



Alexander Marble



Alexander Marble was born February 2, 1902 in a log cabin in Troy, a small town in the northeast corner of Kansas. His father was a school teacher, and he and his two sisters were brought up in a modest and financially frugal environment, but obviously one in which scholarship was prime. His father eventually became superintendent of the regional educational system.

He attended local schools and then the University of Kansas, earning an AB in chemistry in 1922. He stayed at "KU" another two years in preparation for medicine, and received an MA in bacteriology and immunology before departing for Harvard. While at Kansas, a paper by Donald N. Medearis and Alexander Marble, on thymic growth in the foetal pig, appeared in 1922 in the Kansas Science

Bulletin. Dr. Medearis subsequently became a distinguished pediatrician in the midwest and his son, Don Jr., is now the Wilder Professor of Pediatrics at Harvard and Chief of Pediatrics at the Massachusetts General Hospital.

Alex Marble earned his way through medical school working as a chemistry technician at the New England Deaconess Hospital, graduating from HMS in the class of 1927. A paper appeared by Mallory and Marble in *Experimental Medicine* in 1925 on immunization of rabbits with *Staph. aureus*. This was done while a medical student in Dr. Mallory's unit, in addition to his laboratory employment and medical curricular activities. After a year of medical internship at the Johns Hopkins Hospital, he returned to Boston to the Massachusetts General Hospital for two more years of house staff training.

Dating from this house staff period, several papers appeared by Walter Bauer, Alexander Marble and others on synovial fluid composition and on the biochemistry and physiology of irradiated ergosterol. It would appear that Alex Marble was headed for a career in academic medicine in the area of bone, calcium

and phosphorous. One day while checking on some rats in the animal room at the MGH, he lent his assistance to another young researcher, an attractive young lady from the mid-west, Beula Frances Becker, who had received a Master's degree in Nutrition from the University of Iowa. With Dr, Walter Bauer she was studying nutritional effects on bone in rats fed ketogenic diets. Alex and Beula were married September 30, 1930!

The next very significant component in his career was a Moseley fellowship which took the newlyweds to Europe where they first spent 6 months in Vienna in Erdheim's pathology department. They then joined Grafe in Wurzburg, followed by several months at the British National Institute of Medical Research in the laboratory of Sir Henry Dale, and finally back to Berlin for a final 2 months. Publications included papers on pentosuria, renal glycosuria, one in German on xylose metabolism, and even a paper with Sir Henry on large doses of Vitamin D in the dog. Alex Marble was in Dale's lab for only 6 months! He certainly started as a most enthusiastic and productive investigator.

Elliott Joslin kept in close touch with the hard-working, meticulous, gentlemanly medical student who did the blood sugars at the hospital for a number of years. Keep in mind, that the technology was not as simple as today, nor as accurate. Enzymatic analysis was decades in the future, and the standard was the Folin-Wu method. The more accurate and easier Somogyi-Nelson was 15 years to come. Likewise, gasometric analysis for acid-base assessment was the new thing in the management of diabetic ketoacidosis. Joslin hired the young chemically-trained Alex Marble to join him, Howard Root and Priscilla White as the fourth in his rapidly growing clinic. Joslin was a world leader in the treatment of diabetes, perhaps *the* world leader, and the offices on Bay State Road were the mecca for hundreds of diabetic children and adults, as well as diabetologists from around the globe.

Dr. Joslin, in a unique move, gave Alex Marble a small laboratory and some lab help, and more importantly, some time-off from clinical responsibilities. He was later appointed Director of Research, a position he held until 1949. As stated previously, Alex Marble soon became an international authority on the treatment of diabetic ketoacidosis. The Joslin fatality rate was a fraction of all the other centers thanks to early diagnosis, meticulous care with enthusiastic administration of insulin and saline and finally their equally careful record-keeping. Subsequent embellishments by others treating ketoacidosis included hypotonic solutions, and these led to occasional cerebral edema and death. The therapeutic pendulum rapidly swung back to the simpler but successful Marble/Joslin copious isotonic saline as the initial fluid therapy. Also, every Joslin patient was part of at least one study on diabetes management. Alex Marble brought to the clinic the highest level of scientific criticism. He became the ultimate authority on the compilation, interpretation, and dissemination of the immense amount of data collected on the innumerable Joslin patients for use in each edition of Joslin's classic text.

The standard medical resource for diabetes, Joslin's *Diabetes Mellitus*, was first published in 1916. Alex Marble was co-author of a number of editions appearing between the 30's and the 60's, and the principal author of the 11th and 12th, the latter appearing in 1985. Some 50 scientific papers were

published by him and his associates between 1932 and 1941, dealing again with the non-diabetic glycosurias, diabetic ketoacidosis and the use of various insulins. In addition, there were some very significant publications on experimental animal models dealing with glycogen and fat levels and the various effects of different insulin regimens. He was not only an excellent clinical researcher, but also a very competent physiologist. Like the other Joslin "seniors", his day started prior to the 8:00 AM patient review, attended by Drs. Joslin, Root and White and all the fellows and junior staff, with usually a handful of international visitors. Dr. Joslin would stand by the large hall clock on Deaconess 2 awaiting the staff. Dr. Marble was always one or two minutes ahead of Dr. Joslin, and, more significant, had also read the new journals and was prepared to answer Dr. Joslin's queries to the younger staff about their contents. The usual day oftentimes continued through late into the evening.

It was the Joslin tradition that each patient receive a letter from the Joslin physician after every office visit. This was dictated at first at the end of the day in the office and, when the dictaphone came onto the scene, in the evening at home and the "belt" brought in the following morning.

His research activities dealt with measurements of liver glycogen histologically and chemically, effects of various insulin preparations on glucose levels in rabbits, and a series of papers dealing with clinical problems in diabetic patients. One very interesting paper by McDaniel, Marble and Joslin, raised the question whether early, vigorous insulin therapy can "cure" diabetes, a regime now being used successfully for some other-wise normal children with evidence of early immune destruction of their beta cells. One other paper dealt with the local fat hypertrophy at the site of insulin injection in diabetic subjects. This observation was to lead to a major new area of diabetes research a decade later, namely, adipose tissue metabolism.

As might be expected by anyone knowing Alex Marble, he was already in the Army Reserve prior to Pearl Harbor. Much against his wish, his World War II stint was all state-side. After 2 years on Cape Cod, he transferred to Harmon, the 12th General Hospital where he was Chief of Medicine for 2 more years. Again, as expected, he continued as a Consultant in the Reserves for another 30 or so years, rising to the rank of Brigadier General.. His active army years were far more than being a chief of medicine or a consultant in a major hospital. A series of publications between 1942 and 1947 (9 in all) approached the problems of servicemen returning with tropical diseases, mainly malaria, including possible spread as well as therapies directed to permanent cure. He also continued as an active member in the Association of Military Surgeons and the Society of Medical Consultants.

In 1949, a young Swiss research fellow, Albert Renold, was sponsored by Dr. Marble to come to the Joslin to work on the effects of insulin on fat tissue. The Marbles met him at the railroad station and took him home for the next few days until he was able to find his own accommodations. This liaison opened the entire area of adipose tissue metabolism, the effects of insulin on lipogenesis, glycogen synthesis and many other avenues. The alliance was so successful that with strong recommendations from both Alex Marble and Elliott Joslin, Renold was able to complete his clinical studies at the Peter Bent

Brigham Hospital under George W. Thorn, followed by several years at the Brigham's Endocrine Unit. A laboratory floor in the Deaconess Hospital had been built for the Research arm of the Joslin group under Alex Marble's direction. Renold returned to the Joslin as the first full-time Director of Research, supplanting Dr. Marble in the mid-1950s. The latter continued, however, as the mentor to Dr. Renold and the subsequent Directors of the Baker (later the Joslin) Research Laboratories until his retirement. This close relationship with the "Brigham" continues today, and the academic appointments in the Research Division, now headed by C. Ronald Kahn, MD, are through the Department of Medicine at the Brigham & Women's Hospital. This academic and administrative amalgamation was essentially spear-headed by Alex Marble, bringing together the academic depth of the Brigham and the Medical School with the experience and patient population of the Joslin group. Dr. Marble was President of the Joslin Diabetes Foundation, the parent organization of the Research and Clinical Divisions from 1967, following the death of Dr. Howard Root, until 1976. He was succeeded by Dr. Robert Bradley and then, and presently, Dr. Kenneth Quickel. Alex witnessed, and for a major part, guided the clinic from the original 4 "seniors", a nurse and some secretarial and custodial help, to its present 415 employees. There are now at Joslin 51 physicians in clinical practice and 4 more in clinical research, all under the direction of Dr. Edward Horton, and, in the Research Division, 50 PhD's and 77 MD's or MD/PhD's under Dr. Kahn.

Many recognitions and awards came Alex's way, including the Presidency of the American Diabetes Association, Honorary President of the International Diabetes Association, the Banting Medal, the Distinguished Service Award of the University of Kansas, and innumerable lectureships around the world. He was the Senior Editor of Joslin's *Diabetes Mellitus*, and authored or co-authored some 300 papers. More important, he was the physician's physician. As might be expected, more diabetologists have diabetes than other medical specialists, and Alex Marble was both friend, advisor and occasionally a needed physician to these professionals with the disease of their speciality.

A few comments are in order about Mrs. Marble and their family. Beula Marble originally worked in the laboratories of Drs. Joseph Aub and Walter Bauer, looking at nutritional/metabolic interactions. She became one of the country's leading dietitians. For years she directed the nutritional component of the legendary research ward, Bulfinch 4, at the Massachusetts General Hospital. She was elected president of the other ADA, the American Dietetic Association. The Marbles have one daughter, Betsy, Mrs. Elizabeth Hartwell, and a grandson, Richard Alexander Hartwell.

What was probably most significant to others in the life of Alex Marble was his absolutely scrupulous honesty and integrity. Right behind was his intelligence and love of work. The writer of these minutes prepared a chapter for one of the Joslin editions, and Dr. Marble (it never was Alex, in deference to his seniority!) told him that he thought it was OK, but on leaving his office he said: "George, you can do better". Of course, the whole thing was rewritten! He was meticulous and orderly in his patient care, his teaching, and his writing. He was also very active in the church, both the United Parish of Brookline and the Harvard Church. Rev. Dr. Victor Scalise, Jr. a Founding Minister of the former, quoted words

used at the services for another Kansan general, Dwight Eisenhower, in his eulogy for Dr. Marble:

The time for my departure is at hand.
I have fought a good fight,
I have finished my course,
I have kept the faith. Amen.

Dr. Scalise also used the words of John Wesley earlier in his presentation, and how much these applied to Alexander Marble!

Do all the good you can
All the time you can
To all the people you can
For as long as you can

These are what Alexander Marble did until his death, 3:00 AM, September 13, 1992.

Respectfully submitted,

George F. Cahill, Jr. MD

Leo P. Krall, MD

Beula B. Marble, BA,MS (Mrs.Alexander Marble)

Kenneth E. Quickel, MD

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