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IN MEMORIAM

Mary Ella Mascia Pierpont: Geneticist, scientist, mentor, friend (1945–2020)

Mary Ella Mascia Pierpont, MD, PhD (Figure 1), died peacefully surrounded by family in her home in Roseville, Minnesota on August 01, 2020. With her passing, the Department of Pediatrics and University of Minnesota community lost a friend and colleague, and one of the most astute and dedicated geneticists in the country. Mary Ella was born and raised in Tarrytown, NY, a short distance north of New York City on the east bank of the Hudson River. She spent her undergraduate years studying at Mount Holyoke College in Massachusetts, and from there completed graduate work in Genetics at the University of North Carolina in Chapel Hill and Medical School at the University of Miami where she met her husband, Dr Gordon L. Pierpont. She received her PhD in 1971 and MD in 1973.

1 | TRAINING AND ACADEMIC POSITIONS

Mary Ella spent the next 4 years of her medical training in several different positions, as residency and fellowship training were at that time far less regimented than now. Her first 2 years were spent at Georgetown University Hospital in Washington, DC, where she completed an Internship and year of Pediatrics focused on Development and Clinical Genetics. She then made what proved to be her most important move to the University of Minnesota, spending first a year in Laboratory Medicine and Pathology, and then a final year in Pediatrics. By this time, Mary Ella had become interested in the heart and went on to complete a 3-year Fellowship in Pediatric Cardiology in 1980. That same year, she joined the faculty as Assistant Professor of Pediatrics in the Division of Genetics and Metabolism (later becoming Assistant Professor of Ophthalmology as well) and rose to Associate Professor in 1991 and full Professor in 2014. Along the way, she spent 12 years at Children's Hospital of Minnesota, continuing her active academic contributions. She rejoined the University of Minnesota Division of Genetics and Metabolism in 2012 due her desire to increase her opportunities for clinical studies, particularly regarding Ras pathway disorders ("RASopathies") and continuing her clinical, research and teaching efforts in congenital heart disease (CHD).

FIGURE 1 Photo of Mary Ella Pierpont, circa July 2012

2 | CARDIOVASCULAR GENETICS

Mary Ella's most sustained and important scientific contributions involved the genetic basis of heart disease in children. She studied the risks for CHD in relatives of children with heart malformations (Becker, Van Amber, Moller, & Pierpont, 1996; Gobel, Pierpont, Moller, Singh, & Edwards, 1993; Pierpont, Gobel, Moller, & Edwards, 1988; Sletten & Pierpont, 1995) and was lead co-editor of the textbook, *The Genetics of Cardiovascular Diseases* (Figure 2), still regarded as a seminal work in the field of cardiovascular genetics (Pierpont & Moller, 1987). She later served as guest co-editor of a special issue of the *American Journal of Medical Genetics* (Heart Development and the Genetics Aspects of Cardiovascular Malformations; Winter 2000, Volume 97, Issue 4) that explored congenital heart malformations (Lin & Pierpont, 2000; Pierpont, Markwald, & Lin, 2000). She developed productive collaborations with Dr Val Sheffield at the University of Iowa and others to map and clone genes associated with CHD (Cousineau et al., 1994; Sheffield et al., 1997). She also had a longstanding interest in the impact of CHD in adult survivors (Lin et al., 2008). In 2018, Mary Ella served as lead author and Chair for The American Heart Association Scientific Statement on the Genetics of Congenital Heart Disease (Pierpont, Brueckner, et al., 2018). Throughout her career, she was a tireless advocate for participation in and increased funding for research on the genetic causes of childhood heart disease.

During the past 10 plus years, her major research interest involved studies of the RASopathies, especially Noonan and cardiofaciocutaneous (CFC) syndromes. She wrote several expert studies focused on cardiac complications in the RASopathies (McCallen et al., 2019; Menon, Pierpont, & Driscoll, 2008; Pierpont et al., 2014; Pierpont & Digilio, 2018; Romano et al., 2010). She was also a clinical expert in aortopathies, a site investigator for the National Heart, Lung, and Blood Institute (NHLBI)-funded Trial of Beta Blocker Therapy (Atenolol) versus Angiotensin II Receptor

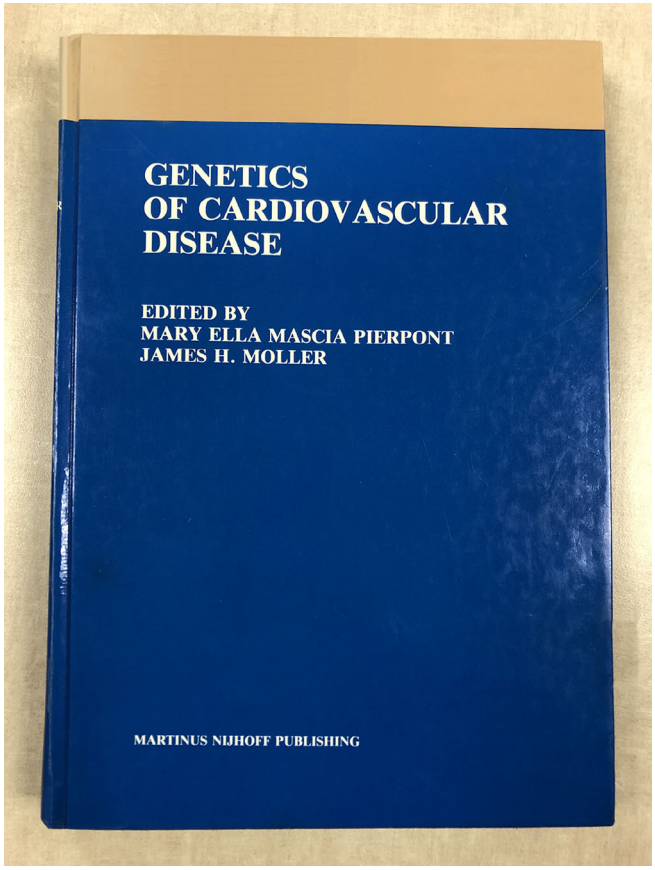

FIGURE 2 Photo of the seminal textbook co-edited by Drs Pierpont and Moller

Blocker Therapy (Losartan) in Individuals with Marfan Syndrome and an influential participant in the resulting study (Lacro et al., 2014).

3 | OTHER RESEARCH INTERESTS

In 1998, Mary Ella reported a novel syndrome in two boys with microcephaly, consistent dysmorphic facial features, and mid-foot fat pads that was later designated "Pierpont syndrome," and contributed to discovery of the causal gene, *TBL1XR1* (Heinen et al., 2016; Pierpont, Moller, Gorlin, & Edwards, 1982). The original report was one of several papers she authored with one of the founders of modern Clinical Genetics, Dr Robert Gorlin (Berry, Pierpont, & Gorlin, 1984; Coad, Angel, Pierpont, Gorlin, & Anderson, 1997; Pierpont et al., 1982; Pierpont, Stewart, & Gorlin, 1998).

In 1999, she published a paper with one of us that changed the narrative regarding Joubert syndrome, then viewed as a single homogenous disorder affecting primarily the brain with occasional retinal problems and renal cysts. Over the course of almost a year, she mentored medical student (now Dr) Dan Satran as he reviewed ~100 publications and defined a broad spectrum of overlapping phenotypes that involved the brain, eyes, kidneys, liver, limbs, and other systems, presaging later discovery of an entire class of disorders that are now designated ciliopathies (Satran, Pierpont, & Dobyns, 1999).

FIGURE 3 Mary Ella and her daughter Rene Pierpont both presented at the fourth International RASopathies Symposium and the coinciding cardiofaciocutaneous (CFC) International conference in Seattle, WA in July 2015. Mary Ella's infant grandson Elijah J. Rassette is also pictured. Photo credit Clifford Conger and Brenda Conger, Founder and previous Executive Director of CFC International

Mary Ella may be unique in having collaborated in research with both her husband, Dr Gordon L. Pierpont (Pierpont et al., 1993, 1985, 1989), and her daughter, Dr Rene Pierpont. Mother and daughter (Figure 3) were familiar participants at the CFC and Noonan syndrome support group meetings where they conducted collaborative investigations into the neurobehavioral profile of the RASopathies (McNeill et al., 2019; Pierpont et al., 2009, Pierpont, Ellis Weismer, et al., 2010; Pierpont, Hudock, et al., 2018; Pierpont, Pierpont, et al., 2010; Pierpont, Semrud-Clikeman, & Pierpont, 2017; Pierpont et al., 2014). In January 2015, the two Drs Pierpont gave the first mother–daughter Grand Rounds in the Department of Pediatrics at the University of Minnesota. For those of you interested, a video is available: https://www.youtube.com/watch?v=wnijZrKczNQ.

4 | AN EXPERT AND CARING PHYSICIAN

While her academic contributions were substantial, Mary Ella's primary focus over many years was the care of children and occasionally adults with genetic diseases. She had deep affection for her patients and their families, and the feeling was mutual. Families often commented on her approachable nature and her ability to convey genuine commitment and interest in each person that she met. The mother of one of her patients remembers that "She was there from 2 days old and there learning with [us] in the NICU when doctors knew little about the severity of Noonan syndrome. She was instrumental in saving [our daughter's] life and helping her get the understanding and help she needed lifelong. [She was] a friend who was always an email away."

Mary Ella served on the Medical Advisory Councils for multiple advocacy groups including CFC International and the Noonan

FIGURE 4 Mary Ella and colleagues (including Drs Katherine Rauen, Kent Reinker, Jaqueline Noonan, Amy Roberts, Judith Allanson and Grace Yoon) at the 2007 meeting of Cardiofaciocutaneous (CFC) International

Syndrome Foundation (Figure 4). One of the adult advocates in the Noonan group remembers that "Dr Pierpont was the most caring, kind, helpful soul you could ever meet. A joy to see her each time, and I always looked forward to catching up, hearing her news, sharing mine etc. She was always there for us as a support group (advising us, presenting for us and being part of the group of doctors at the 'clinic' at our meetings amongst other things), for our families and especially for us adults with Noonan syndrome (she had a special interest how Noonan syndrome affects us, so few doctors/researchers do)."

5 | A PERSON OF JOY

Mary Ella was a person of incredible and infectious joy. She could always be counted on to share a kind word and provide encouragement to colleagues, trainees, and patients alike. Being around Mary Ella was a breath of fresh air. She found deep pleasure in writing and sharing her knowledge, caring for patients, and caring for those around her. She was a mother and wife and her family was first in her heart. As a woman coming up in medicine in the 80s and 90s, she was one of the first to speak about work-life balance. Her love for her husband and children was boundless. Her stories about her family, including her mother who had season tickets to the New York Yankees well into her 90s, were fun and inspiring.

6 | FRIEND AND MENTOR

Mary Ella was an astute dysmorphologist who also participated actively in molecular genetics as it revolutionized the diagnosis, understanding and treatment of disorders of the cardiovascular system in children. She was a "go-to" Geneticist, one of the first to call when a colleague needed expert advice. Mary Ella served as the program director of the genetics training program for more than a decade. She was a generous and productive mentor for students and trainees throughout her career, and for several of her junior colleagues she was an inspiration to pursue dual fellowship training in both genetics and pediatric cardiology. She possessed a special wisdom and could be counted on for sage advice in navigating an academic career. Mary Ella was a wonderful friend, mentor and colleague to many, including the authors of this tribute. She will be greatly missed by her colleagues, friends, and family.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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