

Review: Paul, D. and J. Brosco. *The PKU Paradox: A Short History of a Genetic Disease*. Baltimore: Johns Hopkins University Press, 2013.

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The paradox of phenylketonuria (PKU), according to Diane Paul and Jeffrey Brosco, is as follows: PKU is a relatively rare disease — affecting roughly one out of every 15,000 people in the United States — yet, it has become a potent symbol of the power of scientific medicine, the value of the Human Genome Project (HGP) and large-scale genetic screening programs, and finally, of the fallacy of genetic determinism. Indeed, it is a simple story that biologists, geneticists, physicians, and philosophers of biology all know well: PKU is a classical Mendelian metabolic disorder that leads to profound cognitive impairment in patients left untreated. However, if detected in infancy, patients placed on an appropriate diet (very low in phenylalanine) will develop normally. Our genes were not our destiny, it turns out. However, Paul and Brosco argue that the story of PKU is not so simple, and that to be able to serve the multiple scientific and political agendas that it has, the story of PKU first had to be stripped of all its messy complications, conditions, and origins. The *PKU Paradox* — part of the Johns Hopkins *Biographies of Disease* series, edited by Charles Rosenberg — aims to restore what has been lost in the transformation of PKU into a medical parable. Diane Paul comes to this project as an historian of biology and genetics and Professor Emerita at the University of Massachusetts, and Jeffrey Brosco as a developmental pediatrician and professor of clinical pediatrics at the University of Miami. Together, they weave the biography of PKU through a number of rich historical trajectories, including the history of newborn screening, patient activism, and medical ethics, in addition to the more familiar histories of genetics, eugenics, and psychiatry.

The book's ten chapters trace the history of PKU from its discovery as a defect in the metabolism of phenylalanine by Ivar Følling in Norway in the early 1930's, through the development of dietary treatments and improved testing technologies in the 1950's and 60's, to the emergence and expansion of mandated newborn screening (NBS) programs in the United States beginning in the 1960's. Their focus is largely on the United States — the only country where screening for PKU was mandated by law — although their narrative necessarily takes them across national boundaries as they consider the history

of early research on its etiology, and into diagnostic methods, treatments, and screening programs. Their history contains a wealth of interesting information about the rise of NBS programs, including for example, the critical role that patient activism and political lobbying played in securing state-mandated screening programs for PKU in the US, in spite of lingering uncertainties among scientists about the efficacy of current diagnostic and treatment methods. As well, Paul and Brosco show us how ethical difficulties emerged over time, as screening programs expanded — especially with the advent of newer technologies, such as tandem mass spectrometry — to include a number of diseases that did not fit well within the PKU framework, such as those which have no cure, or for which testing was for the mere *probability* of future disease.

The primary aim of *The PKU Paradox*, however, is to provide a fuller picture of the disease than is found in the traditional success narratives that have come to surround it. The authors accomplish this through two moves: first, by correcting certain historical inaccuracies or omissions that have accrued to the story of the disease — indeed, this work also represents the first book-length history of PKU — and second, by highlighting some of the quotidian difficulties and uncertainties that patients experience while living with and managing the disease.

One of the most compelling aspects of this book emerges out of a detour the authors take from straightforward history to including patient-centered narratives about living with PKU. Over a period of a few years, Paul conducted a series of interviews with individuals with PKU. It was an aim of this book to give nonspecialist readers a sense of the daily realities of managing the disease. These interviews reveal the many personal, social, and economic obstacles that make maintaining the recommended low-phenylalanine diet difficult: from the embarrassment of being perceived as “different” as a child, to the difficulties of maintaining the proper diet during pregnancy, to the many obstacles preventing reimbursement for low-phenylalanine formulas from insurance companies.

The unpacking of symbolic or paradigmatic stories in the history of biology and medicine has become characteristic of the historical work of Diane Paul, and *The PKU Paradox* follows in this tradition. Paul and Brosco reveal that inaccuracies or omissions were introduced to the popular narrative surrounding PKU as its story was transformed into a simplified paradigm used to justify a particular interest or goal. For example, proponents of the Human Genome Project (HGP) in the 1980's frequently appealed to the case of PKU to justify the value of the proposed mapping project in the face of its

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huge costs. The story they invoked repeatedly in newspapers and magazines was one in which genetic research led to the successes of current PKU screening and treatment programs. Yet, as Paul and Brosco point out, genetic research has actually contributed little, if anything, to therapies for PKU — instead, these came largely from biochemical investigations conducted years prior to the identification of the gene for phenylalanine metabolism. Similarly, they highlight how the history of PKU screening has been used to justify both cautionary warnings about, as well as the promotion of, expanded screening programs by alternatively emphasizing the difficulties surrounding treatment and diagnosis, or the successes of PKU screening programs. “The lessons of history,” they remind us, “are rarely self-evident” (p. 202).

Indeed, they require careful consideration, which is what *The PKU Paradox* offers. In the process, Paul and Brosco have written something of a double history, that of PKU the paradigm and of PKU the disease. The biography of so symbolic a disease as PKU necessarily includes the former. Yet, by restoring some of the details and nuances to the history of PKU, Paul and Brosco enable the reader to shift their gaze from PKU the paradigm to PKU the disease, in all its historical and biological complexity. For this reason, this book will be of interest to historians and practitioners of medicine alike. Moreover, it also serves as an excellent example of the constructive possibilities inherent in a collaboration between historians and physicians, and indeed, of the value of such an approach.