Tehilla Brander

“T
de individual is tied to his people both with the chains of fate and the bonds of destiny,” writes Rav Soloveitchik [1]. Fate unites the Jewish people as a result of a shared history. Jews are a people of fate because of events beyond their control. Today, this shared history can be seen not only in historical events, but in the foundation of life itself: the genetic code. Scientists are able to trace mutations that are unique to Jews and link these mutations to various periods in Jewish history. One such example is the BRCA 1/2 mutation, which can increase the risk of different cancers including breast cancer. Scientists have traced this mutation “prior to the dispersion of the Jewish people in the Diaspora,” making it a constant marker for the shared Jewish fate [2]. While fate describes the inevitable, there is another element that characterizes the Jewish nation; Jews are a people of destiny, a people who ask not “about the cause of evil...but rather how it might be mended and elevated” [1]. As a people of destiny, the Jewish community has a responsibility to face challenges that arise, whether they are political or genetic in nature. With new scientific advances, the Jewish people can become a nation of destiny, despite the fate of various genetic mutations.

Before exploring the options in addressing the BRCA-1 and BRCA-2 mutations, it is important to understand the implications of inheriting these mutations. At the phenotypic level, acquisition of the BRCA mutation results in a heterozygote with a dominant predisposition for developing cancer. As noted in pedigree analyses, the development of cancer follows a dominant pattern with incomplete dominance. It is the loss of function of the normal copy of the BRCA gene in a somatic cell that may lead to the actual development of cancer, affecting both men and women. Acquisition of mutated BRCA genes has been linked to an increased risk in breast, ovarian, prostate, and other forms of cancer [3]. The BRCA mutation is a risk factor, meaning that though the predisposition to cancer is inherited in a dominant fashion, it is only a risk. As such, it is possible that a person who has the mutation may not develop cancer. Furthermore, there are procedures that can help prevent and fight cancer, including increased screenings, oopherectomy, mastectomy, and chemoprevention. Yet one must still consider that the risk of developing breast cancer is significantly raised with the inheritance of a mutated BRCA gene. In the general population about 12% of women will develop breast cancer. However 60% of women who have inherited the BRCA mutation will develop breast cancer. In other words, a woman who has inherited the BRCA mutation is five times more likely to develop cancer [4].

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The inheritance of the BRCA-1 and BRCA-2 mutations has particular significance to the Jewish community. Apparently, many generations ago the BRCA mutation originated in a specific individual, termed the founder. Possibly because of persecutions, a small group of Jews separated from the larger Jewish community to live in an isolated region. Within this small group was the founder. As Jews tended to marry within their own limited and isolated communities, a founder effect occurred, magnifying the allele frequency of the BRCA mutation within the isolated community. As a result of the founder effect, certain mutations of BRCA are more commonly found in populations of Ashkenazi descent and were recently discovered in Sephardic communities [2]. In the non-Jewish population it is estimated that a person has a 1 in 300 to 500 chance of inheriting these mutations [5]. However, in the Ashkenazi Jewish community it is estimated that about 2.3% carry this mutation which is five times higher than that found in the general population [4]. With the knowledge that the BRCA mutation is more frequent in Jewish populations, many Jews are genetically predisposed for a higher risk of developing hereditary breast or ovarian cancer. One must consider how to take charge of this challenge and alleviate the predisposition to these malignancies within the Jewish population.
At first glance, one may consider applying the premarital testing model, already in place for preventing Tay Sachs, to BRCA-associated malignancies. However, considering the differences in inheritance patterns and in the diseases themselves, it becomes apparent that this is not an option. Tay Sachs disease is caused by an inherited recessive mutation, which does not allow the breakdown of certain fats, especially in the neurons of the brain. A child born with this disease will exhibit adverse symptoms, starting around 6 months, that progressively worsen until the child dies typically around the age of four or five [6]. There is no medical cure for Tay Sachs disease. To prevent this disease, the Jewish community advocated for premarital genetic screening tests, in which a person is tested to determine that person’s genetic status; that is, whether completely free of the Tay Sachs mutation or a carrier of the mutation. A carrier would typically avoid dating another carrier because marriage between two carriers produces a 25% chance of producing a Tay Sachs baby. This model is possible because the mutation is recessive, the carrier is unaffected, and the concern arises only when two carriers marry each other. A carrier marrying a non-carrier is fine because this match cannot produce offspring with Tay Sachs disease. However, the predisposition to BRCA-associated cancer is inherited in a dominant manner. Therefore, if the normal copy of the BRCA is inactivated in a somatic cell of the carrier, the carrier may be affected and develop a malignancy. Furthermore, regardless of the genetic status of the carrier’s mate, future progeny have a chance of being affected. Unlike Tay Sachs, once a BRCA carrier transmits the mutated gene, a carrier child who inherited one copy of the defective gene has the same risk factors as the carrier parent [7]. Additionally, the issue of stigma and anguish arises, especially during shidduchim, as being labeled a BRCA carrier might deter potential suitors. Another difference is that Tay Sachs disease is incurable, whereas the BRCA mutation is a risk factor and not an absolute predictor of cancer. There are also measures that can be taken to try to prevent cancer that results from the BRCA mutation, including more regular screenings and prophylactic surgeries, like a mastectomy and/or hysterectomy [7, 8]. For the above reasons one cannot apply the same population model of Tay Sachs to BRCA.

While current BRCA carriers have options in dealing with their carrier status, there is still a larger question of how to prevent the continuation of this mutation in future generations. One possible solution is the use of preimplantation genetic diagnosis (PGD), a procedure that utilizes in vitro fertilization (IVF) techniques, allowing couples to select those preembryos for implantation based on their genetic suitability. A woman’s eggs are fertilized in vitro (i.e. in a Petri dish) and tested for genetic constitution. Those preembryos that do not carry the mutation are chosen for implantation into a gestational carrier. Studies have found that “PGD is an acceptable reproductive option for BRCA mutation carriers, especially for those who require IVF due to fertility problems” [9]. When considering applying this technique in individual cases, there are social and halakhic issues that should be taken into consideration.

The question of when one should be tested for the BRCA mutation has been debated. If one is tested before marriage, the carrier may be stigmatized and have a more difficult time getting married. Furthermore, early testing may cause additional mental anguish, as the individual will constantly fear a cancer that, in fact, may never develop. However, to consider PGD, one must be informed of the mutation prior to having children. It is also worth noting that PGD is a challenging process financially, psychologically, and physically. While PGD may be suited for couples who already require IVF treatments due to fertility challenges, using this protocol on a communal scale may be impractical. Additionally, one must address whether it is halakhically permitted to perform PGD in this situation. Machon Pniah, an organization that assists with halakhic issues of infertility, has discussed this issue with major poskim, and “almost all said they would permit a couple to undergo PGD for BRCA mutation” [10]. A few poskim have even asserted that “the birth of a healthy child is paramount and overcomes other halakhic considerations; therefore the couple must undergo PGD” [11]. Other halakhic authorities allow PGD because it can prevent potentially life-threatening diseases. However, these poskim do not make PGD obligatory as the mitzva of having children would be fulfilled even by having a child with the BRCA mutation [11]. There are other poskim who believe that PGD as a method of genetic selection against BRCA is not permitted. Some believe that IVF should only be used in cases of infertility. Others believe that PGD should only be used for life-threatening diseases like Tay Sachs. Since BRCA is only a risk factor and certain cancers can be cured or prevented, PGD should not be used for BRCA [10]. Machon Pniah advocates that each case be dealt with on a case-by-case basis as PGD raises many complexities. In families where the BRCA mutation has historically caused cancer, PGD is worth discussing with a posek.

Just as the Jewish people do not simply accept the fate of historical events, such as the events of the Diaspora, but take an active role in molding and bettering the future, we must address genetic challenges with a similar mindset. The Jewish people should not be passive when addressing BRCA issues, which are as old as the Diaspora itself. With the advent of PGD, the option for screening preembryos for possible genetic mutations allows
for the eradication of the BRCA genes in specific cases. However, dealing with these issues on a communal level and creating a communal protocol is more complex. The issues surrounding a communal response to the BRCA mutation requires further investigation. By raising the issue, exploring solutions presented by emerging technology, and offering support to members of the community facing this challenge, we will transition from a people of genetic fate to a people of genetic destiny.

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REFERENCES