Mitochondrial DNA: A Discussion of Applications in Reproductive Medicine, Biomedical Ethics and Halacha

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Table of Contents

Abstract:

All eukaryotic organisms have mitochondria; a vital double membrane-bound organelle. Unlike nuclear DNA, which is equally inherited paternally and maternally, mitochondrial DNA (mtDNA) is primarily inherited maternally. As such, mutations of the mtDNA are only transferred via the mother. Because of the number of mitochondria needed per cell and the up to 10 copies of mtDNA per mitochondrion, the rate at which a mutation may occur is very high. A mutation within mtDNA may have significant harmful effects on cellular energy production within cells. Mitochondrial diseases have been linked to many serious health conditions, including deafness, blindness, muscle weakness, cognitive impairment, and diabetes, as well as heart, liver and kidney failure (Bleich, 2015). About 1 in 4,000 people worldwide, and some 20,000 in the U.S. have mitochondrial diseases (Park, 2019). There are various methods of intervention that can be done to reduce the inheritance of mtDNA and subsequently prevent the development of life-threatening diseases in off-spring, including mitochondrial replacement therapy (MRT). However, there is much controversy around MRT from both ethical and *halachic* perspectives. From an ethical standpoint, MRT is included in a rider that Congress passed in 2016 under the Consolidated Appropriations Act, which banned germline modifications. This encompasses all genetic engineering of eggs, sperm, or early embryos. From a *halachic* standpoint, MRT is controversial because it involves aspects of egg donations. This raises the question of who the mother of the created offspring is, which is a complicated *halachic* issue. Knowing the exact identity of the mother is crucial, as the mother is responsible for the transmission of Jewish identity. The implications of these complicated ethical and *halachic* matters are discussed.

Background:

All eukaryotic organisms have mitochondria; a vital double membrane-bound organelle. True to its nickname, "powerhouse of the cell," mitochondria play a large role in the production of cellular energy in the form of ATP. In addition to energy production, mitochondria are involved in calcium signaling, cell metabolism, and cell death (Anderson, 2019). Mitochondria are especially interesting in scientific research because they evolved through bacteria endosymbiosis. Ancestral mitochondria developed from bacteria that were endocytosed by another prokaryotic organism, which developed into a eukaryotic cell. Due to this origin, mitochondria contain their own DNA and encode for their own proteins, although they acquire most of their proteins from the translation of nuclear-derived mRNA.

Mitochondrial DNA, discovered in 1963 by Margit and Sylvan Nass. is circular double-stranded DNA lacking histones. mtDNA contains 37 genes and consists of 16,569 base pairs encoding 13 proteins (Figure 1). Although this amount of DNA seems insignificant compared to the total nuclear DNA in a human cell, it is vital for the well-functioning of the cell. Each mitochondrion in the cell contains 2-10 copies of mtDNA and a human somatic cell may contain up to 1,000 mitochondria (Amorim, 2017).

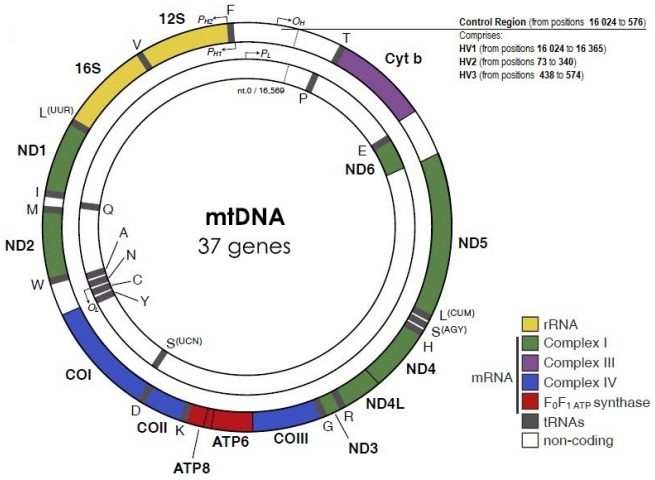

Figure 1: Labeled human circular double stranded mitochondrial DNA (Amorim, 2017)

Unlike nuclear DNA, which is located in the membrane-bound nucleus and is equally inherited paternally and maternally, mtDNA is unique in that it is primarily inherited maternally. With dual inheritance of nuclear DNA, crossing over, and independent assortment there is a great amount of genetic diversity within families. Due to its maternal inheritance, mtDNA lacks any sort of recombination with paternal mtDNA. This means that, without mutation, the mtDNA of siblings and their maternal relatives are identical (Amorim, 2017). Since mtDNA is inherited maternally, mitochondrial-based diseases or mutations are attributed to a mother's mtDNA and are transmitted to all her children (Figure 2).

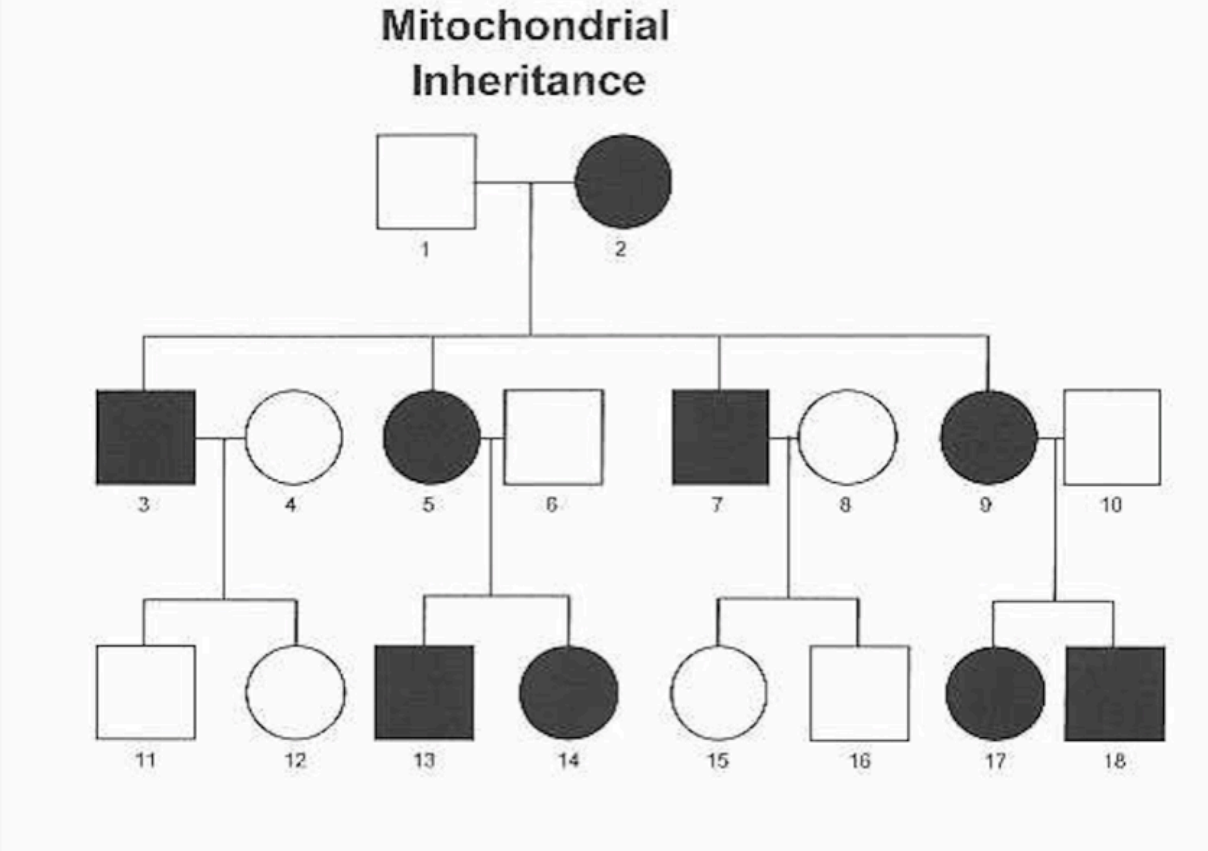

Figure 2: Mitochondrial inheritance pedigree (MI Genetics Resource Center, 2018)

MtDNA has traditionally been thought to be exclusively maternally inherited because during fertilization the tail of the sperm with its mitochondria are excluded and lost from the zygote. This view is a misconception. In fact, in the majority of mammalian embryos, humans included, sperm mitochondria can be identified, although their role and fate are not known (Ankel Simons & Cummins, 1996). Ankel-Simons and Cummins (1996) were critical of those scientists who perpetuated the misstatement about the total omission of paternal mtDNA during fertilization. They made that rebuke with regards to those "theories of evolutionary relationships based on obligatory maternal inheritance of mitochondria" (Ankel Simons & Cummins, 1996). According to Ankel-Simons and Cummins, any model or theory of evolution that relies on mtDNA must consider that paternal mtDNA is not totally excluded during the fertilization process. The fact is we really do not know what happens to paternal mtDNA, perhaps it is just a matter of simple dilution in the vast amount of maternal mtDNA in the embryo. For the purposes of our discussion, we can assume a primarily maternal inheritance of mtDNA.

Except for erythrocytes, all human somatic cells and gametes contain mitochondria, as they are the main organelle for ATP production. A mutation within mitochondrial DNA may have significant deleterious effects on cellular energy production within cells. It is critical to study mtDNA and the effects of mutations in order to understand specific diseases. Mitochondrial diseases have been linked to many serious health conditions, including deafness, blindness, muscle weakness, cognitive impairment, and diabetes, as well as heart, liver and kidney failure (Bleich, 2015). About 1 in 4,000 people worldwide, and some 20,000 in the U.S. have mitochondrial diseases (Park, 2019). However, there may be many more cases, as misdiagnosis rates are high (Bleich, 2015). Some of these diseases arise as a result of nuclear DNA mutations and some from mtDNA mutations either inherited maternally or arising *de novo*, the latter

contributing to a lesser extent because of the sheer volume of nuclear DNA genes as opposed to the 37 mitochondrial genes. Because of the number of mitochondria needed per cell and the up to 10 copies of mtDNA per mitochondrion, the rate at which a mutation may occur is very high. In addition, mitochondria, unlike the nucleus, lack DNA repair enzymes, and mutations in mtDNA, regardless of their origin, are transmitted to progeny.

Mitochondrial diseases:

Recently, interest in mtDNA-based diseases has increased. Diseases such as Leigh syndrome and myoclonic epilepsy with ragged-red fibers (MERRF) syndrome are caused by specific mitochondrial DNA mutations (Viswanathan, 2018). Leigh syndrome is a neurodegenerative disease that develops in the first year of life and is characterized by psychomotor regression resulting in death by two to three years due to respiratory failure (Medline Plus, 2020). One cause of Leigh syndrome is an 8999T>G mutation in subunit 6 of the mitochondrial ATPase gene (Park, 2019). MERRF syndrome is a rare disorder characterized by muscle twitches (myoclonus), weakness (myopathy), and progressive stiffness (spasticity). Clinical features of MERRF may include seizures, ataxia, peripheral neuropathy, dementia, optic nerve atrophy and cardiomyopathy. Mutations in the mitochondrial *MT-TK* gene are the most common cause of MERRF (Medline Plus, 2020). There are no specific treatments for MERRF. Medications are used to control seizures and myoclonus.

Researchers at Newcastle University in the United Kingdom, using data from 2012, estimated that 778 births per year in the U.S. are at risk for inheriting diseases due to mtDNA mutations (Viswanathan, 2018). The reason the words “at risk” are used is because although a woman with a mitochondrial DNA mutation will certainly transmit that mutation to her offspring, the results in the offspring are ambiguous. The mutations affecting mitochondrial

DNA produce varying effects on cells, resulting in a range of phenotypes. A woman that has a mitochondrial DNA mutation may be totally asymptomatic, depending on the mutation load of her own mitochondria. The eggs produced by such a woman may have very different mutations loads resulting in a severely affected child or a perfectly healthy child (Park, 2019). According to Mary Herbert, professor of reproductive biology at Newcastle University, the biggest problem with women with mitochondrial disease is that there is no way of knowing what level of mutation their child will have (Park, 2019). One way to reduce the unpredictability and risk of transmitting mitochondrial DNA diseases is *in vitro* fertilization (IVF) with preimplantation genetic diagnosis (PGD). This technique is already used to diagnose a wide variety of genetic disorders caused by nuclear DNA aberrations (Park, 2019). While mitochondrial PGD is available in the UK, its use in the U.S. remains confined to research studies for reasons that will be discussed below.

Methods to reduce inheritance of mutated mtDNA:

While mitochondrial PGD can reduce the risk of transmitting a mitochondrial DNA disease to a child, there is a relatively new procedure that doctors have begun using that can eliminate the mtDNA disease because the process replaces mutated mitochondria with healthy mitochondria from a donor. The procedure of mitochondrial replacement therapy, or MRT, has made headlines for producing three parent-parent babies (Viswanathan, 2018). The procedure replaces the mother's mutated mitochondria with healthy mitochondria from another woman; there is no physical interaction with the biologic mother's or father's nuclear DNA.

The predecessor for this procedure was cytoplasmic transfer. Researchers were not looking for a cure for genetic diseases but rather were focused on a procedure for women who previously failed standard IVF treatments. The idea was that the cytoplasm of older eggs may

lack something and so they attempted to use a small amount of cytoplasm from younger female donors. A small amount of donor cytoplasm was injected into the ovum of the infertile woman. Subsequent fertilization with the husband's sperm was then performed *in vitro* and eventually the early embryo was transferred into the woman. The first baby conceived in this way was born in 1997 in New Jersey. Coincidentally, no donor mtDNA was found in that infant but it was subsequently found in other children conceived in this manner. Reproductive endocrinologist Jacques Cohn performed this procedure at St Barnabas Medical Center in New Jersey and delivered 17 babies. Three children born through this technique were found to have developmental disorders: two cases of Turner's Syndrome and one case of a pervasive developmental disorder. In 2002, the United States Food and Drug Administration (FDA) banned this procedure.

MRT offers couples in which the mother carries a mitochondrial DNA mutation a way to assure that their child will not harbor the mutation and removes the uncertainty involved in the expression of these diseases in offspring. There are currently two methods for performing MRT: pronuclear transfer and spindle transfer. In pronuclear transfer the mother's and donor's eggs are both fertilized *in vitro* with the father's sperm. The fertilized nucleus of the donor (pronucleus) is removed and destroyed and replaced with the mother's pronucleus which was removed from her fertilized egg. The reconstituted embryo is then transferred to the mother for gestation (Viswanathan, 2018).

In spindle transfer, the mother's nuclear DNA is transplanted to a donor's enucleated egg. The newly constituted egg is then fertilized by the father's sperm via intracytoplasmic sperm injection (ICSI). The embryo that ultimately forms is implanted into the mother for gestation (Viswanathan, 2018). Since the pronucleus is bigger it is easier to work with and therefore a

cheaper and easier procedure (Figure 3). However, it also poses some moral and religious questions because it involves the destruction of fertilized nuclei, which some consider akin to abortion (Viswanathan, 2018).

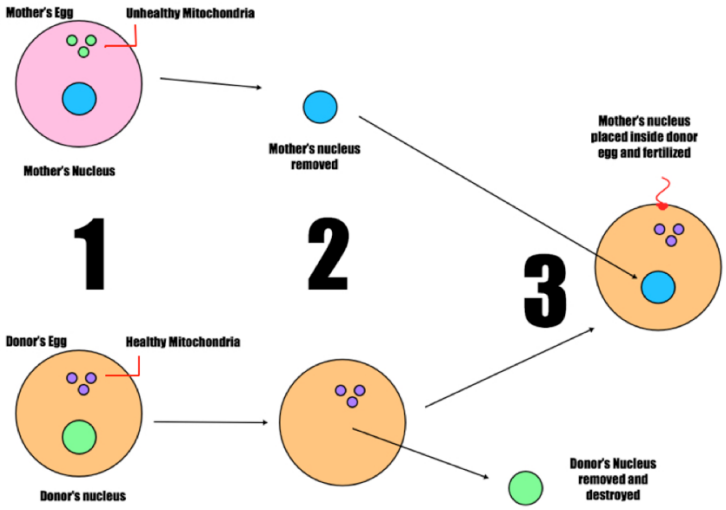

Figure 3: Mitochondrial Replacement Therapy, spindle transfer (Ramanathan, 2016)

Ethical/Legal issues with MRT:

MRT was first performed in 2009 at the Oregon National Primate Center, in which scientists successfully performed MRT in *Rhesus* monkeys. Follow up studies concluded that MRT had the potential to be performed in humans. In 2014, the FDA concluded that more research was needed before it could be legalized. In 2015, the FDA requested a committee from the National Academy of Sciences review the procedure. That committee published a report noting, that with oversight, MRT could be justified. Yet progress came to a halt in 2016, when Congress passed the Consolidated Appropriations Act. The bill included a rider that banned germline modifications which encompasses all genetic engineering on eggs, sperm, or early embryos - modifications that are transmitted beyond a single generation (Viswanathan, 2018).

There are currently permitted genetic treatments studied to treat cancers or other diseases. The procedure used, known as somatic gene therapy, involves replacing a single abnormal gene with a healthy gene; these modifications are not passed to future generations because there are no changes to the sperm or eggs (Bleich, 2015). MRT is considered a form of genetic editing and crosses the "germ line" by altering eggs, sperm or embryos, producing modifications that can be passed onto future generations, and as a result, ethicists and lawmakers have not been ready to accept the social implications of such a scientific leap (Park, 2019).

Despite the ban on MFT in the U.S., Dr. John Zhang, a New York reproductive endocrinologist, reported in 2016 the first live birth involving MRT. He used spindle transfer reconstituted oocytes to assist a couple in which the wife had a mtDNA mutation known to cause Leigh syndrome. She was clinically well with only a 24.5% mutation load, but she had suffered pregnancy losses and the death of 2 children at 8 months and 6 years from Leigh syndrome. Those 2 children had a >95% mutation load that caused their disease. The couple chose the spindle transfer over pronuclear transfer for religious reasons. Zhang fertilized five reconstituted oocytes, four of the embryos were aneuploid but PGD showed one euploid 46XX embryo which was transferred. The woman had an uneventful pregnancy and delivered a healthy girl at 37 weeks' gestation. Subsequent to delivery, newborn cells were analyzed and showed that the average transmittal of maternal mtDNA was around 1.6% (Wu, et al., 2016).

Because of the U.S. ban on the procedure, Dr. Zhang performed the procedure in Mexico. He subsequently received a letter from the FDA notifying him that he broke the law. Currently, he is affiliated with a clinic in the Ukraine and is offering this procedure to Americans. In 2015, the UK became the first, and so far, the only country to officially legalize the procedure, under strictly regulated conditions, exclusively for the prevention of genetic diseases.

The rider on the Appropriations Act of 2016 is why the procedure continues to be banned in the U.S. and the rider has continued to be renewed as recently in the 2018 Reiteration Act. According to Josephine Johnson, an ethicist and director of research at the Hastings Center, a bioethics research institute, "The starting position of the federal government has been that we're not going to do research on human embryos -we won't fund it and we won't condone it" (Park, 2019). Many believe the law was created because of concerns in technologies like clustered regularly interspaced short palindromic repeats (CRISPR) that allow for gene-editing on a wide scale and could one day lead to engineer babies with preferred traits.

There is considerable disagreement with how MRT should be viewed. Is it a form of gene-editing that puts us on that slippery slope encroaching on the germ line? Or should it be viewed as another form of IVF with PGD that does not alter the nuclear DNA? In a 2014 op-ed piece in the New York Times, Marcy Darnovsky, executive director of the Center for Genetics and Society, explained why MRT should not become legal. She noted that beyond scientific considerations, the ethical issues are even more worrisome. She advocated for safer alternatives to this experimentation such as IVF or adoption. "Simply being able to something doesn't mean we should do it," she wrote (Viswanathan, 2018).

MRT is a form of genetic editing and according to Brown University professor of reproductive biology Eli Adashi, it got swept up into that rider because it may be construed as a germline modification (Viswanathan, 2018). The main concern has been technologies like CRISPR which can work on all DNA, but MRT involves a very small amount of DNA with only 37 genes. "Obviously there are ethical considerations," Adashi said. "Everybody's always concerned about state-led eugenics" given what happened in WWII under the Nazi regime (Viswanathan, 2018). There is a big difference between MRT and eugenics and while we should

always scrutinize and remain diligent, Adashi considers the UK's method for licensing MRT the gold standard of how to adjudicate difficult ethical questions (Viswanathan, 2018). Australia and Singapore are currently developing programs based on the UK's gold standard approach. Adashi has co-authored a paper in *Obstetrics and Gynecology* advocating for the removal of the U.S. ban on MRT research so that eventually MRT can be carried out safely for those who really need it to have a healthy child.

The present concerns over MRT and the *de facto* moratorium regarding genetic research that would or may involve crossing germlines echo concerns that surfaced following the introduction of IVF in the 1970s. There were serious medical, ethical and theological concerns that were raised over the years. Yet despite these qualms, to date, IVF, has resulted in the birth of over 5 million babies (Bleich, 2015). Since the early days, advances in *in vitro* fertilization in reproductive medicine have presented rabbis and *halachic* authorities with many issues. These issues included: semen procurement, ovum donation, disposition of defective embryos, fetal reductions and parental identity (Bleich, 2015). The questions of parental identity have certainly posed some of the most difficult and challenging *halachic* questions.

The *halachic* issues with MRT:

A 2015 article Rabbi J. David Bleich stated that a pregnancy achieved with additional genetic material contributed by someone apart from the couple in the marriage conforms neither to the traditional notion of the nuclear family nor to the notion of a family dictated by natural order (Bleich, 2015). Pregnancies and children achieved via ovum or sperm donation or by same sex couples represent a departure from the traditional family structure which, he said, has been the "bedrock of the natural order" (Bleich, 2015). Bleich cited several examples from the Torah and the Talmud that the "Divine wish is that parental identity be established with certainty and

that individuals be clearly identified in terms of family identity" (Bleich, 2015). The Talmud (*Sotah* 42b) discussed the meaning of the phrase "*ish ha-beinayim"* (I Samuel 17:23) in reference to Goliath. The Talmud questioned who was *beinayim*? Rabbi Yochanan answered that Goliath was the son of a hundred fathers and one mother. Rashi understood it to mean that Golaith's paternity was indeterminable and could have been any of his mother's many sexual partners. Tosafat understood differently, explaining that Goliath's paternity was not ambiguous, rather "that as long as sperm remains viable in a woman's genital tract, multiple sperm can contribute to a single pregnancy" (Bleich, 2015). In scientific terminology, this is described as polyspermy. While the scientific understanding of the process of conception is different, "Tosafot accepted the empirical possibility of a child having not only 2 fathers, but a hundred fathers" (Bleich, 2015). There is no reason to believe that this concept could not also be extended to multiple mothers. According to Bleich the cited scriptural passage disparages not only the immoral behavior of those involved but also the concept of multiple maternity. Rabbinic interpretation of the census noted in the Book of Numbers offered further proof of the sanctity of the family. As it says in Numbers 1:18: "And they assembled all the congregation together on the first day of the second month and they declared their pedigrees (*va-yityladu*) according to their families..." *Va-yityladu***,** "and they gave birth" would not make sense if taken literally. Rashi, citing the *Sifri,* explained the phrase …. that they brought genealogical records or witnesses who testified to presumptions surrounding their birth for purposes of tribal identification (Bleich, 2015). Rashi's larger point explained the need for a second counting of the Jewish people after the sin of the Golden Calf. The census at the beginning of Numbers was shortly after the erection of the Tabernacle and subsequent to resting of the Divine presence, the *Shekhinah,* in it. The Talmud (*Kiddushin* 70b) noted that the "Holy one …does not cause His *Shekhinah* to rest other than upon

genealogical identifiable families (*mishpachot meyuhasot)* of Israel." According to Rashi the genealogical records mentioned in Numbers 1:18 to establish familial identity were critical to guaranteeing the presence of the *Shekhinah*. Very practically the Mishnah in *Yevamot* 41a stated that a woman may not remarry until three months after the termination of a previous marriage. Elaborated upon in the Talmud (*Yevamot* 42a), Rav Nachman stated in the name of Samuel, "Scripture said 'to be unto you for a God, and to your progeny after you'(Genesis 17:7) to distinguish the seed of the first and the second." (Bleich, 2015) The Talmud added the same applied to a convert who wanted to enter a marital relationship. The waiting period allowed to distinguish between a "seed planted in sanctity" from one that was not. Rashi explained that the Talmud (*Yevamot* 4b) cited Genesis 17:7 because of the principle formulated in *Kiddushin* (70b) that *mishpachot meyuhasot* were a prerequisite for the presence of the *Shekhinah.* Moreover, in Genesis 18:19 Abraham was told to command his progeny to observe "the way of God." For Bleich the "way of God," the *mesorah* and the covenant, can only be transmitted "by means of the family relationship… to do so the family unit must be clearly defined, and its members unequivocally identified."

One of the universal precepts taught to students of healthcare, doctors, nurses, *etc*. is *Primum non nocere,* translated as "first do no harm." It reminds healthcare personnel to always consider what harm may be caused to a patient by a specific treatment or therapy. Most maintain, Bleich included, that this must also extend to the unborn. Extrapolated from that, Bleich stated that in Judaism the existence of an individual is not "an unmitigated blessing and hence his or her personal welfare might have been better served had he or she not been born. 'Better for man had he not been created' (*Eruvin* 13b). Consideration of the possibility of less than a satisfactory outcome is not a matter of human concern." (Bleich, 2015) This is illustrated in the incident of

King Hezkiah recorded in the Talmud (*Berakhot* 10a). The king was childless because he feared that his offspring would worship idols, *avodah zarah*. In rebuking the king, Isaiah the prophet told him that the secrets of God should be of no concern to him. Procreation is part of God's natural order but for Bleich that was interpreted to mean that miscarriages, stillbirths and congenital anomalies were also as part of that order. According to Bleich, "to man, procreation appears to be a form of Russian roulette but fortunately the odds are in our favor" as these events represent a small part of the reproductive process. Certainly, Bleich would agree that all appropriate measures should be used to extend human life, even when we cannot understand the purpose to that life. However, there is no obligation to "harness use of heroic or artificial measures in the genesis of life." (Bleich, 2015). Certainly, Bleich would empathize with the emotional pain of the infertile couple or with the couple who experienced recurrent pregnancy loss, but elimination of their pain would "not justify the risk of imposing congenital burdens upon the yet to be born" (Bleich, 2015). Even if new procedures and technologies are shown in retrospect to be no more hazardous than a natural pregnancy, a positive outcome does not "retroactively serve to exculpate an act inherently unethical at the time at which it was undertaken." The end does not justify the means if the means were "immoral." Bleich referenced the infamous Tuskegee syphilis episode and emphasized that positive results did not make the study moral. Bleich cited Professor Paul Ramsey who considered all fetal experimentation unethical because there may be unknown harmful effects not yet identified and the unborn fetuses' inability to provide consent. At the time of publication of his article in 2015, Bleich considered MRT a procedure that "may pose risks to the yet to be conceived fetus and that such experimentation should be deemed unethical" (Bleich, 2015).

Rabbi Professor Avraham Steinberg, M.D., an associate clinical professor of medical ethics at Hebrew University Hadassah Medical School in Jerusalem, took a different approach. According to Steinberg, “science and technology are morally neutral” (Steinberg, 2018) but they are now here and are part of our everyday life. The question is, if and how can we ethically and *halachically* use medical technology. It is important to understand what *Chazal's* position are on such innovations. In commenting on the Talmud’s discussion of new crops that germinated before the month of Nissan, the Hatam Sofer declared, “*Hadash asur min ha”Torah”, "*the new is forbidden by the Torah." The Hatam Sofer elaborated that innovation was forbidden, and we must take a step back and think about it. On the other hand, the Tiferet Yisrael commenting on a Mishnah in *Taharot, Yadayim* 4:3 stated that if something was not explicitly forbidden then we were permitted to do it without finding a reason. A middle of the road approach seemed the best approach when faced with something new, especially in the area of reproductive medicine. According to Steinberg (2018), when innovations in assisted reproduction arise, we should ask ourselves two questions. Is what we are doing tantamount to playing God? And, do we have a right to interfere with nature? Perhaps, as Bleich suggested, we should accept the seemingly Russian roulette of God's natural order. Steinberg would seem to disagree. According to him, the term “playing God” has no relevance to normative Jewish thought. We cannot understand the "what or why" of God's actions and therefore one cannot be “playing God.” Rather, advances in reproductive medicine or science in general should represent our enhanced understanding of nature and the natural order created by God. If anything, it should strengthen our belief in an omnipotent God. As to the second question, according to Steinberg, not only are we allowed to interfere with nature, we are mandated to do so. He cited the Talmudic discussions in *Bava Kama* 85a and Rashi’s comments regarding the famous verse in Exodus 21:19, *Ve’rapo yerapeh*

- and heal, he shall be healed. The Talmud there discussed the types of damages for which a person may cause to another. The Torah required the person causing the damage to pay five types of compensations to the person who was damaged. One payment was for medical treatment. In other words, the damager must pay the victim's medical expenses. If medical healing *per se* was forbidden, then the perpetrator would not be required to pay the medical expenses. This verse in I Samuel 17:2 is the source for the *halachic* authorization for a doctor to heal. The seemingly obvious question that follows is why is there a need for Biblical permission to practice medicine? Rashi explained that one might assume that an illness or injury that befalls a person is because God wanted that person to experience the health issue. By healing a sick or injured person, is a physician interfering in God's plan? Therefore, the Torah needed to clarify that medical practice is different and by stating *ve'rapo yerapeh,* God is giving a doctor the permission to heal. According to Steinberg, the Torah allows one to "heal" because of *tikun olam*; we are partners with God in creating and improving the world. "To fulfill our role as partners, we must discover and innovate as long as our interventions do not involve a prohibition" (Steinberg, 2018). Furthermore, now one can fully understand statements of the Hatam Sofer and the Tiferet Yisrael: an innovation should only be contemplated when the potential benefits outweigh the risks and, even for something is not expressly prohibited, the resulting consequences may trigger *halachic* issues. With that in mind, does innovation and technology in the area of reproductive medicine fall within the mandate of *tikun olam, i.e.,* to "repair the world" by acting constructively and beneficially?

From the various stories of barren women in Tanach it seems obvious that fertility is a blessing and infertility a curse. In Genesis 30:1 Rachel cried to Jacob, "give me children, otherwise I am dead." The Talmud (*Nedarim* 64b) noted that one of the four types of people

considered to be dead while alive is the childless person (Steinberg, 2018). Infertility is a problem for approximately ten percent of the world's couples. Causes of infertility differ between men and women, with, for example, ovulatory dysfunction and tubal adhesions in women and azoospermia in men. In some cases, the cause of infertility is unknown. Recurrent pregnancy loss, transmission of genetic diseases, and mitochondrial DNA disorders are hereditary disorders of concern for couples planning a family. A complete discussion of the *halachic* implications for the treatment of couples facing any of the above problems is beyond the scope of this review. There are many options to treat infertility and health issues and, undoubtedly, new technologies - triggering new *halachic* analyses - will emerge in the future. Therapies, including egg donation and/or surrogacy, raise the question of the identity of the *halachic* mother. The same question could be asked regarding MRT and the so-called "three-parent" baby.

Halachic importance of identifying the mother:

Moving beyond Bleich's admonition about the sanctity of the nuclear family, there are very practical *halachic* concerns posed by the technology and methods involved in assisted reproductive technology (ART), including MRT. Bleich cited the famous previous Intel CEO, Andrew Grove, that "in technology, whatever can be done, will be done." For Bleich, advances in ART, gene therapy, and MRT are a *fait accompli* and the *halachic* challenges that accompany these technologies must be addressed (Bleich, 2015). Besides the obvious overarching question of Jewish identity, determination of maternity presents *halachic* authorities with very specific and nuanced cases. The main issue involved in the older and more established technologies of egg donation and surrogacy is who is the *halachic* mother: the biological mother, the gestational mother, or maybe it is both. MRT may, as we will see, add an additional dimension to the idea

of multiple mothers. Some of the many issues that may arise in cases of using a donor egg or a surrogate include prohibitions of marrying full of half siblings, honor due a mother (*kibbud em*), inheritance, and, of course, conversion if either the egg donor or the surrogate is not Jewish (Steinberg, 2018). To address each of these and other questions would be rather simple if there were just one nuance to the issue. According to Steinberg, contemporary *poskim* group into three categories (Bleich, 2015) the genetic mother or egg donor is the *halachic* mother, (Steinberg, 2018) the gestational mother or the surrogate is the *halachic* mother, and (Sharon, 2017) the issue cannot be resolved and therefore both are considered *halachic* mothers *l'humra.*

It is worthwhile to consider the sources from the Torah and the Talmud used to formulate these three opinions regarding maternal identification. The famous debate between the Roman Emperor Antonius and Rebbi Yehudah Ha'Nasi over when the soul enters the body serves as the basis for one opinion; the Emperor held that the soul enters at conception and Rebbi held at birth. The Talmud recorded that at the end of the debate Rebbi reversed his position and agreed with the Emperor. This would support the egg donor as the mother. (Steinberg, 2018)

There is a different approach found in the Talmud, *Yevamot* 97b, discussing the case of a pregnant gentile woman who converted during pregnancy and subsequently gave birth to twins. The logic involved in this case is quite interesting. Consider, for example, the situation in which a non-Jewish woman pregnant with twins converted to Judaism while pregnant, are her children Jewish or do they require conversion? Similar cases noted in the Talmud (*Yevamot* 22a; *Bekhorot* 47a) concluded that a convert is like a newborn who lacks relatives. If so, those twin babies would have neither a mother nor siblings. The Mishnah (Yevamot 22a) ruled, however, that the twins cited above are maternal brothers, and that is a possibility only if they share a mother. Thus, it is "gestation that establishes the maternal-filial relationship." (Bleich, 2015). Apparently,

there can be a *halachic* change in the status of a fetus post-conception, with the birth mother being the *halachic* mother.

Further proof for this line of thinking is found in the Talmud *Megilla* (13a). In Esther 2:7, it cited Mordechai taking Esther for a daughter to himself because she had no father or mother. The Talmud elaborated that Esther's father died after her conception and her mother died in childbirth (Bleich, 2015) This supported the idea that maternal relationship is based on birth. An additional support along this line of thinking is noted in Tosfot's comments in the Talmud *Ketubot* (11a) discussing a minor child with property but with no heir. The question raised is how this could occur. Tosafot explained that it was a case where a pregnant woman converted to Judaism and died after delivering the baby. The child inherits from her, although the child has no other relatives. This line of reasoning corroborated the idea that the birth process created the maternal-filial relationship (Bleich, 2015)

The Targum Yonatan also related a Midrash about Leah and Rachel. Leah knew Yaakov would have 12 sons. When she became pregnant for that last time, she already had 6 sons, each of the maid servants (or, *shivchots*) already had 2 sons each, and Rachel had Yosef. Leah, pregnant for the 7th time, knew that the fetus she was carrying was a boy and that Rachel was carrying a girl. Leah thought it would be humiliating for her sister to have less sons than the *shivchot.* According to the Midrash, Leah prayed that the fetuses should be exchanged. (i.e., an *in utero* transfer and exchange). Thus, Leah she gave birth to a daughter, Dinah, and Rachel gave birth to a son, Binyamin. This Midrash is further evidence that the surrogate is the *halachic* mother. (Steinberg, 2018)

There are also more contemporary examples; one very interesting one is recorded in the *Even Yekarah*, authored by Rav Binyamin Aryeh Hakohen Weiss. The case occurred

approximately 150 years ago and interestingly concerned an ovarian transplantation from one woman to another woman. The question focused on the identity of the mother of a child produced under this circumstance - was the *halachic* mother the egg/ovary donor or the birthing mother? Realizing that this was technically impossible in the 1800s, the *Even Yekarah* analyzed the question by bringing a related example involving grafting a fruit tree and the issue of *orlah,* forbidden fruits from a tree less than three years old. The Talmud in *Sotah* 43b recorded the debate of the status of fruit that grows on a branch of a tree less than three years old but was grafted to a tree older than three years. The Talmudic ruling was that fruit from this branch was considered part of the older tree and, thus, was permissible to eat. The *Even Yekarah* concluded that if an ovarian transplant was technically possible the recipient birthing mother would be considered the *halachic* mother (Steinberg, 2018).

Apparently, there are sources for both opinions: whether the biological mother or the gestational mother was the *halachic* mother. Bleich presented the opinion cited by the former Sephardic Chief Rabbi of Israel, Rabbi Eliyahu Bakshi-Doron, that it was not permitted to engage in activities that lead to an ambiguous situation. This is based on the previously cited verse from Genesis 17:7, "to your progeny after you," used as the basis to establish the 3-month waiting period before a woman's remarriage. The reason was to avoid creating a situation of parental ambiguity and *halachic* doubt.

In addition to the problem of maternal ambiguity, Bleich cited both written and oral opinions of Rav Woszner, who believed that the use of donor semen or egg was prohibited in all cases. Writing in *Teshuvot Shevet ha-Levi,* III, no.175, Rav Woszner noted, God said to Adam, "therefore a man shall leave his father and his mother and cleave to his wife, and they shall be one flesh" (Genesis 2:24). The Talmud in *Sanhedrin* (58a) derived the prohibition of adultery

from this verse and also construed that the concluding phrase of "one flesh" referred to the child born to this couple. Therefore, for Rav Woszner, the use of donor genetic material violated this prohibition, because the conception of such a child was viewed as participating with "the wife of his fellow" rather than his own wife. Bleich stated that Rav Woszner agreed that the same reasoning applied for negating a married woman from being a surrogate. Rabbi Bakshi-Doron said that Rav Wozner's reasoning extended to any somatic material contributed by a married woman to conceive a child. Interestingly, as we shall see below, Rav Eliashiv also prohibited cytoplasmic transfer from one woman's egg into the egg of another woman. It is, however. not clear whether he was concerned about ambiguous maternity or whether he shared Rav Woszner's view that it constituted an adulterous parenthood. (Bleich, 2015).

Rav Shlomo Zalman Auerbach refuted all the sources offered to prove whether the *halachic* mother was the biological mother or the birth mother. According to Steinberg it was not an issue of ambiguity but rather a *taku.* Many issues the Talmud remain as *taku*, a question without an immediate solution and with a conclusive decision waiting until the arrival of the Mashiach. Rav Auerbach held that in cases involving both a biologic and birth mother, both women were considered the *halachic* mother *l'humra.* Returning to the questions raised about marriages between siblings, inheritance. and conversion the implications of this approach are clear. The child of a such a birth could not marry the children of either the egg donor or of the surrogate; if either of the two women were not Jewish, the child would need to be converted as a *giyur l' humra* because of the uncertainty of the *halachic* mother. Such a child could not inherit from either mother because of the lack of proof of the identity of the *halachic* mother. According to Steinberg, Rav Auerbach applied this rationale to handling the very sensitive case of a circumcision (*bris*) when either the egg donor or the surrogate was not Jewish. Typically, two

blessings (*brachot*) are made at a *bris*: *al ha'milah* and *l'hakhniso b'vrtito she Avraham Avinu.* If the baby is to be converted, the second *bracha* is changed to *la'mul et ha'gerim.* The first *bracha al ha'milah* is generic and can be recited in all cases, but depending on the case, one of the two second *brochas* might constitute a *bracha l'vatalah*, with some suggesting it should be omitted entirely. One can just imagine a potentially embarrassing situation where the second *bracha* was omitted entirely. Rav Auerbach was so sensitive to this matter that he held that the *mohel* must only recite "*Baruch ata"* and then mumble an inaudible phrase that does not contain God's name as the second *bracha*. With this approach, no one will be the aware of the delicate situation. (Steinberg, 2018).

A similar situation is recorded regarding the position of Rabbi Yosef Shalom Eliyashiv. Steinberg related a case of a colleague who asked Rav Eliyashiv whether a child resulting from a non-Jewish surrogate and a Jewish egg donor needed to be converted. Rav Eliyahsiv replied in the affirmative. This indicated that the surrogate was the *halachic* mother. A different colleague asked Rav Eliyashiv if the child of a Jewish surrogate and non-Jewish egg donor needed a conversion and again, he replied in the affirmative. Apparently, this indicated that he considered the egg donor as the *halachic* mother. There seemed to be some confusion as to Rav Eliyashiv's opinion or, perhaps, he changed his opinion. When asked about the seemingly different opinions, Rav Eliyashiv replied that both colleagues were wrong because either the surrogate or the egg donor was not Jewish. A *giyur l'humra* was required because of the uncertainty of the identity of the *halachic* mother. (Steinberg, 2018).

Contemporary ramifications of the issue of motherhood:

This *halachic* question of the identity of the halachic mother found its way into Israeli legislation with two contradictory laws currently recorded. In large part the contradictions are

due to the fact that there were different chief Rabbis when each law was written and the rabbis differed in opinion regarding what determines motherhood - the egg donor or the fetus carrier, or perhaps the matter was unanswerable *halachically*. When the Surrogacy Act of 1996 was formulated, the Sephardi, Chief Rabbi was Rabbi Mordechai Eliyahu who was of the position was that the birth mother was the mother. He did not consider the source of the egg in the *halachic* definition of motherhood. Therefore, according to him a child born from a married Jewish surrogate would be a *mamzer,* since the fetus being carried was from an egg fertilized by another man other than her husband. Therefore, Rabbi Eliyahu insisted that a Jewish surrogate must be a single, unmarried woman. Because the identity of the *halachic* mother is unclear (Rav Elyashiv and Rav Auerbach), special provisions were formulated within the Surrogacy Act. When born, the child was not registered as the son of anyone. The couple who arranged for the surrogacy then petitioned the court for an order of parenthood. A registry of surrogate children is kept so that when that child marries the registry will be checked to assure that that a marriage between half siblings was avoided, which is a *halachically* prohibited marriage. At the time of the Egg Donation Law of 2010 the Sephardi Chief Rabbi was Rabbi Shlomo Amar who held like Rav Ovadiah Yosef that the egg donor, not the surrogate, was the *halachic* mother. As such, according to Rabbi Amar the *halachic* mother was the one who donated the egg; the birth mother or surrogate was irrelevant. This created a political stir within the Knesset: hypothetically, how could the donor of an egg fertilized in a laboratory have the exclusive role as the child's mother over that of the birth mother who will raise the child. Therefore, the Egg Donation Law ruled that the birth mother was the real mother, and the genetic mother was irrelevant. Since this Law took a clear position on maternity it was *halachically* problematic, and it contradicts the

Surrogacy Act. According to Steinberg, new legislation is being worked on that will consider all the positions while remaining practical for day-to-day issues (Steinberg, 2018).

Thus, there are three opinions regarding egg donation and surrogacy and the identity of the *halachic* mother. Those that rule the genetic mother is the *halachic* mother, those who rule that the nurturing mother is the *halachic* mother and those like Rav Auerbach and Rav Eliyashiv who hold that the matter cannot be resolved and, with abundance of caution, consider both women as the *halachic* mothers *l'humra.* This brings us back to the issue of MRT. Does MRT introduce an additional mother? Is it possible the child may have multiple mothers since each "donor" of genetic material is to be considered an *halachic* mother? Or since the mtDNA contains only 37 genes, whereas the nucleus of the egg contains 37,000 genes, should mtDNA be considered insignificant as a *miyut shel miyut* (a minority of a minority). Both Bleich and Steinberg have difficulty with such an approach. Bleich stated that the principle of *rav* (majority) does not apply, citing Rabbi Bakshi-Doron's opinion on cytoplasm transfer, that the quantity of the donated material is not the determining factor. *Bittul be-rav* exists in cases where the identity of the minority material is suppressed. "That principle does not apply in situations in which the lesser component remains readily discernible in the composite mixture." (Bleich, 2015). Although the nuclear genes determine the overall health and phenotype of the child, mitochondrial genes are crucial for production of cellular energy and life without them is not possible. Furthermore, the case for MRT is to replace a mother's diseased mitochondria. As such the donated mitochondria must be viewed as a *davar ha-ma'amid* - a substance that holds up. According to Bleich, although those genes do not necessarily express themselves in observable characteristics, they are essential for life and thus a "*da-var ha-ma'amid* that is not subject to

nullification." (Bleich, 2015). So what of our question: does MRT introduce an additional mother by virtue of *da-var ha-ma'amid* ?

Steinberg compared mitochondria to a heart: they are both vital and life is not possible without either one. Surely everyone would concur that a heart can be transplanted from one person to another and that transfer would not make the donor the "parent" of the recipient. Mitochondria, like the heart, "are necessary for existence but do not define the very identity of the human being" (Steinberg, 2018). Thus, for Steinberg, even if we assume egg donors and surrogates both are *halachic* mothers *l'humra*, the same does not apply for MRT. "The miniscule amount of genetic material in the mitochondria cannot be considered as genetic motherhood."

Of course, this point may be argued because the analogy may not be valid in that the transplanted mitochondrial genes will cross the germ line to subsequent generations, whereas the transplanted heart or kidney will not. Ethicists may continue to have issues with this type of genetic editing but if viewed, as Steinberg suggested, MRT may not pose any real *halachic* question.

Moving beyond the general ethical concerns involved with MRT, it is almost certain that the future widespread use of this promising innovation will require approval from the United States Food and Drug Administration (FDA). Before a new treatment or medication is eligible for approval by the FDA, it must pass through three phases of clinical research. The treatment or medication must be proven to be safe and beneficial at each phase of testing to move to the next phase. Before Phase I trials the treatment or medication must have already shown some promise in the laboratory. In general Phase I clinical trials are concerned with the overall safety of the treatment or medication and its tolerance by the body. The number of participants in this phase of testing is usually under 100 and may contain healthy volunteers and those who are in need for

which the specific therapy. Phase I volunteers may also include those seeking a financial reward, and as well as those with altruistic goals.

Once shown to be relatively safe during Phase I trials, the safety evaluation progresses to Phase II trials. Participants in Phase II trials comprise up to several hundred people with the condition. Phase II trials last from months to several years and are primarily concerned with efficacy of the treatment or medication. Additional safety information is collected, and any side effects are noted during this phase. Phase III trials only begin once there is evidence of clinical benefits and efficacy from Phase II trials. Phase III trials contain a few hundred to several thousand volunteers, including with the medical condition, and span one to four years (FDA, 2018). Phase III studies "are designed to gather more information about safety and effectiveness, studying different populations and different dosages, and using the drug or protocol in combination with other drugs and protocols"(Tendler & Loike, 2015). There are different reasons people volunteer for clinical trials or research. Volunteers with the condition include those for whom there is no alternative therapy or treatment and those who have an alternative treatment.

In designing trials for MRT as a treatment for preventing transmission of a mitochondrial disease, like any other trials, volunteers, representing both women who have mitochondrial diseases and women who will provide healthy mitochondria, are required. In addition to monitoring the health of these groups, the study must focus on the children produced via MRT-associated IVF. With regards to this last point there is some concern over potential negative interactions between donor mtDNA and recipient nuclear DNA. Moreover, in more than 50% of the animal studies of MRT, faulty mitochondria were inadvertently transferred during the procedure. A recent study of MRT with primates showed neither birth defects or congenital

anomalies in their offspring (Tendler & Loike, 2015). In addition to the concerns discussed above of MRT crossing the germline, bioethicists may raise issues with informed consent from the embryo/fetus, which is an impossibility.

Rabbi Dr. Moshe Tendler and Dr. John Loike (2015) analyzed the Jewish *halachic* perspectives involved in volunteering for clinical trials, in general, and MRT, specifically. *Halachically* it is forbidden for a Jew to place his or her life/health into a dangerous situation. Their article acknowledged that Rambam proscribed that a person should aspire to a healthy lifestyle. Rabbi Tendler and Loike listed several examples mentioned by *Chazal* that promote health, including eating healthy and not being overweight, not putting one's mouth over a pipe to drink water, not drinking water from a river at night because you cannot inspect for parasites, not drinking from unattended liquids for fear that a venomous snake drank from it, and not engaging in activity that causes physical wounds or injuries. These are but a few examples. In contrast, however, there is a Biblical command "Do not stand by idly over your friend's blood" (*Leviticus* 19:16). What degree of danger can a person incur to save the life of another life? According to Rav Naftali Zvi Yehuda Berlin, a.k.a. the Netziv, a people cannot place themselves in severe danger to save someone else. One can accept a small degree of risk as an act of beneficence or *midas chassidus*. With regards to medical risk each case must be individually assessed, by consultations with a physician and an *halachic* authority (Tendler & Loike, 2015).

With regards to those women who would volunteer for MRT, initial studies focused on the major health risk encountered with medically-induced ovarian hyperstimulation to retrieve eggs. Hyperstimulation is an infrequent but well-known complication of ovarian stimulation that is part of any IVF cycle. While a serious complication, it is treatable and should not discourage a couple from participating in IVF. Furthermore, volunteering as an egg donor for a clinical trial of

MRT is certainly an act of beneficence or *chesed.* Women with mitochondrial diseases who volunteer for MRT trials, accomplish the *chesed* of having others birth healthy children. Rabbi Tendler and Loike noted that there are subjects who volunteer for clinical trials for financial compensation, which perhaps lessens the standard of the chesed, though not against *halacha*. He made an analogy between the risk associated with being a fireman or policeman for financial gain and the risk encountered when enrolling in a clinical trial. According to Rabbi Tendler and Loike, since *halacha* permitted a healthy person to volunteer in a clinical trial for *midas chassidus,* even for financial compensation, it is surely permitted a person with a medical condition for which there is no alternative therapy. Understood this way *halacha* would permit a woman with a mitochondrial disease to engage in MRT in order to have healthy children, so long as she fully understood the risks and benefits involved in the procedure (Tendler & Loike, 2015).

Having established that *halacha* permitted one to volunteer for a clinical trial, such as for MRT, Rabbi Tendler and Loike enumerated the positive and negative reasons for participating in clinical trials, in general. The Torah instructed the Jewish people to contribute positively to society. Rabbi Tendler and Loike cited examples of the conduct of our forefathers, Avraham and Yaakov, and how that contributed to society and to the overall honoring of *Hashem*. The Talmud (Arachin 16b) stated that when Avraham returned from Egypt, he stayed in the same lodgings as on his initial trip down to Egypt. He did this because, not only did he not want to show dissatisfaction with the establishment, but he wanted to show that "customer" loyalty was a virtue of society. Yaakov taught social responsibility in Shechem. The Talmud (Shabbos 33b) stated that he taught them about currency, markets in which to sell goods, and the necessity of bath houses - all of which promote the well-being of society. Thus, according to Rabbi Tendler and Loike volunteering in clinical trials, like those for MRT, promote social responsibility and

bring honor God. The negative *halachic* reason for volunteering for clinical trials falls under the prohibition of *aiva* (animosity against Jews). According to Rabbi Tendler and Loike "failure to participate in societal responsibility can incur the disdain of society" (Tendler & Loike, 2015) This concern is the *halachic* basis for allowing Jewish doctors to violate Shabbat to treat non-Jews. Although far beyond the realm of discussion here Rabbi Tendler and Loike discussed the consequences of *aiva* related to organ transplantation. Rabbi Tendler and Loike encouraged Jews to volunteer for MRT, because we live in a society where Jews and non-Jews interact daily, and it promotes goodwill and prevents *aiva* (Tendler & Loike, 2015).

Although MRT remains stalled in the United States legislature, the potential benefit of ensuring healthy offspring, in cases of women with mitochondrial diseases, is clear. One additional potential use for MRT to discuss is for the treatment of infertility. There is a percentage of women for which conventional IVF was not successful. In 2019 a Spanish company, Embryotools, headed by Nuno Costa Borges, announced the first IVF pregnancy to use MRT for treating infertility. The woman was a 32-year-old Greek woman who failed four previous IVF cycles but was able to become pregnant through MRT with donor mitochondria. Embryotools is collaborating with the Greek firm, Institute of Life, in a pilot study using MRT as a treatment for infertility. The laws are vague in both countries regarding the legality of MRT. The pilot study planned to show that the early stages of MRT are safe and thereafter plan to conduct long term studies on children conceived through MRT and IVF. If the ethical and safety concerns can be resolved favorably, the use of MRT/IVF as an adjuvant to current IVF protocols may increase success rates even further. Adjuvant MRT may also open up IVF to older patients, who because of poor quality of their eggs, are not suitable candidates for

traditional IVF. Donor mitochondria and cytoplasm may improve an older woman's prospect for successful IVF pregnancy (Molteni, 2019)

Another and perhaps equally controversial use of mtDNA and its analysis is in the area of Jewish genealogy and proof of Jewish descent. The rationale is that since mitochondria are inherited primarily from the mother, "genetic markers in this DNA can be traced back many generations to determine a person's maternal ancestors within a high degree of certainty" (Sharon, 2017). Jewish genealogists have determined that 40% of Jews of Ashkenazic background are descendants of one of four women who settled in Europe over 1,000 years ago. According to a report by geneticists Dr.Karl Skorecki and Dr. Shai Tzur of the Technion-Israel Institute of Technology and Rambam Medical Center, Israel, there is a certainty of "at least 90% and up to 99% that someone bearing specific genetic markers in their mitochondrial DNA is descended from one of these women" (Sharon, 2017). The information in this report was welcomed by some in Israel and was the cause for concern by others. The issue at hand was the possibility of using this genetic information as proof of one's Jewishness, particularly important in Israel. In the State of Israel, the Chief Rabbinate grants the marriage license. A Jew is defined as having been born to a Jewish mother. To be recognized as a Jew one must provide proof of Judaism for several generations through birth certificates or marriage certificates. If someone cannot provide the required proof of their Jewishness, they are considered "undefined" and will need to complete a long conversion process to be allowed to marry as a Jew by the Chief Rabbinate (Ben Kimon, 2017).

One million Jews from the former Soviet Union (FSU) have immigrated to Israel since the collapse of Soviet regime in 1991. While this has been a blessing for the State of Israel, issues have arisen regarding proof of their Jewish identity. This is particularly important when it

comes to issuing marriage certificates. Many immigrants from the FSU do not possess the necessary documents to prove their Jewish roots. In 2017 Rabbi Yosef Carmel head of the Eretz Hemdah Institute for Advanced Jewish Studies and senior judge on the private Eretz Hemdah rabbinical court in Jerusalem published a ruling that permitted using a mtDNA test as proof of Jewish descent in certain Ashkenazi Jews. The ruling was based on responsa involving a case in Munich, Germany, in which a woman having no other way to prove her Jewish status took a mtDNA test and submitted it as evidence that she was Jewish (Sharon, 2017). According to Rabbi Carmel for the 40% of Ashkenazi Jews who descend from the four women " the mtDNA test would be a breakthrough in their efforts to prove their Jewish status, especially important if they lack other forms of conventional proof, such as Soviet-era documentation and witnesses" (Sharon, 2017). Following the release of Skorecki's original report many claimed to possess the so-called Jewish gene. Rabbi Carmel stated there was no such thing as a Jewish gene but explained that the mtDNA test determined ancestry and not Jewishness. He insisted that the absence of specific markers on the test would not and could not be used to revoke someone's status as a Jew since 60% of Ashkenazi Jews don't possess these markers (Sharon, 2017). Carmel and the co-head of Eretz Hemda submitted their report to the Chief Rabbinate in 2017 claiming that if the Rabbinate accepted the genetic test it would represent "a significant change for the hundreds of thousands who are considered 'undefined'."(Ben-Kimon, 2017)

Not everyone agreed with the claims made by the Eretz Hemdah report. Rabbi Seth Farber, head of ITIM (seasons in Hebrew), a religious services advisory organization, expressed concern that relying on a laboratory test would be "the beginning of a slippery slope to greater reliance on scientific methods to prove Jewishness." He said these methods run counter to the established tradition in existence for over two millennia in all Jewish communities. The

presumptions based on that tradition are what allowed Jews from the next neighborhood or shtetl to marry each other and created a sense of community (Sharon, 2017).

Farber was concerned that rabbinical courts would reject valid traditional mechanisms of establishing Jewish status in favor of genetic testing. He pointed to the following case in making his point. The Supreme Rabbinical court overturned a ruling of a lower court that rejected a man's Jewish status following a traditional investigation. The Sephardic Chief Rabbi Yitzhak Yosef ruled according to the principal of *rov.* He opined that since the overwhelming majority of people undergoing such investigations are found to be Jewish, the man in question could also be presumed to be Jewish (Sharon, 2017). Farber was concerned that the use of mtDNA tests could threaten the traditional *halachic* process and the idea of presumption which rabbinical judges have always relied on.

In a Jerusalem Post article, in March of 2019, it was reported that Chief Rabbi David Lau admitted that rabbinical courts are using this mtDNA testing in certain cases to determine if someone is Jewish. Yisrael Beytenu Party leader, Avigdor Liberman, respond by saying the Chief Rabbinate is engaging in "institutional discrimination." He was most concerned that the rabbinate would force people to take such tests if they wanted to be considered Jewish and marry in Israel. ITIM echoed these concerns, reporting that they were aware of 20 cases where the rabbinical courts requested the test be done to prove Jewish status while registering for marriage. Rabbi Lau maintained that the mtDNA genetic test would only be helpful to an applicant who lacked documentation to support a claim of Jewishness. Rabbi Lau stated, "we would never force someone to do this. Also, it should be emphasized that a DNA test is not used to determine Jewish status ...it is used only in the clarification process." Rabbi Seth Farber, director of ITIM

remained skeptical and maintained that asking someone to undergo a mtDNA test to uphold their Jewish status is a form of coercion (Montenu, 2019).

Conclusion:

In summary, the debate remains about the ethical status of MRT in fertility to treat and prevent diseases from transferring to offspring. The hope is that, in time, with more study and more progressive movement in legislature, that scientific innovations and *halachic psak* can catch up, and those carrying mtDNA mutations can have a fair chance of conceiving a healthy child.

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