HEMOPHILIA: THE FIRST RECORDED GENETIC DISORDER

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Centuries before hemophilia became a medically recognized blood disorder, the rabbis in the Talmudic era recognized its symptoms. The Talmud (*Yevamot* 64b) relates Rabbi Judah the Prince's ruling that if a woman's first two children died from blood loss after circumcision, the third son should not be circumcised. Rabbi Simeon ben Gamliel disagreed and ruled that the third son may be circumcised, but if this infant died then the fourth child should not be circumcised. These two Rabbis agreed that the abnormal bleeding was hereditary, but disagreed as to how many repetitive events were required to establish a pattern and therefore exempt a child from circumcision. While three events are usually required by Jewish law to establish a pattern, Rabbi Judah ruled that in matters of life and death, two repetitive events were enough to establish a trend.

The Talmud continues with another story about four sisters from *Tzippori*. It related that the first three sisters each had a son who died from circumcision, and when the fourth sister had her first son, she came before Rabbi Simeon ben Gamliel and asked him if she should circumcise her newborn. Rabbi Simeon ben Gamliel ruled that her son should not be circumcised. This ruling shows that Rabbi Simeon ben Gamliel thought the disease was passed down maternally. The Talmud goes on to state that some families have "*Rafei D'ma"* (loose blood), while others do not.

Since the cases discussed here involve sons with bleeding disorders, the Rabbis were probably talking about a recessive mutation transmitted on the X chromosome. Females have a much lower risk of being affected by disorders that are carried on the X chromosome, since a deficient gene with a recessive mutation on one X chromosome can be masked by the equivalent normal gene on their second X chromosome. However, males who have a deficient gene on an X chromosome are always affected, since they do not have a second X chromosome to compensate for the defect. The disease discussed in the Talmud, thus, was most likely a maternally-transmitted hereditary bleeding disorder.

Later codifiers of Jewish law based their rulings for circumcision of hemophiliacs on these Talmudic discussions. Rabbi Issac Alfasi, an eleventh-century scholar, ruled that the law was in accordance with Rabbi Judah the Prince. Moses Maimonides, a well-known scholar and physician who lived in the twelfth century, added to Rabbi Judah's ruling and stated that even if the first two sons who died after circumcision were from different husbands, the third son should not be circumcised. Instead, the surgical procedure should be postponed until the child matures and establishes his strength. Rabbi Yosef Karo, in his commentary on Maimonides, cited the above Talmud and stated that the disease being discussed involves loose blood and is hereditary.

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Although Maimonides believed that this bleeding disease was maternally transmitted and that an abnormal bleeding pattern could even be established in siblings who were only maternally related, other commentators held that the disorder could be transmitted by either parent. Rabbi Jacob Reischer, among others, ruled that if a man's first two sons died from loss of blood after circumcision, the third son should not be circumcised. Although there was some debate as to whether the bleeding disorder could be paternally inherited, everyone agreed that it could be passed on from the mother. Fred Rosner [1] has reviewed this in detail.

A simple reading of these sources indicates that the bleeding disorder being discussed is hemophilia. Hemophilia is a genetic bleeding disease which is caused by a deficiency in one or more protein clotting factors. Clotting factors work in a chain reaction, and each protein is needed in order to complete the reaction and cause the blood to clot. When there is a deficiency in at least one of the plasma clotting factors, the body's ability to control bleeding is impaired. The two most common forms of hemophilia are hemophilia A and hemophilia B. Hemophilia A is caused by a lack of clotting factor VIII, while hemophilia B is caused by a lack of clotting factor IX. Both of these forms are inherited as X-linked recessive genes, so most hemophiliacs are male and the gene is maternally inherited. The severity of the disease depends on the

individual. Although for some hemophiliacs scrapes and cuts can be life-threatening, others only experience complications during surgery and internal bleeding [2].

Although Maimonides believed that the bleeding disease was only passed down maternally, he was also of the opinion that the disorder would improve over time and that the child could undergo circumcision at a later age. Hemophilia generally does not improve over time. Additionally, in Maimonides's discussion of delaying the time of circumcision, he does not directly quote the passage of Talmud that discusses hemophilia. Instead, he brings a case where the circumcision "enfeebled his strength", and does not talk about a thinning of the blood. Therefore, it is possible that Maimonides was not referring to a blood disorder, but to a different disorder altogether.

As mentioned above, there was a disagreement among the Rabbis as to whether the faulty gene was only able to be transmitted from the mother or whether it could also be passed down from the father. It is possible that the Rabbis who believed the bleeding disorder could be passed down from the father were referring to a third type of hemophilia, known as hemophilia C. Hemophilia C, caused by a deficiency of clotting factor XI, is transmitted as an autosomal recessive and can therefore be passed down from either parent. Additionally, while it only makes up 2-3% of those affected with hemophilia, it predominantly occurs in Jews of Ashkenazi descent [2]. It is possible that the Rabbis referring to this blood disorder were in fact discussing hemophilia C.

While it can be suggested that the different rabbinic commentators were indeed referring to different blood disorders and not just hemophilia, the Talmud and Rabbi Isaac Alfasi's suggestions that the child should not be circumcised imply that even when they get older they should remain uncircumcised. Their answers, especially in comparison to Maimonides's ruling that circumcision should merely be pushed off, suggest that the bleeding disorder they were referring to was indeed hemophilia. When the first accurate description of hemophilia in medical literature was initially discussed in the nineteenth century, it served as a confirmation of what the rabbis noted and recorded in the Talmud many centuries ago [3].

In evaluating the rabbinic response to the various bleeding disorders, it must be remembered that these rabbinic figures only wrote about what they themselves came into contact with in their own communities. They did not have access to the scientific knowledge that we do today. Hemophiliacs and people with other blood disorders were diagnosed solely through their sibling history. Some believed that those affected by bleeding disorders could mature and become stronger, and therefore be fit to undergo circumcision at a later time. Others felt that individuals who were affected by blood coagulation diseases should at no point in their lives be circumcised. However, no rabbi would have stated that a known hemophiliac should ever be circumcised. Since the rabbis did not have a detailed understanding of hemophilia, it could have been possible that its symptoms were confused with those of neonatal morbidity. Thus, certain rabbis did not easily distinguish between these two disorders and ruled that circumcision should be performed once the child matured and grew stronger.

While hemophilia was once considered a dangerous, and even fatal disease, recent medical advances have led to greater control over its symptoms. Although there is still no cure for hemophilia, those affected by the disease can be treated with regular injections of a clotting factor replacement, depending on which form of hemophilia they exhibit [2].

The availability of treating a child affected by hemophilia with clotting factors before and after a surgical procedure led Rabbi Shlomo Zalman Auerbach to rule that according to Jewish law, circumcision should be performed on hemophiliacs. According to Rabbi Auerbach, the dearth of clotting factors is not reason enough to prohibit circumcision, since supplemental clotting factors may be injected and the person's blood clotting system will temporarily behave normally during and after the surgical procedure. Rabbi Yehoshua Neuwirth challenged this opinion, and stated that as long as there is no cure for hemophilia, temporary treatments should not be depended on and do not change the child's status as a hemophiliac. Rabbi Yechiel Yaakov Weinberg ruled that, in relation to an adult male convert candidate who is medically unable to safely undergo circumcision, the person cannot, according to Jewish Law, accept the risk and be circumcised. However, this judgment was given at a time when clotting treatments were not yet available. In his manuscript, Rabbi Dr. Richard Weiss concluded that since current treatments in surgery for hemophiliacs do exist, such an adult convert should undergo circumcision [4]. There is some thought of using laser technology for circumcision on hemophiliacs. The reader is directed to Dr. J. David Bleich's article on laser circumcision for more information on this subject [5].

Although the Talmudic rabbis prohibited circumcision from being performed on a known hemophiliac, today's medical advances should be taken into account when deciding whether an affected individual should undergo circumcision. Modern technological discoveries made in surgical procedures pertaining to hemophilia and other blood disorders can be applied to circumcision. Thus, it may be possible for affected individuals to undergo circumcision with special safeguards and precautions in place. ■

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