day at the Peabody Hotel in Memphis, in an upper room, when William Rose announced his discovery of threonine, the last essential amino acid to be discovered. That must have been shortly after 1935.

At that meeting, with perhaps a hundred nutritional scientists present, L.A. (Stub) Maynard was chairman, and he asked me to operate the slide projector because he knew me from my time at Cornell. People realized that this discovery was a nutritional landmark, and when Rose had finished, everyone stood up and cheered, a standing ovation. In

Attending a nutrition conference in Atlantic City, April 1954. L to R: James Waddell; Elmer Nelson; A. Rae Patton. Dr. Nelson was Chief, Food and Nutrition Section, FDA.

honor of the occasion, I made up a silly little mnemonic: "Any help in learning ten little molecules proves truly valuable." Thus, arginine, histidine, isoleucine, leucine, tryptophan, lysine, methionine, phenylalanine, threonine, valine. Somehow this spread across the nation.

Trouble began to appear with the vitamin D-3 product. There were complaints that in poultry feed, it didn't "keep," it wasn't "stable," it "oxidized." In some batches only. Top management announced that solving this problem was the number one priority. I figured out a way to solve it. By labelling the carrier I devised a way to detect it, even the tiny bit mixed in the formula.

Feed manufacturers mixed rations by dropping ingredients from hoppers onto a moving belt. I was able to prove that the complaints came not from instability of vitamin D-3, but from it not being in the feed at all. Every so often the carrier in the hopper would arch at the bottom, and for some seconds none fell onto the moving belt. The whole difficulty was solved with electric vibrators on the hoppers. Nothing in my ten years of college training had prepared me for solving this "nutritional" problem.

Most of my personal research at DuPont was concerned with improving the nutritive value of soy-bean oil meal. With methionine of course; but something else was lacking which was present in sardine (pilchard) meal. We called this unknown factor APF, meaning "Animal Protein Factor," but in more discouraging moments we called it "Apple Pie Flavor." Others found out ahead of us, that it is a very complex molecule containing cobalt, required in extremely small amounts, and called vitamin B-12.

Because of my interest in methionine I followed the outstanding research of Dick Block and Vincent DuVigneaud. Dick was

later killed in a small plane crash in South America. DuVigneaud was a stately man who always reminded me of Paul Whiteman, famous in the twenties as "the king of jazz." The research report I wrote was published *(J. Nutrition* 31: 485-496 [1946]); and a later article by DuVigneaud stated that I was the first person to prove a relationship between vitamin B-12 and transmethylation.

About 1944 the National Research Council asked me to set up an RDA for the essential amino acids, similar to the vitamin Recommended Dietary Allowance. This I reluctantly refused to do, because I thought it would depend on what else was in the diet.

Meanwhile, a lot of vitamin D-2 was being made elsewhere from ergosterol, because that is cheaper. Another company was irradiating without paying royalty to the Wisconsin Alumni Research Foundation (WARF), which brought suit for patent infringement in a Federal District Court. When the judge read in the patent that it included the sun, he said "you can't patent the sun," and invalidated the patent. DuPont had so far paid $7,000,000 royalty, which it didn't seek to recover.