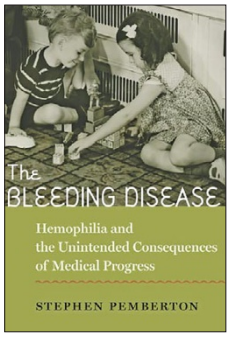
The history of hemophilia



The Bleeding Disease: Hemophilia and the Unintended Consequences of Medical Progress

Stephen Pemberton

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Reviewed by Katherine A High

Few stories in modern medicine oscillate as dramatically between triumph and tragedy as the history of hemophilia. *The Bleeding Disease*, by historian Stephen Pemberton, combines classic history of science with sociological analysis to tell this story in a style that should appeal to both medical and lay audiences.

The book's early chapters focus on hemophilia's history in the nineteenth and early twentieth centuries and are arguably the best reading in the book. The author traces the evolution of the modern understanding of hemophilia, from the initial description in the medical literature by the Philadelphia physician John Conrad Otto in 1803 to our current grasp of a whole range of clotting factor deficiencies, both sex-linked and autosomally inherited; and from early concepts that the disease was a type of systemic disorder to the realization that the defect was in the blood and, more specifically, that it was a deficiency of a substance in the plasma.

The author's discussion of the role played in the British medical literature by the presence of hemophilia in Queen Victoria's descendants is fascinating; Prince Leopold's disorder was described for years as "weak veins" at a point when many medical men knew otherwise but were reluctant to identify the devastating inherited disorder in the British royal house. The physician John Legg, who served briefly as Prince Leopold's tutor and medical attendant, had a firm grasp of the heredity in the disorder when he argued that "bleeders" ought not to marry, as even if the sons escaped the disease, it would reappear in the daughters' sons. Clearly, these ideas would be anathema to a royal household with many sons and daughters, and open discussion of hemophilia was thus constrained, at least in Britain, during Victoria's reign.

As Pemberton notes, the realization that the defect was in the blood led to the concept of treatment by blood transfusion. A few bold practitioners, motivated by the desperate circumstances of patients, sought to act on this realization as early as the mid-1800s, but lack of knowledge of basic principles of donor-recipient blood compatibility made this a risky undertaking until the discovery of blood types made their way into practice in the early twentieth century. Pemberton skillfully demonstrates how progress in hemophilia treatment was absolutely dependent on progress in transfusion science.

Pemberton also covers in lively detail the series of incorrect observations and blind alleys that were pursued on the path to the current formulation of the blood clotting cascade. That hemophilia was thought as late as the 1930s to be a platelet defect will come as a surprise to many, and the concept advanced by one earnest hematologist that the disease arose in men from lack of some female sex hormone persisted for longer than one might guess.

The excellence of the author's early history of hemophilia makes one wish that this part of the book would never end. It is thus disappointing that certain crucial accomplishments in the science of hemophilia are not included in the book. The isolation and characterization of the genes encoding factor VIII and factor IX, the development and licensing of recombinant clotting factor concentrates and the recent delineation of the mutation in Queen Victoria's line, by sequencing of DNA derived from the bones of the Romanovs, might all have been well told stories in the author's capable hands. Instead, the next section of the book veers off into a history of the formation of a community of people affected by hemophilia in the US during the post–World War II era and the rise of the National Hemophilia Foundation.

The author recounts in a particularly vivid way the burdens imposed on families of hemophilic sons, who were expected to 'replace' the units of blood consumed by their sons by inducing friends and family members to donate blood. The development of clotting factor concentrates thus seems to have been a major relief for these families; not only do clotting factor concentrates allow boys with hemophilia to lead near-normal lives, but also the pharmaceutical and plasma fractionation companies absorb the task of locating donors, reducing the families' obligation to a purely financial one. The author points out, however, that this was a Faustian bargain, as the plasma fractionation industry relied heavily on paid donors, which clearly contributed to the spread of hepatitis and then of HIV into the hemophilia community. Pemberton makes it clear that this reliance on paid donors was not well understood by most consumers at the time.

The book takes a surprising turn at the end, where it unfortunately seems to devolve into a polemic against a whole range of individuals and organizations involved in decisions surrounding use of plasma-derived clotting factor concentrates. HIV transmitted in the older plasma-derived concentrates resulted in an AIDS epidemic that affected the majority of those with severe hemophilia in the Western world. It is hard to argue with the proposition that these patients were poorly served by whatever safety systems were in place as HIV entered the blood supply. I remember, though, how reluctant most blood bankers were, for example, to institute *any* measures that would reduce the flow of units into the blood banks; in retrospect, this was wrong, but faulting them as a group fails to recognize that they had spent their professional lives in a seemingly hopeless battle to have blood available when it was needed. Other players in this drama come in for criticism, as well, including the plasma fractionation industry, the US Food and Drug Administration and physicians, but this part of the book contains more heat than light and suffers from a much less objective presentation than the earlier parts. Nevertheless, the best parts of the book outweigh its shortcomings and are well worth the read.

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