Jerusalem Science Contest

החידון המדע הירושלמי

Judaism, Genetic Screening and Genetic Therapy Part 1

Judaism, Genetic Screening and Genetic Therapy

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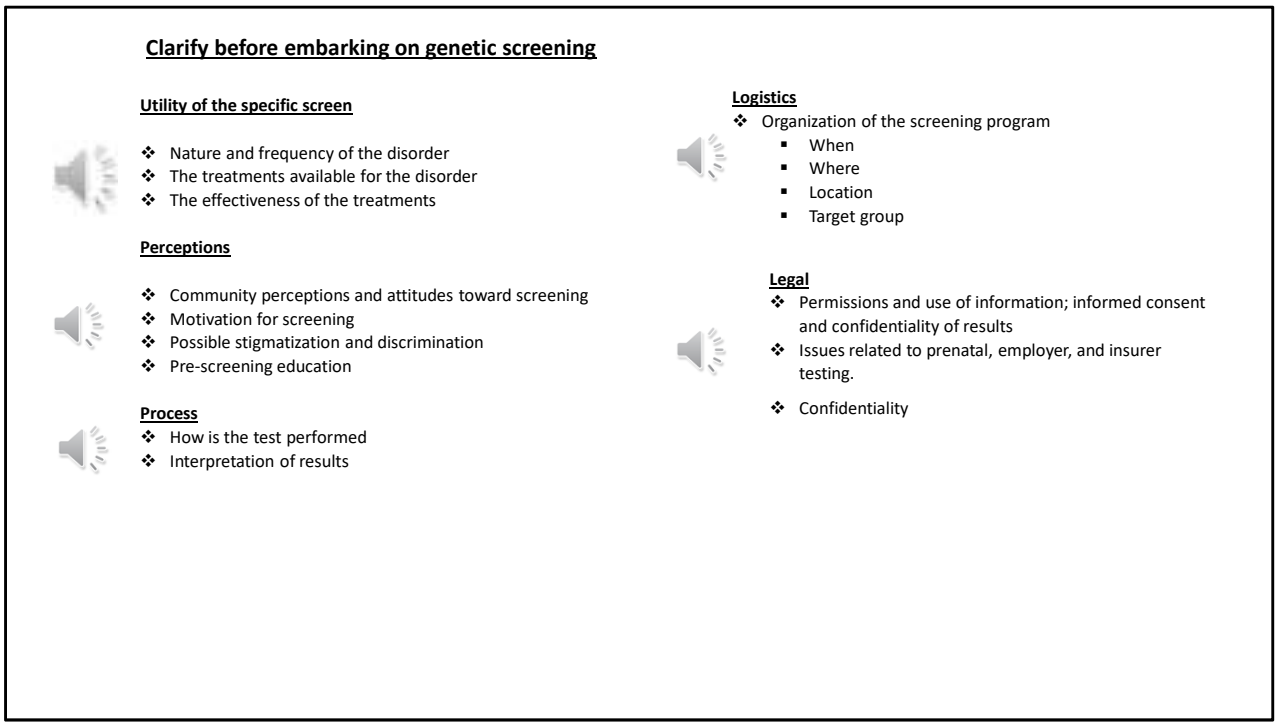
Abstract

Genetic screening, gene therapy and other applications of genetic engineering are permissible in Judaism when used for the treatment, cure, or prevention of disease. Such genetic manipulation is not considered to be a violation of God's natural law, but a legitimate implementation of the biblical mandate to heal. If Tay-Sachs disease, diabetes, hemophilia, cystic fibrosis, Huntington's disease or other genetic diseases can be cured or prevented by "gene surgery," then it is certainly permitted in Jewish law.

Genetic premarital screening is encouraged in Judaism for the purpose of discouraging at-risk marriages for a fatal illness such as Tay-Sachs disease. Neonatal screening for treatable conditions such as phenylketonuria is certainly desirable and perhaps required in Jewish law. Preimplantation screening and the implantation of only "healthy" zygotes into the mother's womb to prevent the birth of an affected child are probably sanctioned in Jewish law. Whether or not these assisted reproduction techniques may be used to choose the sex of one's offspring, to prevent the birth of a child with a sex-linked disease such as hemophilia, has not yet been ruled on by modern rabbinic decisions. Prenatal screening with the specific intent of aborting an affected fetus is not allowed according to most rabbinic authorities, although a minority view permits it "for great need." Not to have children if both parents are carriers of genetic diseases such as Tay-Sachs is not a Jewish option. Preimplantation screening is preferable. All screening test results must remain confidential. Judaism does not permit the alteration or manipulation of physical traits and characteristics such as height, eye and hair color, facial features and the like, when such change provides no useful benefit to mankind. On the other hand, it is permissible to clone organisms and microorganisms to facilitate the production of insulin, growth hormone, and other agents intended to benefit mankind and to cure and treat diseases.



Utility –Before even embarking on a genetic screening program, some of the following issues need to be clarified. And this list is not all inclusive. But, it does include primary questions to answer:
What is the utility of the specific screening program? In other words, what is the benefit that we expect to derive from the program. This can be driven by:
The Nature of the disease; be it treatable or not; be it fatal or not.
The treatments available for the disorder. If treatments are unavailable in this locality, is there still a point to do the screening? Maybe treatments are available elsewhere.
How effective are the treatments? Minimally or very effective?

Perceptions – Regarding perceptions about genetic screening. It is very important to educate the screening participants, and all those who make up their environment: family, friends, co-workers, their entire social milieu about the purposes and processes of genetic screening. Misperceptions abound about why people get screened and what, if any, are the effects of the test results upon the participants and environment. Members of the community have their perceptions and attitudes about screening; right or wrong. Many need clarity about why screening is done and what motivates people to be screened. Unfortunately, screening participants are subjected

to stigmatization and unwarranted discrimination. For these reasons, community screening program education and pre-screening education are very important.

Process – Anyone involved in genetic screening need to be clear about the process of screening. How is the tests performed? What preparation, if any, is needed? When can we expect the results? Who interprets the results? Once we understand the interpretation, what are the next steps? The greater detail that is provided to the participant, the less mystifying and frightful will be the experience.

Logistics – There are many logistical issues in organizing a screening program that take a great deal of planning, time and effort. When is the best time to offer the tests? At night? On weekends? On work time? Avoid vacation times? What's the best location? Clinic? School? Community center? Who are we targeting as participants? Adults or children? How do we promote the program? How do we maintain confidentiality?

Legal – And, there are legal issues that must be recognized. As we will note later in this lecture, Jewish law requires a high level of confidentiality. Who has access to the test results? Who needs to give permission to view the results and who needs to obtain permission? Participants needed to have informed consent. This means that before giving permission to use the results, the participants are to be informed as to who uses the results and why the results need to be shared. This is not a frivolous issue. Different confidentiality laws apply to medical professionals in a prenatal screening, or to employers and insurance companies. and the manner in which permissions are given and obtain vary.

Decisions for society to make and limits to set:

- Data obtained from screening results
  - Control the obtaining and use of genetic information
  - Decide who owns the genetic information
  - Decide how genetic information is to be used
  - Whether or not we have enough data to judge the pros and cons of testing
- Controls, so as not to infringe upon ethical and legal issues
- Who decides the screening program's target population
- Should limits be placed on testing
- When or not to abort a pregnancy.
- Testing should be available for those who seek it

The society supporting gene screening must face decisions in regulating the program so that the benefit derived should be maximized while potential injury be minimized. These decisions include how society can control how the data is obtained and used. Testing should cease once it is clear that enough data has been culled to solve the issue for which the test was done. Rules defining ownership of the test result data rules must be set. And, for what purposes only, and none other, may the data be used.

Society must formulate controls to make sure that the screening program does not violate or infringe upon ethical and legal issues. And, society must decide if there are situations that testing will not be allowed and limits set as to who qualifies for the program and who does not.

Sometimes, screening results in being faced with the decision whether or not to abort an existing fetus. Should society be allowed to pre-empt parental decisions by regulating and limiting when abortion is permitted or prohibited?

Even if screening is available only to a qualified population, society should make sure that testing is available to all segments of a qualifying population; not easier and

accessible for one group more than another.
These are not all the issues that society faces when implementing a gene screening program; but these are some of the important ones.

In these last two slides, Dr. Rosner delineates some of the many legal and ethical issues that must be part of the decisions and planning of a gene screening program. The following slides will now examine some of the sources in classic and contemporary Jewish writings that speak to what ought to be Judaism's role regarding gene screening programs.

Genetics and Eugenics in classic Jewish sources
(Genetics is the science; Eugenics is discriminatory legislation as a result of the science).

- Jacob's speckled and spotted sheet and Mendelian genetics? (Gen. 30)
- Hemophilia (Yevamot 64b). Sages had a remarkable knowledge of the genetics of this sex-linked disorder. Females transmit the disease but do not suffer from it. The case of the 4 sisters, 3 of whom had hemophiliac sons and the 4th asked R. Shimon b. Gamliel if she should give her son a brit mila. He said "no".
- Hereditary absence of menstruation (Ketubot 10b) and childlessness. No other anatomical or physiological abnormality is described. Rabban Gamliel researched a family in which the women did not menstruate.
- Prohibition to marry into a family of epileptics or lepers (Yevamot 64b, MT Issurei Biyah 21:30, Shul. Aruch. Even HaEzer 2:7) lest the illness be transmitted to future generations. The reason is supplied by Rambam in the Mi
- Rashi (Yevamot 64b) any hereditary disease is included in this prohibition. Rashi says "Sick people" and makes no distinctions.
- Rabbi Yehuda HaHasid (the Pious) prohibited marriages between first cousins and uncles and nieces, in his ethical will.
- Marriages between Uncles/nieces and first cousins are encouraged in Sanhedrin 76b.

Genetic disease

- Maimonides MT Deot 4 – Recognizes the construct of an inherent health defect, in his promise to those who adhere to his health regimen.
  - Dr. Rosner states 'hereditary or genetic' defect.
  - It is not apparent from MT that Rambam ascribes the defect to genetics or hereditary.

For brevity reasons, we will not be presenting Dr. Rosner's cited sources in full. However, you may get a better understanding by reading the source cited text. Reading the sources is not mandatory and no questions will be related solely to those sources.

In Beresheet 30, Genesis 30, we read about Yaakov Avinu agreeing with Lavan to be paid for his shepherding work with speckled and spotted sheep. The Torah describes some ingenious maneuvering on Yaakov's part and all of the sheep were born speckled and spotted. Although God did inform Yaakov in a dream that he saw how badly Lavan treated him, so the product could have been simply a nature defying miracle. Some have opined, among them, Dr. Yehuda Feliks and others, that Yaakov produced the speckled and spotted sheep through expert genetic manipulation through crossbreeding.

Talmud Yevamot 64a speaks of 4 sisters, 3 of whom had sons who died from their brit mila, apparently due to hemophilia. The 4th sister had a baby boy and was told by Rabban Shimon ben Gamliel not to give him a brit mila. It appears from this piece that R. Shimon ben Gamliel presumed that she was a hemophilia carrier because her sisters were demonstrated carriers. It is interesting that you do see evidence that the

Talmudic sages were aware of the concept of being a carrier. And, that hemophilia generally strikes males.

Hereditary absence of menstruation (Ketubot 10b) and childlessness. In defense of an accusation made by her new husband, a woman claimed that she came from a family in which the women did not menstruate. Rabban Gamliel researched the family and found her claim to be based upon reliable evidence. Here is evidence of a sage becoming aware of a hereditary syndrome and researching it.

Prohibition to marry into a family of epileptics or lepers (Yevamot 64b, MT Issurei Biyah 21:30, Shul. Aruch. Even HaEzer 2:7) lest the illness be transmitted to future generations.The reason is supplied by the Rambam in the Mishna Torah and is not recoded in the Talmud. However, it seems obvious that this is the reason.

Rabbi Yehuda HaHasid (the Pious) prohibited marriages between first cousins and uncles and nieces, in his ethical will. R. Yehuda HaHasid does not say why he disallows it. Dr. Rosner is presuming that the reason is health. That may or may be the reason. It may have mystical ramifications.
Marriages between Uncles/nieces and first cousins are encouraged in Sanhedrin 76b. In context with the Mishna's other examples such as loves his neighbors, keeps his relatives close, lends a poor man money, it appears that marrying one's niece is an act of kindness, and not motivated by any health or genetic factors. It appears that the real reason is that one will extend his love for his sister to his niece.

In terms of Genetic disease, Dr. Rosner cites…….

- Maimonides MT Deot 4 – Recognizes the construct of an inherent health defect, in his promise to those who adhere to his health regimen.
  - Dr. Rosner states 'hereditary or genetic' defect.
  - It is not apparent from MT that Rambam ascribes the defect to genetics or heredity. Rambam does consider the syndrome as natural but we can't be sure that he understood that in a genetic sense.

This concludes part 1 of our lecture on Genetic screening by Dr. Fred Rosner. Due to the large content of Dr. Rosner's essay, we have split this presentation into 2 lectures for the Jerusalem Science Contest. The discussion of slides 7 to the end will comprise the next lecture.

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BEGINNING OF REQUIRED READING FOR PART 1 (UNTIL PAGE 4)

Abstract

Genetic screening, gene therapy and other applications of genetic engineering are permissible in Judaism when used for the treatment, cure, or prevention of disease. Such genetic manipulation is not considered to be a violation of God's natural law, but a legitimate implementation of the biblical mandate to heal. If Tay-Sachs disease, diabetes, hemophilia, cystic fibrosis, Huntington's disease or other genetic diseases can be cured or prevented by "gene surgery," then it is certainly permitted in Jewish law. Genetic premarital screening is encouraged in Judaism for the purpose of discouraging at-risk marriages for a fatal illness such as Tay-Sachs disease. Neonatal screening for treatable conditions such as phenylketonuria is certainly desirable and perhaps required in Jewish law. Preimplantation screening and the implantation of only "healthy" zygotes into the mother's womb to prevent the birth of an affected child are probably sanctioned in Jewish law. Whether or not these assisted reproduction techniques may be used to choose the sex of one's offspring, to prevent the birth of a child with a sex-linked disease such as hemophilia, has not yet been ruled on by modern rabbinic
decisions. Prenatal screening with the specific intent of aborting an affected fetus is not allowed according to most rabbinic authorities, although a minority view permits it "for great need." Not to have children if both parents are carriers of genetic diseases such as Tay-Sachs is not a Jewish option.

Preimplantation screening is preferable. All screening test results must remain confidential. Judaism does not permit the alteration or manipulation of physical traits and characteristics such as height, eye and hair color, facial features and the like, when such change provides no useful benefit to mankind. On the other hand, it is permissible to clone organisms and microorganisms to facilitate the production of insulin, growth hormone, and other agents intended to benefit mankind and to cure and treat diseases.

Key Words: Premarital screening, genetic diseases, Judaism

Introduction

Genetic information about a person's health and health prospects can be inferred from family history or by direct genetic testing. Such testing can involve sophisticated molecular analysis for the mutant gene (e.g., cystic fibrosis) or simple biochemical (e.g., hypercholesterolemia), enzymatic (e.g., Tay- Sachs disease), hematological (e.g., Sickle cell diseases), or chromosomal (e.g., Down's syndrome) analysis of blood or body fluids or tissues.

Points to consider before embarking on carrier screening programs include the nature and frequency of the disorder and availability and effectiveness of treatment, community perception of the disorder and attitudes to screening, motivation for screening, how the test is done and what the results mean, obtaining informed consent

and maintaining confidentiality of results, when to screen, education before screening, possible stigmatization and discrimination, and the organization of the
screening program (1). The Council on Ethical and Judicial Affairs of the American Medical Association has addressed ethical issues related to prenatal genetic testing (2), genetic testing by employers (3) and insurers (4), and carrier screening for cystic fibrosis and other disorders (5).
How does society control the way genetic information is obtained and used? How does society monitor and review genetic screening programs? What criteria should be set to make maximum use of the potential good that the Human Genome Project offers, without infringing on the ethical and legal principles of privacy, autonomy, beneficence, confidentiality and nondiscrimination? Who owns genetic information? How should genetic information be used? Who decides which people should be screened? Are there or should there be limits to preimplantation, prenatal and neonatal screening? How should employers and insurers receive and use genetic information? Do we have sufficient data to judge the pros and cons of genetic testing and screening? The Orthodox Jewish community relies on the traditional use of biblical and talmudic law and rabbinic responsa to answer such questions. This approach is described in this essay on traditional Jewish views on genetic issues.

The genetic testing and counseling of children and adolescents is associated with special ethical, legal and psychological implications (6). The risks and benefits of testing have to be assessed to determine whether it is in the child's best interests to be tested (7).

[The following section, in red, is not required reading for the Jerusalem Science Contest]

Specific Examples

Breast Cancer

About 5 or10% of all breast cancer cases are hereditary. The breast cancer genes known as BRCA1 and BRCA2 are responsible for most inherited breast cancer, especially in women who develop the disease before the age of 40 years. The BRCA1 mutation known as 185delAG is found in approximately 1% of the Ashkenazi Jewish population (8) and in 20% of Ashkenazi Jewish women who develop breast cancer before 40 (9) or 42 (10) years of age. This gene is also associated with an increased risk of ovarian cancer. These findings and observations are cause for concern (11). Early interventions may be appropriate in high-risk women who test positive (e.g., more frequent breast examination and mammography, prophylactic mastectomy, hormone prophylaxis). There are many other issues of concern, including confidentiality; access; autonomy; and informing the patient about the implications of a positive or negative test, including its technical accuracy and cost.

The availability of a test does not require that it be offered universally. The American Society of Clinical Oncology recommends that cancer predisposition testing be offered only when the person has a strong family history of cancer or very early age of onset of disease, when the test can be interpreted adequately, and when the results will influence the medical management of the patient or family member (12). However, many other prestigious organizations emphasize that BRCA1 testing remains a research activity for the time being (13). The pitfalls of genetic testing (14) and the psychological issues in testing for breast cancer susceptibility (15) should not be minimized. People at risk must fully understand the risks, benefits, and limitations of genetic testing, the risk of psychological harm, and the possibility of insurance discrimination and subsequent loss of health care coverage, before they undergo testing (16).

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Tay-Sachs Disease

Debates continue about the screening of large populations of Jewish people for the carrier state of Tay-Sachs disease to prevent the Ainappropriate@ marriage of two carriers. Also controversial is the performance of amniocentesis for the prenatal detection of the fatal disease, with the subsequent possible abortion of an affected fetus. Selected termination of affected fetuses may not be acceptable in Judaism, although some rabbis might sanction it. Mass screening programs may produce a psychological burden on those young people who screen positive. Should a carrier of the Tay-Sachs gene refuse to marry an individual who has not been tested? Should a couple break up their engagement if they learn that both are carriers? Should a young person inquire about the Tay-Sachs status of a member of the opposite sex prior to meeting that individual on a social level? Must a person who knows he or she is a carrier divulge this fact to an intended spouse? The stigma of being a carrier of the Tay-Sachs gene may not be fully appreciated. Misinformed or uninformed people may shun and ostracize such carriers. Job and insurance discrimination is also possible if confidentiality of testing results is not assured. If the purpose of Tay- Sachs screening is to provide information and genetic counseling about mating and reproductive options, few will oppose screening. If the purpose, however, is to suggest prenatal diagnosis with the specific intent of recommending abortion of affected fetuses, religious and moral objections might be raised. Preimplantation diagnosis of in vitro fertilized eggs, with the discarding of affected zygotes, if any, avoids the issue of pregnancy termination since pregnancy in Judaism does not begin until zygote implantation into the wall of the uterus.

Genetics and Eugenics in Classic Jewish Sources

Ancient Jewish writings, including the Bible and Talmud, are not devoid of material relating to genetics. One writer describes in some detail how the laws of Mendelian genetics were applied by Jacob in the biblical narrative (Genesis 30:32 ff) of the speckled and spotted sheep (17). Hemophilia and its precise genetic transmission is described in the Talmud (Yebamot 64b). The Sages in the Talmud and subsequent rabbinic authorities had a remarkable knowledge of the genetics of this sex-linked disorder (18). All rabbis recognized that females transmit the disease but do not suffer from it. A few rabbis also considered the possibility of its transmission through males.

Elsewhere (Ketubot 10b), the Talmud portrays a family whose women had hereditary absence of menstruation and no blood of virginity, and were obviously childless. The exact nature of the anatomical or physiological abnormality is not described.

It is prohibited in Jewish law to marry a woman from a family of epileptics or lepers (Yebamot 64b; Maimonides' Mishneh Torah, Issurei Biyah 21:30; Karo's Shulchan Aruch, Even Haezer 2:7) lest the illness be genetically transmitted to future generations. According to Rashi (Yebamot 64b), any hereditary disease is included in this category. This Talmudic ruling (19a) may well represent the first eugenic enactment, and the only legislative bar to the procreation of a diseased progeny, in ancient and even medieval times.@ On the basis of the higher frequency of defective births resulting from unions among blood relatives, Rabbi Judah the Pious, in his ethical will, prohibited marriages between first cousins and between uncles and nieces. Yet such marriages are sanctioned in the Bible and expressly encouraged in the Talmud (Yebamot 62b and Sanhedrin 76b). Since consanguineous marriage increases the probability of birth defects, some rabbis ban such marriages (20, 21), while others strongly caution against them (22 & 24).

Judaism, Genetic Screening and Genetic Therapy

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Genetic disease was recognized by Maimonides, who prescribes a regimen of health for all Jews to remain healthy, since one cannot serve the Lord when one is ill (Mishneh Torah, Deot 4:1). He guarantees that anyone who follows his regimen will be healthy all his life, except for those who were born with hereditary or genetic defects (Ibid. 4:20).
END REQUIRED READING FOR PART 1

The Genome Project and Judaism

Is the genome project an encroachment on the Divine plan for this world by interfering with nature as God created it? Would genetic engineering tamper with the Divine arrangement of Creation? Although one rabbi answers in the affirmative (25), most rabbis consider the acquisition of knowledge for the sake of finding cures for human illnesses to be divinely sanctioned, if not in fact mandated. God blessed mankind with the phrase: replenish the earth and subdue it (Genesis 1:28).

This phrase is interpreted by Nachmanides (Ramban) to mean that God gave man dominion over the world to use animals and insects and all creeping things for the benefit of mankind (Ramban, Genesis 1:28). To subdue the earth, according to Samson Raphael Hirsch (Hirsch, Genesis 1:28), is to master, appropriate, and transform the earth and its products for human purposes. To have dominion over the fish and over the birds and over every living thing on earth (Genesis 1:28) means to use them for the benefit of mankind. The pursuit of scientific knowledge does not constitute prohibited eating from the tree of knowledge (Genesis 2:17). Whatever is good for mankind must be permissible and praiseworthy. However, good often is not pure good, but may contain potentially dangerous elements. Although the genome project is intended to cure diseases, it has raised many concerns.

In the general introduction to his Commentary on the Mishnah (26), Moses Maimonides discusses the existence and purpose of all living and inanimate things in the world. He clearly enunciates the thesis that the purpose of everything that God put on this earth is to serve mankind. Thus, scientific experiments on laboratory animals, during the course of medical research that might find cures for human illnesses, are sanctioned in Jewish law as legitimate utilization of animals for the benefit of mankind (27). However, whenever possible, pain or discomfort should be avoided or minimized in order not to transgress the prohibition in Jewish law against cruelty to animals.

King David said that The heavens are the Lord's heavens but the earth He has given to mankind (Psalms 115:16), further supporting the concept that knowledge and its pursuit are legitimate activities for human beings and not considered an encroachment upon Divine prerogatives. Thus, therapeutic genetic engineering and gene therapy that may result from the knowledge derived from the genome project do not undermine God's creation of the world by manipulating nature (Ramban, Leviticus 19:19). On the contrary, it is a legitimate modification of the natural order. The use of scientific knowledge to benefit mankind is biblically mandated (Ramban, Genesis 1:28). The use of such knowledge to heal illness and cure disease is also allowed biblically, based on the Talmudic interpretation (Baba Kamma 85a) of the phrase and heal he shall heal (Exodus 21:19), or even biblically mandated, based on Maimonides' interpretation (Mishnah Commentary, Nedarim 4:4) of the biblical obligation to restore a lost object (Deuteronomy 22:2) to include the restoration of one's lost health. The healing of illness