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Newton E. Morton (1929–2018)

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(Top left) Newton E. Morton, professor of genetic epidemiology (December 21, 1929, to February 7, 2018). Photograph courtesy of Patricia Jacobs.
(Bottom left) Sewall Wright and Newton Morton at the board in the Population Genetics Laboratory (1979). Photograph courtesy of D.C. Rao.
(Right) Newton Morton's 70th birthday celebratory symposium in St. Louis (1999). Sitting (left to right): Robert Elston, Arno Motulsky, James Crow, Patricia Jacobs, Newton Morton, W. Jack Schull, and C.C. Li and his wife. Standing (left to right): Henrique Krieger, P. Michael Conneally, Bronya Keats, Charles MacLean, Jean-Marc Lalouel, D.C. Rao, Mark Skolnick, Stephanie Sherman, and Tim Bishop. Photograph courtesy of D.C. Rao.

Newton Ennis Morton died on February 7, 2018, at the age of 88 after a long struggle with Alzheimer disease. Morton was a legend in human genetics, population genetics, and genetic epidemiology for the nearly six decades of his active career not only for his scientific scholarship and contributions but also for the remarkably unique style in which he engaged with colleagues in scientific discourse. Morton was an avid tennis player (nearly to the end of his life), and his highly competitive spirit and passion for the game transcended into many aspects of his scientific career; he often sparred intellectually in tennis-match-like scientific arguments, disagreements, and disputes, which he always relished. He was also brilliantly witty, the manifestation of which could often be observed at meetings and in his writings. As any tennis player will attest, nothing improves one's game as much as an able opponent, and the same was true of Morton because he sought out intellectual equals (should they exist) with whom he could have a lively interaction. It would be a mistake to interpret his critique of others as

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a lack of respect—rather, it was typically the exact opposite.

Morton was also remarkably prolific: he published over 500 peer-reviewed articles, books, commentaries, and the like. He not only touched on a very broad array of topics that were the trend at the time, often with valued colleagues and collaborators, but also created new topics through the introduction of novel concepts and approaches to human genetics. He was amazingly well read—in many fields and in several languages—allowing him to frame his questions and interpret results within a well-supported context. As his trainee, Sarah Ennis described, "He was truly a fountain of knowledge ranging from the utterly bizarre to the pointedly relevant." He also did not shy away from controversial topics, such as the genetics of IQ and racial disparities, although he always shunned the introduction of politics into scientific discourse.

It is also true that Morton's passion was for science and discovery and not for the notoriety that it can sometimes bring. In many respects, he was actually a modest man and not self-promotional, and did not seek out prominent leadership positions in the human genetics community. Nonetheless, his groundbreaking contributions were recognized first early in his career as the first (and youngest at 33 years old) recipient of the prestigious William Allan Award from the American Society of Human Genetics (ASHG) in 1962 and then later in life by his election to the US National Academy of Sciences in 1990.

It would be impossible to recount with justice the career of such a brilliant and prolific scientist, so here we only provide some highlights. Along with these highlights, we provide background information about Morton's early years and time in Wisconsin from two interviews, one in 2005 by Peter Harper[1] and the other in 2012 by D.C. Rao.[2]

Early Years

Morton was born in 1929 in Camden, New Jersey, to parents who descended from the pilgrims of Massachusetts. The family soon moved to Connecticut, where his younger brother was born. Neither of his parents had a great interest in science. His father worked in transportation and had an early career working with the railway in Pennsylvania. Later, during the war, he became an instructor in transportation at Yale. He enjoyed teaching and, after the war, went to Kent State University in Ohio and spent the rest of his life teaching.

As a child, Morton got interested in science through butterflies (a story similar to many others of his generation) and thought that he would become an entomologist. He attended the Hopkins School in New Haven, Connecticut (the third oldest secondary school in the US and all male at the time), and then went to Swarthmore College in Pennsylvania for 2 years. Although still interested in entomology, Morton realized that he did not want to make a career of it. Feeling depressed, he spent hours at the biology library, where he voraciously read a variety of biology texts to find a new direction. He delved into the works of Theodosius Dobzhansky, Ernst Mayr, and George G. Simpson. He was greatly influenced by Dobzhansky's book *Genetics and the Origin of Species* and decided that population genetics would be an excellent career choice, also because he appreciated the combination of mathematics and biology (which is surprising, because the book is decidedly non-mathematical!). He finished his last 2 years of undergraduate work at the University of Hawaii in Honolulu, to which he was drawn by a young woman from the islands—he subsequently married this woman and had five children with her. Morton was also drawn by work in insular speciation, a very popular subject at the time, and he saw an exciting opportunity to study *Drosophila*. He enjoyed these efforts and continued working with this model system into his graduate years. He also became intrigued by human genetics after a course with Gordon Mainland. Mainland advised Morton to apply for graduate studies at the University of Wisconsin under the mentorship of James Crow. So after graduating in 1951 with a bachelor's degree in zoology, Morton traveled from the warmth of Hawaii north to the snowbound land of Wisconsin.

Graduate School and Junior Faculty Years at Wisconsin (1951–1962)

Morton recounted his memorable first interaction with Crow. Of course, they talked about several potential projects at their first encounter, but Crow advised Morton to first get settled before making any decisions about his graduate studies—Crow knew that housing was poor after the war and that it might take some effort. Nonetheless, Morton immediately chose to study effective population size in *Drosophila*. Somewhat reluctantly, Crow let Morton get started. Morton jumped in and completed his master's degree in 1 year, during 1952. One of the other highlights during his Wisconsin years was getting to know and interact with Sewall Wright, who had moved to Wisconsin from the University of Chicago.

In 1952, Morton also became interested in human genetics. He credits Crow, a generalist, for encouraging him and for introducing him to James Neel, who was working as a geneticist for the Atomic Bomb Casualty Commission in Japan. As Morton recalled, Neel was looking for someone competent to analyze the data but not senior enough to take it out of his hands. "So I was happy, he was happy, and I had a marvelous time there."[2]

Morton's interaction with Neel presaged others to come. There was a disagreement between the data analyses done in Michigan (by Neel) and those done in Japan (by Morton). When Morton returned to Wisconsin, he received a telegram telling him to report to Washington, DC, at 1400 hr. Morton was worried because he was clearly the underdog—Neel had been a captain in the medical corps. So when he entered the meeting room with admirals and generals sitting at a table a "mile long," he was fairly

certain he was going to have to fight or be "squashed like a fly." However, the group included Curt Stern, a prominent human geneticist from the University of California, Berkeley (and for whom the ASHG Curt Stern Award is named). Stern told a story about "how maggots would go into a piece of cheese from different directions, and by coming from different directions, they could eat it all instead of just part of it." He used this as an analogy for science, where disagreements are needed, and in this case, both points of view on the table were highly defensible. The disputes with Neel would continue for decades. What is most revealing about Morton, however, was what happened when, decades later, Neel was accused of unethical practices during his research studies on the Yanomamo and Xavante tribes of South America. Morton immediately came to Neel's defense and eloquently wrote the following:

> In his long and influential career Neel contributed to almost all aspects of genetic epidemiology from mutation to ethical and philosophical issues. His research spanned North America, Japan, Africa, and Latin America in a fascinating equipoise among clinical, biochemical, epidemiological, and molecular studies that have stimulated hundreds of researchers who enjoyed the controversies he generated as much as the insights he provided. Without exception, we treasure recollections of a high-principled and warm-hearted colleague whose field studies were a model for their generation.[3]

In other words, his disputes with Neel were born of deep respect and not of contempt. Yet, they published only a single paper together—the important initial work on the effect of exposure to the atomic bomb in Japan.[4]

Morton came into contact with many others during his time in Japan; these encounters influenced his and the future work of others. One example is Motoo Kimura, a gifted geneticist who was not well known at the time. Morton recognized Kimura's remarkable understanding of the higher mathematics used by Wright and Fisher in evolutionary genetics. It happened that Morton carried Malecot's classical paper,[5] one that Kimura was anxious to understand, with him to Japan. Morton translated the French (in which he was fluent) into English for Kimura, who easily grasped the equations that had slowed Morton down. After Morton wrote to Crow about this extraordinary exchange, Kimura was convinced to go to Wisconsin, where he and Morton shared an office until the end of their doctorates with Crow. Although Morton and Kimura never ended up collaborating, that was not true of Crow and Kimura. They published several iconic papers and a textbook on quantitative population genetics together.

Another influential colleague from the days in Japan was Jim Renwick, a British medical doctor who served as part of the British Medical Corps stationed in Hiroshima. He was interested in the classification of malformations and also had a keen interest in linkage analysis. He and Morton talked about the linkage application to dominant disorders in humans. Renwick published many significant papers on his return to England, and Morton, on his return to Wisconsin, turned his focus and his PhD thesis to this topic. He developed the idea that Wald's sequential analysis using common logarithms of exact probability ratios (called LODs) could be applied to the problem of human linkage. In so doing, he also showed how to create LOD score statistics for a pedigree of any type. He earned a PhD in genetics in 1955 from the University of Wisconsin for this work, and his thesis was published *in toto* in the *American Journal of Human Genetics* that same year.[6] This landmark paper provided the basis for accumulating evidence across pedigrees for statistical analysis and is still his most cited. One of the first successful applications of this method was for elliptocytosis, which was shown to map to more than one locus.[7] In this paper, he also introduced a statistical approach for testing genetic heterogeneity, which proved its existence for this disorder. Although genetic heterogeneity was a familiar finding in *Drosophila* genetics, it was new to human genetics. Importantly, Morton introduced the need to control for type 1 error in linkage studies (e.g., LOD ($Z > 3$)) by using a probability argument, a criterion that was subsequently validated empirically[8] and continues to this day.

After graduation, Morton continued to work at the University of Wisconsin as an assistant professor (1956–1960) and then as an associate professor (1960–1962). During his years in Wisconsin, he extended classical models of segregation analysis with the use of the computer, furthered the concept of genetic load and showed the large contribution of recessive genes to idiopathic deafness (which was subsequently validated by molecular studies), and characterized the genetics of spherocytosis. He also turned his attention to the genetics of interracial crosses to answer questions about the effects of outcrossing. During 1958–1959, he and his colleagues collected data on about 180,000 live births and late fetal deaths from 1948 to 1958 from Hawaii. Hawaii was the best place for this type of study because of the relative equality and short outbreeding history of many racial groups. Morton and his colleagues showed that individuals from first-generation outcrosses are intermediate between the parental groups in size, mortality, and morbidity.[9] This work led Morton to go back into the field and collect data on high-mortality populations. He spent 1962 in Brazil, where he collected data from more than 1,000 large nuclear families, about 7,000 people in total, who were emigrants from northeastern Brazil and attended the Hospediaria de Imigrantes in Sao Paulo. He and his Brazilian colleagues (Drs. C.A. Barbosa, H. Krieger, and E. Azevedo to name a few) published over 25 papers on the genetics and epidemiology of various disorders—including endemic goiter, acheiropodia (the handless and footless), and Chagas disease—and of common traits such as height, weight, and blood pressure. It was at the same time that Morton and colleagues pioneered continental admixture analysis, as applied to the Brazilian

population. This work preceded, by decades, modern studies of genetic admixture.

Back to the University of Hawaii at Manoa and the Population Genetics Laboratory (1962–1985)

During the year in Sao Paulo, Morton accepted an offer from the University of Hawaii to start a new department of genetics. After 2 years, he realized that administration was not his avocation and that it very much interfered with his science. In 1968, he created the university's Population Genetics Laboratory (PGL), which was devoted solely to research. He remained director of the PGL until 1985. Although situated in Hawaii, it was never insular. Morton invited the top geneticists to visit and work in the laboratory for extended periods of time, which was made possible by a grant from the World Health Organization. To support his research, he amassed computer power with enough capacity to attack novel analytical problems. However, trying to keep the "computer room" cool under the Hawaiian sun in a wooden building with no insulation was always a challenge. He had a devoted team of programmers and analysts, most notably Shirley Yee and Ruth Lew, who supported him and his collaborators during those PGL years. You see their names on all of the major publications from the PGL. Behind the scenes were those who supported all the PGL'ers—Evelyn Yoshioka, Evelyn Hiraki, and Helen Tomiyasu.

Once the word was out, no one could pass up the opportunity to work in such a stimulating environment and play in such a beautiful setting. Morton's graduate student trainees during the PGL years included Norikazu Yasuda, Henrique Krieger, Anne Campbell Spence, and Wick Williams, many of whom also became prominent in the field of human genetics. Morton's trainees and colleagues were exposed to some of the loudest and most contentious arguments in the small breakroom at the end of the barrack because he made sure that all sides of a topic were attacked. If you couldn't join in, you had to at least stay seated and take it all in. Morton, the tennis enthusiast, would also occasionally challenge his students to a game of tennis, or if that didn't materialize, to a comparable intellectual exchange back in the barracks. And, according to Anne Spence, a graduate student at the time, if tennis did not provide a stress release for the students, then bouncing a ping pong ball around the graduate student office in teams in a game of table tennis without the table sufficed.

In the early 1970s, Morton launched a series of innovative advances with assistance from his close colleagues Charles J. MacLean and D.C. Rao; they wrote a series of papers that introduced methods associated with deconstructing family resemblance into its causal components.[10–14] Methods included segregation and path analysis, group differences expressed in families of hybrid ancestry, linkage, mutation screening, parentage exclusion, and recurrence risks. Jean-Marc Lalouel joined the PGL in the 1970s and also worked closely with Morton on the study of kinship relationships in various unique populations, building tools for linkage, gene mapping, and complex segregation analysis (e.g., POINTER[15]) and later was instrumental in promoting the Centre d'Etude du Polymorphisme Humain (CEPH) as a reference set of families for gene mapping.[16]

The late 1960s through the early 1980s were distinguished by PGL visits from prominent scientists such as Sewall Wright (genetics) and C.R. Rao (statistics). Early on, C.S. Chung, an epidemiologist at the University of Hawaii, collaborated with Morton on the application of these methods to cleft lip or palate, natural selection at the ABO blood group locus, and periodontal disease. Many of Morton's collaborators—Tim Bishop, Robert Cloninger, Charles Cotterman, Robert Elston, Walter Fitch, Tobias Gedde-Dahl, John Grove, Henry Harpending, Don Harris, Irene Hussels, Lennart Iselius, Henrique Krieger, Kenneth Lange, Ian Shine, Mark Skolnick, Anne Spence, Craig Stevenson, John Sved, Peter Workman, and numerous others—visited the PGL multiple times and for extended periods to further develop methods of addressing new problems. Morton was not just interested in developing methods for others to apply. He was completely absorbed in trying to characterize the genetic underpinnings of disorders such as muscular dystrophy, leprosy, multiple sclerosis, type 2 diabetes, neural tube malformations, schizophrenia, etc. International collaborators would arrive at the PGL with their extensive datasets to delve into these methods and worked with Morton to develop new ones if necessary to find answers to their questions. Everyone would agree that Morton had a remarkable intuition about the directions to take on a project after just a few days of concentrated analysis.

During the 1970s, a celebrated controversy developed in terms of models and approaches for segregation analysis. Morton had always focused on nuclear families for such analyses. But in the early 1970s, Robert Elston and his colleagues developed efficient computer algorithms for analyzing extended pedigrees for both linkage analysis and segregation analysis. The two extant models were both created to address the question of major gene effects for both quantitative and discrete traits. But a computational limitation created a fissure. Morton believed that it was critical to include a polygenic component in the models because polygenic inheritance and distributional skewness could mimic major gene effects. In the pedigree models of Elston and his colleagues, a polygenic component challenged the computational efficiency of their models; however, they included transmission parameters (called tau) that estimated the transmission probabilities of presumed major genes from parents to offspring, and these were tested against their Mendelian expectations. Because DNA data in those days were scant, the models were based solely on trait distributional patterns in families. The dispute between Morton and Elston became sufficiently intense that Morton, no doubt seeking a tennis-match equivalent, proposed a "Genetic Analysis Workshop" in which data were simulated and offered to

participants to try to resolve the methodologic conflict. He persuaded Jean MacCluer, in collaboration with other colleagues, to lead this workshop series. The workshop was such a success (although not at resolving that controversy) that it has persisted to the present; it focuses on a broad array of methodologic questions in genetic epidemiology by using both simulated and real datasets.

Elston first met Morton at an ASHG meeting in 1965, after which Morton invited him to Hawaii, where he spent several summers and a complete year. As was true of the case with Neel, despite the public displays, the two got along well, and as Elston recounts, "Newton taught me a lot, both while I was in Hawaii and when we met at meetings." Morton and Elston did end up collaborating on a number of papers, but one in particular, on a "Unified Model of Segregation Analysis" led by Jean-Marc Lalouel,[17] in which the transmission tau parameters were included in the mixed model (including both a major gene and a polygenic component) for nuclear families, stands out. With the advent of DNA-based genetic markers, first for linkage analysis and then for genome-wide association studies, the controversy eventually dissipated as the field learned the inherent complexity of nearly all inherited traits and as statistical models that included direct genomic assessments began to arrive.

The methods developed by Morton and others laid the foundation for the field of genetic epidemiology. Morton attributes to Neel and Jack Schull the idea that epidemiology did not have the needed tools for genetic studies. In addition, he noted that population genetics considered environmental variables noise. Early studies by Morton in Hawaii on inter-racial crosses pointed to the need to have these two disciplines come together.[9] He recalled that he mistakenly advocated for the order of words as "genetic epidemiology" whereas Neel suggested "epidemiological genetics." As Morton said, he opposed Neel on any topic—that is just what he did. In retrospect, Morton agreed that Neel's choice was better. Nonetheless, the name "genetic epidemiology" stuck, and Morton authored two books outlining the concepts and the tools of genetic epidemiology.[18,19] D.C. Rao created the journal *Genetic Epidemiology* in 1984. In 1992, the International Genetic Epidemiology Society was launched, and Morton was the one who strongly recommended that Neel be invited as the founding president.

Also during his time in Hawaii, Morton met his second wife, Patricia Ann Jacobs, an internationally recognized human geneticist with cytogenetics as her focus. They commuted between Scotland, where Jacobs had a professorship at the University of Edinburgh, and Honolulu for some time before Jacobs took a position in the Department of Anatomy at the University of Hawaii School of Medicine. The move for her was not without challenge—she started with none of the resources she had available in Edinburgh to support her work. Nonetheless, she was eventually able to set up her laboratory and research group. Plus, she had the added advantage of having Morton there at her side for advice and collaboration. No doubt, Jacobs was Morton's favorite collaborator, and they co-authored 20 papers together; Morton provided the statistical and population genetic expertise to Jacobs' cytogenetics projects. It is notable that Jacobs was the first (and youngest) female William Allan Award recipient from the ASHG (in 1982), making Jacobs and Morton the first "power couple" of human genetics. Jacobs also brought her love for Scottish traditions to the islands. She and Morton hosted "Burn's Night" suppers, loved Scottish dancing and music, and to that end, helped organize the Lanikai Scottish Formation Team—they were a dashing couple in their tartans. They remained devoted to each other through the rest of Morton's life.

In the late 1970s and early 1980s, new challenges coming to the forefront involved the integration of family linkage data, radiation hybrid data, and human-rodent somatic cell hybridization data for the mapping of genetic markers on each chromosome (e.g., Rao et al.[20]). Working with Morton, Bronya Keats at the PGL came to the forefront of the International Human Gene Mapping Workshops.[21] She was very instrumental in encouraging investigators to share their data and collaborate, a unique contribution at that time.

The group of people at the PGL and in the Department of Anatomy with Jacobs in the 1980s—Terry Hassold, Patricia Hunt, Stephanie Sherman, Tim Bishop, Bronya Keats, Charlie MacLean, Shirley Yee, Ruth Lew, and others—had the great fortune to work, learn, and enjoy life in the setting that the pair had created. Sherman had the unique opportunity to work with both Morton and Jacobs to study families with fragile X syndrome. Jacobs and her international colleagues had collected a large series of families with what was then called marker X syndrome. Morton guided Sherman through complex segregation analyses to characterize the inheritance of this unusual X-linked mutation as a postdoctoral project. Both let Sherman learn, falter, and grow without pressure to quickly publish in a high-impact journal. The novel scientific discoveries from these studies were career shaping for Sherman. The friendships created among this group continue to this day.

A Short Stint in New York City (1985–1988) and Then on to the University of Southampton (1988–2011)

Morton left Hawaii in 1985 as he and Jacobs recognized that the field of molecular genetics needed to be incorporated into their work and they required different resources to stay abreast. They had a brief stay in New York City, Morton at the Memorial Sloan Kettering Cancer Center as chair of the Department of Biostatistics and Epidemiology and Jacobs at Cornell University Medical Center. Josh Lederberg, president of Rockefeller University at the time, gave Morton rights to play tennis at their courts, a significant incentive. During this time, Morton also created an active group involving new trainees and colleagues, such as Chris Aston, Leigh Pascoe, and Andre Rogatko, in addition to

others who migrated with him from Hawaii, such as Sherman and Bishop.

Being in the New York metropolitan area also afforded Morton the opportunity to connect with many colleagues at other universities in the region, including Yale University in New Haven, Connecticut, where his mother was also living. On one such trip up to New Haven to visit his mother, he took the occasion to visit with a favorite colleague, Neil Risch, who was a professor at Yale at the time. Morton had graciously agreed to visit Risch's genetic epidemiology class. Risch did not forewarn the students. Morton and Risch were sitting in the front of the class as the students began to arrive. No doubt they were curious who the visitor was. After everyone was settled, Risch announced, "We have a distinguished visitor here today who has agreed to answer any questions you might have about what you have learned about genetic epidemiology during this course. This is Newton Morton." Risch recalls watching their jaws drop in amazement. No doubt, his status among the students was elevated many fold as he recognized this day as a career-high-point classroom experience.

After 2 years and the recognition that their positions in New York did not fully satisfy their needs, Morton and Jacobs moved to the UK in 1988. Jacobs took up a position as director of the Wessex Regional Genetics Laboratory in Salisbury, and Morton became a professor of genetic epidemiology at Southampton University. Once again, they set up a formidable team to answer questions in human genetics and continued to train the next group of human geneticists. Morton's influence continued to be strongly felt in this new environment. John Crolla, a colleague and close friend, summarized Morton's strongly argued stand that "the key is not in the technology but in how to analyze, interpret, and utilize complex data sets." Sarah Ennis, one of Morton's postgraduate fellows and now a professor of genomics at the University of Southampton, noted that Morton's scientific prowess was based on his "exemplary scientific rigor and extraordinary insight—both strongly bolstered by a fiery competitive drive."

Morton's arrival in Southampton coincided with the formal launch of the (15-year-long) Human Genome Project. He was an active participant in the construction of the CEPH Consortium linkage maps and developed algorithms for the integration of often fragmentary genetic and physical data, which formed the scaffold for the emerging human genome reference sequence. Much of this work was achieved through a long-standing and fruitful partnership with Professor Andrew Collins. Morton was a pioneer in methodological development of disease association mapping, including linkage disequilibrium maps.[22,23] His work advanced efforts to identify genetic variation involved in common diseases and the establishment of techniques for screening whole genomes, which paved the way for the genome sequencing era.

Morton retired in 2011, when his Alzheimer disease was beginning to limit his capabilities. He continued to play tennis, take long walks, work in his garden, and spend time with his five adult children and seven grandchildren, who live in the western continental United States, Alaska, and Hawaii. Jacobs made sure that he remained independent as long as possible.

Epilogue

We are grateful that we were able to celebrate Newton Morton's achievements at his 70th and 80th birthdays. In 1999, a symposium organized by D.C. Rao, Morton's devoted friend and colleague throughout his career, was held for his 70th birthday in St. Louis. The talks from that symposium were subsequently organized into a book edited by D.C. Rao and Michael Province.[24] In 2009, at his 80th birthday, a celebration of Morton's accomplishments was arranged at the ASHG. Organized by Bronya Keats and Neil Risch, it was entitled "The Evolution of Human Population Genetics and Genetic Epidemiology, 1955– 2009. A Symposium in Honor of Newton Morton's Birthday" and included contributions from D.C. Rao, Neil Risch, Aravinda Chakravarti, and Hua Tang.

At Morton's funeral, John Crolla quoted Morton's own words, which sum up his goals for human genetics. In 2012, Morton said:

> The discovery of DNA took more than 25 years to make a strong impact on genetics. If dramatic success of the search for causal genes takes that long, many of us will not see the exciting day. Meanwhile, increasing genetic and environmental information about pathways underlying disease will guide classification, prevention, and treatment. If that information isn't the main focus of human genetics, what is?

At the 1999 meeting in St. Louis, Dan Weeks, a professor of human genetics at the University of Pittsburgh, introduced the Morton number as reflecting the distance to Morton or one of his collaborators on the basis of coauthorship on publications and noted how well connected the human statistical and population genetics community was to Morton.[25] Indeed, he directly influenced the careers of the many students, postdoctoral fellows, and colleagues with whom he worked over the years. Those who had the opportunity to work and benefit from Morton helped to move the field of genetic epidemiology to the forefront.

Those who did have the privilege of working or interacting with Morton know what an insightful, creative, and unique (if positively provocative!) scientist he was. He did not hold back on stating opinions or critiques. His attendance at meetings always promised something entertaining—whether a critical barb, a new insight, or a brilliant historical perspective—which typically delighted the audience. Probably no one of his generation knew more about the history of human genetics than Newton Morton. His impact over six decades went far beyond those with whom he directly interacted and collaborated by

stimulating generations of scientists in human population genetics and genetic epidemiology.

Morton is survived by his wife, dear friend, and colleague of so many years, Patricia Jacobs. He also was a brother to Stephen, father to five children (Teru, Peter, Amy, John, and Robert), and grandfather to eight grandchildren (Paul, Andrew, Gregory, Adolphus, William, Teru, Mika, and Charly). He passed along his love for biology, wide-open spaces, long hikes, and curiosity. We celebrate Morton's life, his family, his friendships, and his many, many contributions to human genetics and genetic epidemiology.

We conclude this tribute with a quote from his illustrious graduate advisor James Crow on the occasion of Morton's 70th birthday:

> Newton Morton has pioneered in one area after another. Human genetics is a far richer field for his having been involved in it.[26]

Acknowledgments

We would like to thank all of Newton Morton's friends and colleagues who immediately gathered on hearing of his passing to make sure that a tribute was written. There was the immediate heart-felt sadness of recognizing his last years living with Alzheimer disease. What followed were the stories, the laughter, and the comradery among those who knew Morton. We sincerely thank everyone for their contributions.

References

1. Newton Morton, interview by Peter Harper, March 14, 2005. https://genmedhist.eshg.org/fileadmin/content/website-layout/interviewees-attachments/Morton,%20Newton.pdf.
2. Rao, D.C. (2013). A conversation with professor Newton Ennis Morton. Genet. Epidemiol. *37*, 131–135.
3. Morton, N.E. (2003). Recollections of James Neel. Mutat. Res. *543*, 97–104.
4. Neel, J.V., Schull, W.J., McDonald, D.J., Morton, N.E., Kodani, M., Takeshima, K., Anderson, R.C., Wood, J., Brewer, R., Wright, S., et al. (1953). The effect of exposure to the atomic bombs on pregnancy termination in Hiroshima and Nagasaki: Preliminary report. Science *118*, 537–541.
5. Malecot, G. (1948). Les mathématiques de l'hérédité (Masson).
6. Morton, N.E. (1955). Sequential tests for the detection of linkage. Am. J. Hum. Genet. *7*, 277–318.
7. Morton, N.E. (1956). The detection and estimation of linkage between the genes for elliptocytosis and the Rh blood type. Am. J. Hum. Genet. *8*, 80–96.
8. Rao, D.C., Keats, B.J.B., Morton, N.E., Yee, S., and Lew, R. (1978). Variability of human linkage data. Am. J. Hum. Genet. *30*, 516–529.
9. Morton, N.E., Chung, C.S., and Mi, M.P. (1967). Monographs in human genetics; Genetics of interracial crosses in Hawaii (S. Karger).
10. MacLean, C.J., Morton, N.E., and Lew, R. (1975). Analysis of family resemblance. IV. Operational characteristics of segregation analysis. Am. J. Hum. Genet. *27*, 365–384.
11. Morton, N.E. (1974). Analysis of family resemblance. I. Introduction. Am. J. Hum. Genet. *26*, 318–330.
12. Morton, N.E., and MacLean, C.J. (1974). Analysis of family resemblance. 3. Complex segregation of quantitative traits. Am. J. Hum. Genet. *26*, 489–503.
13. Rao, D.C., MacLean, C.J., Morton, N.E., and Yee, S. (1975). Analysis of family resemblance. V. Height and weight in northeastern Brazil. Am. J. Hum. Genet. *27*, 509–520.
14. Rao, D.C., Morton, N.E., and Yee, S. (1974). Analysis of family resemblance. II. A linear model for familial correlation. Am. J. Hum. Genet. *26*, 331–359.
15. Lalouel, J.M., and Morton, N.E. (1981). Complex segregation analysis with pointers. Hum. Hered. *31*, 312–321.
16. Dausset, J., Cann, H., Cohen, D., Lathrop, M., Lalouel, J.M., and White, R. (1990). Centre d'etude du polymorphisme humain (CEPH): Collaborative genetic mapping of the human genome. Genomics *6*, 575–577.
17. Lalouel, J.M., Rao, D.C., Morton, N.E., and Elston, R.C. (1983). A unified model for complex segregation analysis. Am. J. Hum. Genet. *35*, 816–826.
18. Morton, N.E. (1982). Outline of genetic epidemiology (S. Karger).
19. Morton, N.E., and Chung, C.S. (1978). Genetic epidemiology (Academic Press).
20. Rao, D.C., Keats, B.J., Lalouel, J.M., Morton, N.E., and Yee, S. (1979). A maximum likelihood map of chromosome 1. Am. J. Hum. Genet. *31*, 680–696.
21. Keats, B.J., Sherman, S.L., Morton, N.E., Robson, E.B., Buetow, K.H., Cartwright, P.E., Chakravarti, A., Francke, U., Green, P.P., and Ott, J. (1991). Guidelines for human linkage maps: An international system for human linkage maps (ISLM, 1990). Genomics *9*, 557–560.
22. Collins, A., and Morton, N.E. (1998). Mapping a disease locus by allelic association. Proc. Natl. Acad. Sci. USA *95*, 1741–1745.
23. Maniatis, N., Collins, A., Xu, C.F., McCarthy, L.C., Hewett, D.R., Tapper, W., Ennis, S., Ke, X., and Morton, N.E. (2002). The first linkage disequilibrium (LD) maps: Delineation of hot and cold blocks by diplotype analysis. Proc. Natl. Acad. Sci. USA *99*, 2228–2233.
24. Rao D.C. and Province M.A., eds. (2001). Genetic dissection of complex traits (Academic Press).
25. Weeks, D.E. (2001). Newton Morton's influence on genetics: The Morton number. Adv. Genet. *42*, 7–10.
26. Crow, J.F. (2001). Newton Morton: The Wisconsin years. Adv. Genet. *42*, 3–5.