**SENIOR THESIS**

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Introduction

“A revolution is underway, with profound implications for all spheres of life. It is fueled by rapid advances in the ability of genetic information and the capability to intervene in response to it,” says John Kilner, Rebecca Pentz, and Frank Young.\(^1\) Within the last twenty-five years, our understanding of genes and their protein products has been greatly increased. One of the triumphs that has significantly advanced our knowledge in this scientific revolution is the Human Genome Project. The Human Genome Project, completed in 2003, was designed to produce genetic and physical maps, as well as a complete typical nucleotide sequence of human chromosomes.\(^2\) This new knowledge has led scientists to novel ideas on how to treat genetic diseases. Genetic engineering has revolutionized the way in which biology is accomplished, and the hope is that these new technologies will create a world without genetic diseases and scourges such as AIDS and cancer. Medicine would be able to cure the disease at the nucleotide level rather than simply treating the symptoms. However, like all new advancements in medicine, the uses of genetic techniques to treat disease has led to discussions about the means by which it is ethical to treat a patient and more specifically that patient’s genome. Before one can start to discuss the ethical issues involved with genetic treatments, such as genetic screening and gene therapy, it is crucial to understand the scientific breakthroughs that have advanced us to this point.

It was not until the twentieth century that the gene revolution as we know it began, but for millennia humans have understood, at least intrinsically, that there are traits that get passed down from one generation to the next. This concept was reflected in the practices of selective breeding; their goal was to pass on desirable traits by breeding together the animals that
possessed them. However, while selective breeding is efficient at improving a stock of animals, there are many limitations. It can take at least several decades to see the desired trait in an entire population. Furthermore, it is impossible to predict which traits will be passed on from parents to children, and genetic traits cannot be shared among species that lack the ability to mate naturally. These restrictions to selective breeding are removed when genetic engineering enters the picture. In 1858, Charles Darwin and Alfred Wallace announced their theory of natural selection. They stated that individuals in a population that possessed advantageous traits better suited for their environment would survive and pass those traits on to future generations, as opposed to those individuals who had detrimental traits and would die. These new traits arose as a result of spontaneous mutations. Mutations are not necessarily detrimental to the organism; in fact, antibiotic resistant strains of bacteria have a vast advantage over unresistant strains when they come in contact with that antibiotic. Evolution through mutation is what has allowed for the survival and diversity of species on this planet, so evolution could be considered nature’s form of selective breeding. It was during this same period that Gregor Mendel published the result of his famous pea experiment. While Mendel did not know what was physically being passed down from one generation to the next, he did discover proportionality principles to predict the phenotypic results of a particular cross. He bred true breeders which are plants that were homozygous for a specific trait, and from these true breeders he made hybrid crosses. It is from Mendel’s work that much of our basic understanding of genetics and rules about genetic assortment originated.

It was in the 1970s that advances in biology allowed for genetic engineering as we understand it. Hamilton Smith and Kent Wilcox isolated the first restriction enzyme, a protein
capable of cutting DNA at specific locations. Since that discovery, hundreds of other restriction enzymes have been identified. DNA that is cut by a restriction enzyme creates nucleotide sequences with sticky ends which are predisposed on a molecular level to accepted foreign DNA molecules or blunt ends which are easily modified to create the same phenomena. These modified nucleotide sequences can form complementary base pairs with other cut pieces of DNA and can be made permanent by DNA ligase creating a new sequence of DNA. Often the restriction enzymes are used to insert a gene into a plasmid, a small, self-replicating, circular piece of DNA. The plasmid is then incorporated into a competent bacteria cell, a cell that has been treated in a way that increases the permeability of its membrane allowing for the uptake of extracellular DNA. The transformed bacterial cell then replicates the desired gene and uses its own machinery to create numerous copies of the final gene product and its resultant protein. Initial recombinant DNA (rDNA) work focused on the production of medical compounds such as insulin and human growth hormones. The production of human insulin by E. coli has created a chemically identical version of insulin to the natural product found in humans. This has allowed diabetics to inject more effectively human insulin rather than a bovine or porcine form, decreasing the likelihood of an allergic reaction to the non-human insulin.

The goal of medical practitioners according to the Hippocratic Oath is to “concern oneself with the well-being of the sick and to do no harm”. It was not until the nineteenth century and the development of germ theory, as well as the acknowledgment of the roles of bacteria and viruses in diseases, that medicine underwent its first revolution in understanding and controlling diseases. Illness, as it then became understood at that time, was the “loss of
good health due to the invasion of an infectious agent.\(^9\) Disease was a result of microorganisms invading the body, and not, as was often formerly believed, a result of the individual’s behaviors or as a divine punishment. It was possible to prevent the spread of disease by either avoiding the infectious agent or inoculating a person against a specific agent. Furthermore, the uses of antibiotics and other medicines could kill the infectious agent within the body. These advancements in medicine greatly decreased the rate of death due to infectious diseases in western societies.\(^{10}\) With the advancements of molecular biology in the last century, scientists have come to understand the role that genes play in certain diseases. They hope that treatments such as gene therapy and genetic screening will be able to treat or cure genetic disorders just as antibiotics and vaccines were able to cure many infectious diseases.

Our classical understanding of human disease has metamorphoses with the knowledge that genes are the source of some diseases. Genes, in many ways, are responsible for the individual’s phenotypic characteristics, and there are clear cases where a single mutated gene can cause horrific conditions like Huntington’s disease, a late onset autosomal dominant disease that is characterized by behavioral changes, abnormal movement and progressively worsening dementia.\(^{11}\) Yet genes are also responsible for basic traits such as skin color, hair color, height, and even play a role in the potential development of intelligence. This begs the question: what is a disease? Many surveys have shown that short individuals are frequently bullied, viewed as inferior, and may have greater difficulties in their relationships, and careers.\(^{12}\) Does short stature constitute a disease since the lack of height seems to correspond to adverse outcomes? Should it be something that we “cure”? Would it not be better for all
parties if everyone’s intelligence was elevated to an IQ of 150? Would the world not be a better place if everyone had blue eyes and blonde hair? With the power of genetic engineering these changes may one day be possible.

In this paper, I will discuss the goals and ethical concerns involved in genetic screening and genetic testing. I will examine what effects the introduction of these new technologies may have on medicine as we understand it today, as well as a basic understanding of the procedures themselves. I will look at the conflicts that can arise from these new procedures such as the rights and the protection of patient confidentiality. I will examine the role genetics serve in eugenics both past and present. In addition, I will compare the differences between single gene therapy, multifactor gene therapy, and enhancement gene therapy; as well as the ethical concerns and possible abuses these therapies may permit.

**Gene Testing and Screening**

According to Hippocrates in *The Epidemics*, the goal of a healer is to, “Declare the past, diagnose the present, and foretell the future.”

Prognosis is a crucial role of the physician, and techniques such as genetic testing and screening allow physicians to treat not only present malady but potential future illness as well. The CDC reports that genetic tests have been developed for over 2,200 diseases, of which approximately 2,000 are currently available in a clinical setting. They state that the majority of tests developed so far are for rare single gene disorders, but that an increasing number of tests are designed for the identification of multiple genes that may increase an individual’s chances of developing a common disease such as diabetes or cancer. It is important to take a moment to note the differences between genetic
testing and genetic screening. A genetic test is performed on a single individual looking for the presence of a specific mutation within their genome. This test is normally performed because of a family history showing an increased risk of the disorder or as a result of phenotypic abnormalities. Genetic screening, on the other hand, is done on a large population. The goal of genetic screening is to “reduce the impact or incidence of illness on a large scale.”\(^{16}\) When a genetic screening is performed there is usually no family history to suggest that the individual has the disease for which they are being screened. The most commonly performed genetic screenings are done on newborns shortly after their birth. The disorders included in newborn screening programs vary a great deal from state to state and from country to country. All U.S. states screen for Phenylketonuria (PKU) and hypothyroidism, but only some screen for sickle cell disease, galactosemia, maple syrup urine disease or cystic fibrosis.\(^{17}\)

Historically, there are several ways to go about performing genetic screening or genetic testing. The oldest method is looking at the individual’s karyotype. Some genetic disorders are a result of improper segregation of the chromosomes during mitosis or meiosis. During both of these processes the chromosomes are in a condensed form and can be visualized by exposing the cell to a hypotonic solution causing the nuclei to burst, freeing the chromosomes to be treated with trypsin and stain.\(^{18}\) This allows for the identification of chromosomes based on characteristic banding patterns and the location of the centromere. From an individual’s karyotype, any major chromosomal abnormalities can be identified such as Down’s syndrome (trisomy 21) or Edwards syndrome (trisomy 18). Another method is DNA Sequence Analysis which can be used when the objective is to look at one specific gene. First the DNA must be extracted from the individual’s cells, and then it needs to be amplified millions, if not billions, of
times through polymerase chain reaction (PCR). At this point the nucleotide sequencing of the DNA can be performed. It is important to keep in mind that this method is only looking for mutations at the level of one specific gene or a part of a gene. It does not look at mutations throughout the entire genome but rather focuses on a specific region of the genome. The final technique discussed is DNA Mutation Screening. This procedure identifies the presence of a mutation by comparing it to a control sample, not by identifying the mutation on a molecular level. The DNA is amplified through PCR and then annealed to form a double helix with the complementary control strand. This piece of double stranded DNA, as well as a double stranded control standard, is run on a Denaturing Gradient Gel Electrophoresis (DGGE). The DGGE allows for the identification of a single point mutation because double stranded DNA with a mutation will have a different rate of mobility in the gel when containing a mismatched pair as opposed to the control sequence with no mismatched pair. An alternative way to use DNA Mutation Screening is through Single-Strand Conformational Polymorphism analysis (SSCP). SSCP is based upon the principle that single stranded DNA will form complex structures with itself and that even a single base pair change will have drastic changes on the final outcome of the complex structure. The DNA is once again run on a denaturing gel and compared with a control sequence. Keep in mind that for both techniques DNA Mutation Screening only shows the presence of a mutation, not the location of the mutation or whether the change is necessarily detrimental. Further testing would need to be performed to obtain this information.

There are limitations to that which can be discovered through genetic testing or screening. For some genetic diseases, the mutation that causes the disease is located in the
same position for all individuals with the illness; however, there are many diseases that can have a mutation somewhere across the entire span of the gene. Further complicating the picture is the fact that the mutation does not necessarily need to be in the coding region of the gene at all. Mutations located in the promoter region of the gene can have just as dire an impact as if the gene itself was mutated. With the potential for so many different mutations, some of which will not be detrimental, it is impossible to design a genetic test to examine for all possible options. Tests tend to focus on the most likely location of the mutation, but this can lead to the potential of a false negative result. Take the test for Activated Protein C Synthesis, a disease which predisposes patients to form blood clots. In the majority of cases, it is caused by a specific mutation in the factor V molecule which is detected by this genetic test. However a patient may get a false negative for the test if he or she does not possess the specific mutation the test looks for but rather a mutation at a different site. Another limitation that one faces in genetic testing and screening is its sensitivity. Suppose a test has a 90% accuracy rate at identifying those with an abnormal gene. In a population of true carriers for that disease 10% would have false negative test results. On the other hand, a test might have a 90% accuracy rate at identifying the absence of the gene. In a population without the mutated gene, 10% of individuals would falsely tests positive for the disorder. This is especially important when looking at genetic screening, because individuals with no family history may be incorrectly told that they possess a disease affecting all aspects of their life. It is for this reason that Dr. Hook recommends that only tests with 100% accuracy or as close to 100% as possible be employed in genetic screening. A final issue to consider is penetrance meaning that even if a test comes back positive, the result of the test itself cannot predict the degree to which the disease will
physically manifest. This is because not all genes are expressed at the same time or at the same level. A gene may possess a mutation, but if that final gene product is not expressed or only does so in a limited fashion then there could be no phenotypic change.

According to Dr. Hook, “the idea of confidentiality has a long history in the practice of medicine dating back to the Hippocratic Oath.” One of the major ethical issues involved with genetic testing and screening is access to the acquired knowledge and how to prevent sensitive information from falling into the wrong hands. Once an individual’s genetic information has been disclosed, there is the possibility of them suffering from genetic discrimination. Furthermore, it is not only the individual themselves that may face difficulties. Since genes can be passed on to future offspring or shared by siblings, individuals with a relative having a genetic disorder may find themselves discriminated against even though they themselves do not possess the disease. A 1996 study conducted by Harvard and Stanford Universities documented 206 cases of genetic discrimination by employers, schools, insurance companies, blood banks, and the military. However, different parties may claim that they have the right to know a person’s genetic history. Some family members believe that they should be informed if they have the possibility of a genetic disorder. Parents might want to know if their child has a genetic disease. Employers claim that knowing their employees genetic histories allows them to better tailor the hiring process. Insurance companies believe that they have a right to be told because they are often paying for the tests and can use that knowledge to better assign premiums or possibly deny coverage. While many might think that it is a moral imperative to tell those family members who may also be affected, there are many people who would prefer not knowing their genetic history.
It is important that individuals be aware of their test results, so that he or she can make informed decisions about his or her life. It is also important that no one but the patient and his or her physician have access to the test results both to protect the individual’s confidentiality and possibly prevent discrimination based on genetics. The question that arises from this conflict is where to store this sensitive information so that only the appropriate individuals can access it. One suggestion advocated was to place the results from genetic testing in a separate location from the rest of an individual’s medical history, or even create a pseudo history. The main issue with this proposal is that a person may be treated by another physician who is not their normal physician. This new physician would be unaware of the existing genetic condition, and without documentation in the individual’s medical history the physician would have no way to become informed of the condition.

The issue of whether a future spouse should be informed of their spouse’s genetic history brings up another interesting ethical question. Since procreation is a major part of most married lives, should spouses know about the potential genetic diseases of their children before they decide to get pregnant? This decision is further complicated depending on the mode of inheritance; or put another way, if the person has a disorder or if they are a genetic carrier for it. One model that currently exists dealing with recessive genetic disorders is the Chevre Dor Yeshorim program created by the Committee for the Prevention of Jewish Genetic Disease. One in twenty-five Ashkenazi Jews is a carrier for Tay-Sachs gene, the cystic fibrosis gene, or both. Both diseases are inherited in an autosomal recessive manner, meaning that an individual needs both maternal and paternal copies of the gene to express the disease. Individuals having one copy do not express the disease but are still considered genetic carriers.
In this program, men and women are given a number around marrying age and their blood is tested thus ensuring the confidentiality of the individual’s results. When two Jewish individuals decide to get married they can call a telephone number, give their individual number and hear the results of their blood test. If an individual’s test is negative, there will be no problems with future children having Tay-Sachs or cystic fibrosis. It should be noted that the children can still be genetic carriers for the disease. If however, both individuals have positive results as carriers for Tay-Sachs or cystic fibrosis, then the couple will have a one in four chance of having a child with one of the diseases. In the example above, both parents needed to have a copy of the defective gene to pass it on to their offspring. There are some genetic disorders, however, that are expressed when only one copy of the mutated gene is present. In these cases known as dominant conditions, only one parent would be responsible for the offspring inheriting a disorder. Should a spouse be required to share if he or she has a gene that is inherited in a dominant fashion? In this scenario, the parent will have a fifty percent chance of passing on an autosomal disorder if he or she is heterozygous for the gene, and a hundred percent chance of passing it on if he or she is homozygous for the gene. As of now, it is at the spouse’s discretion to share genetic history.

According to the President’s Commission for the Study of Ethical Problems in Medicine and Behavioral Research, and the Committee on Genetic Risks of the Institute of Medicine, there are certain conditions under which a patient’s confidentiality could ethically be breached. These conditions include situations where all previous attempts to elicit voluntary disclosure from the patient have failed. Also there must be a high possibility of irreversible or fatal harm to a relative without disclosure; as well as the disclosure of this information
preventing that harm. Finally, the disclosure is limited to information necessary for the
diagnosis and/or treatment of the disorder. This criterion only corresponds to situations in
which the committees believe that it is ethical to breach confidentiality; it does not constitute a
legal duty on the physicians’ part to intervene. However, there have been some state court
cases that may indicate a movement towards disclosure regardless of the impact of that
disclosure.\textsuperscript{31} In 1996, the court case of \textit{Safer v. Estate of Pack} extended the physician’s duty to
warn to individuals that were known to be at risk of avoidable harm from a genetically
transmissible condition.\textsuperscript{32} Today in the federal government of the United States, there is no
overall legal duty to rescue. This means from a national standpoint, health care professional
are under no legal obligations to warn at-risk relatives, unless other statutory obligations
exist.\textsuperscript{33}

Prenatal testing is one of the most rapid areas of growth for genetic screening and
testing. According to John A. Robertson, a professor at the University of Texas at Austin:

“As advances in genetics grow, persons contemplating procreation will also have more
genetic information about potential offspring, including their susceptibility to chronic
illness and late-onset diseases as well as the more common autosomal recessive diseases
not tested. They may then choose to procreate, avoid conception, or terminate a
pregnancy that has already begun.”\textsuperscript{34}

Prenatal testing is usually linked with a reduction in the number of genetic diseases. Genetic
testing and screening cannot fix a mutation that exists in the fetus; therefore, the only way that
these two methods could decrease the overall number of fetuses born with genetic disorders is
by aborting the fetuses that test positive.\textsuperscript{35} This notion is supported by Robertson who further
states, “As tests to identify fetal cells in maternal blood are perfected, the genetic condition of
every fetus will become a routine part of prenatal care, followed often by pregnancy
termination when the tests are positive.”\textsuperscript{36} In fact, some medical texts use the term amniocentesis to refer to “not only the testing but also the abortion that the authors assume a couple will authorize if their fetus is discovered to have some genetic defect.”\textsuperscript{37}

The presence of genetic disabilities discovered as a result of prenatal testing is a main justification for aborting a pregnancy, but there are some important points to remember when thinking about prenatal testing. Just like all genetic tests, prenatal tests or screens have margins of errors. Alphafetoprotein (AFP) tests examine maternal blood looking for the possible presence of neural tube defects and Downs syndrome. The AFP test, however, is notorious for producing false positives and often requires retesting; even amniocenteses are not 100\% reliable in diagnosis genetic disorders.\textsuperscript{38} Prenatal genetic tests also have no way to predict the penetrance of the disease and it may be that even though an individual has a genetic disorder they can still live a relatively normal life. Some may believe that for an individual with a genetic disease, life is so terrible that their life is not worth living. This, however, is not a medical judgment, but a value judgment, and no one has the right to make a value judgment upon another person especially when the result of that judgment is death.\textsuperscript{39}

From a Catholic perspective, life begins at the moment of conception and it is morally wrong to take the life of another human being. But persons who support aborting the fetus due to genetic abnormalities must believe that the fetus is a lesser form of human life. Without this assumption there is no moral difference between terminating a fetus due to genetic abnormalities and executing an adult with a genetic disorder.\textsuperscript{40} For many this idea is tantamount to eugenics and reminiscent of the horrors perpetuated by the Nazis. Sociologist Marque-Luisa Miringoff offers a somber warning when she declares:
“In pursuit of good health, we have begun to tread a fine line in ‘human selection’. We choose to rule out certain diseases or, more accurately, certain human beings with those diseases. Clearly, it is a just and meaningful desire to prevent fatal and debilitating diseases. Yet in pursuit of this goal, we may pay unobserved costs. In eliminating individuals with unwanted diseases, we also create a mind-set that justifies the process of human selection. We thus move into the questionable arena of human worth, and to some degree eugenic thought. We forgo the idea of therapeutic change and opt instead for elimination. Individuals are seen as flawed. It is easier and more desirable to prevent their existence than work for their survival.”

It may be asked why expecting parents would undergo prenatal genetic testing if the goal is not to abort an abnormal fetus. After all, it can be a painful and somewhat risky endeavor. Although amniocentesis is considered to be a safe procedure, it is recognized as an invasive diagnostic test that does pose potential risks; the primary risk being miscarriages. Although extremely rare, it is possible for the needle to come in contact with the baby. For this reason, great precautions are taken using a sonogram to guide the needle away from the baby. The mother may experience a sharp pain when the needle enters the skin and again when it enters the uterus. That being said, there are still many reasons to have prenatal genetic tests. Knowing that your future child has a genetic disorder gives parents the chance to prepare mentally and make arrangements before the birth of the child. Furthermore, some genetic diseases can be treated immediately before or shortly after birth so it is helpful to know what preparations are needed before delivery begins.

Eugenics

As discussed earlier, these new genetic techniques can be abused and manipulated to target and eliminate “undesirable” individuals. One of the greatest fears for these new
genetic methods is their potential use in eugenic practices. It was a fear that James Watson, discoverer of DNA, reaffirmed as the Director of the Genome Project. He warned that:

“There is no avoiding the fact that arguments drawn in part from genetics have been politically misused in the past, most egregiously by the Nazis but also elsewhere in Europe and North America. Indeed, the specter of coercive government eugenics programs persists even today in statutes still on the books in several nations... The only way to ensure that history does not repeat itself is for scientific and medical communities to remain constantly vigilant for abuses of genetics.”

The term eugenics is most often associated with the Nazis, but the word was actually coined in 1833 by British biologist Frances Galton. Galton, cousin to Charles Darwin, created the term to apply to an individual who was well born or possessed “good genes.”

Galton defined the science of eugenics as “the study of the agencies under social control which may improve or impair the racial qualities of future generations physically or mentally.”

Galton’s goal was to institute public policy that would allow the more suitable set, the wealthy and well born, to prevail over the less suitable set, the poor and uneducated. Galton, like many of his contemporaries, did not recognize the role that environment could play in an individual’s traits; he attributed all characteristics to genes. In his book, *Natural Inheritance*, published in 1889 he claimed to have found evidence linking inheritance to disease, artistic abilities, alcoholism and many other human characteristics.

Social Darwinism was a movement that arose from the scientific information obtained through eugenic studies. Social Darwinism stressed the notion of the survival of the fittest, a term linked to evolution. These individuals believed that medical care and public assistance was interfering with the natural order in which the fit and well born survived and the poor and weak died. Many scientists and governments, including the United States
and Great Britain, embraced this notion; German eugenics, also known as racial hygiene, emerged as a direct response to the rising number of poor Germans. Racial hygiene attacked medical practices that helped individuals but “endangered” the race due to the fact that these practices allowed people who would have died to survive and reproduce, passing down their taint.  

The eugenics movement quickly spread from Europe to America and became the foundation for many social policies within the country. In 1904, Charles Davenport set up the Station for Experimental Evolution in Cold Spring Harbor, New York. Using Mendelian rules of genetics, Davenport argued that patterns of inheritance were evident in many human traits such as insanity, epilepsy, pauperism, criminality, alcoholism, and feeble mindedness. He believed that the best way to defend the quality of the American population was to halt the influence of bad genes from foreigners by keeping them out of the United States of America. Eugenics thus became a “legitimate” justification for racism. According to Russo and Cove, many Americans feared that the new immigrants would make the country “darker in color, smaller in stature, and more given to larceny, murder, and sexual-immorality.” It became scientifically proven to the intellects of that era that some individuals were inferior to others. These conclusions were based upon pedigree analysis, examined back to the third generation, and Intelligent Quotient (IQ) tests. The IQ test became the most popular method for measuring the fitness of an individual. It should be noted that these IQ tests did not take into account the educational or cultural backgrounds of the individual being tested. As a result these tests told very little about the individual’s intelligence, and nothing about the inheritance of intelligence or
differences in intelligence in different races. Yet according to Carl Brigham in his book *A Study of American Intelligence* published in 1923, “it was clear that Alpine and Mediterranean ‘races’ were inferior to the representatives of Nordic race, and that the black Americans were much less intelligent than their white counterparts.” This idea of racial inferiority was reflected in the 1924 Law of Immigration Act that restricted immigration into the country.

The Immigration Act “solved” the issue of foreign masses polluting America with substandard traits, but the question remained about what to do with the genetic inferior individuals already present in the country. The solution, according to Dr. Harry Clay Sharp and other physicians, was state enforced sterilization programs as a way of minimizing the number of individuals with genetic or physical disabilities. They believed that if the state had the right to execute a murderer and thus denying that individual the right to life, it also had the right to deprive persons of the lesser right of procreation. By involuntarily sterilizing undesirable individuals, Sharp believed that it would be possible to prevent the perpetuation of bad genes. Over 60,000 of these involuntary sterilizations were carried out in the early to mid 20th century in the United States. The fact that this happened in America and the magnitude of the numbers of involuntary sterilizations may surprise some individuals, but this number is dwarfed next to the number of sterilizations performed by the Nazis. The German Eugenic Sterilization law went into effect on February 1, 1934 and for the next three years approximately 400,000 individuals were involuntarily sterilized. Half of these sterilizations were performed on the “feeble-minded.” This was only the beginning of the Nazi’s eugenics movement. By the end of World War II, five to six million
Jews had been exterminated as well as an unknown number of gypsies, psychopaths, anti-socials, and homosexuals. It took the horrifying brutality of the era of National Socialism in Hitler’s Nazi Germany to show Americans the ultimate destination of programmed eugenics. The United States’ enforcement of sterilization laws dropped in the 1940s and was almost non-existent after the end of WWII in the 1950s.

After the horrors of the Holocaust were revealed, most people would like to believe that as civilized rational human beings we have moved beyond eugenic practices and that an event such as the Holocaust could never happen again. Unfortunately this belief is not true as seen previously with the case of aborting abnormal fetuses. About 90 percent of women, who learn they are carrying a fetus with the extra 21st chromosome (Trisomy 21) that causes Down syndrome, choose to abort the fetus. Furthermore, studies have shown that many women choose to abort the fetus for diagnoses of less serious conditions.

There is widespread support among Americans agreeing with this position. According to a 2006 poll conducted by the National Opinion Research Center, 70 percent of Americans said they believe that women should be able to obtain a legal abortion if there is a strong chance of a serious defect in the baby. Bently Glass, a former president of the American Association for the Advancement of Science, has stated, “No parent has the right to burden society with a malformed or incompetent child.” Governments may no longer have laws that legalize involuntary sterilization of individuals to prevent them from passing on their genes, but there are still laws designed to prevent the inheritance of certain characteristics. In 1970, the Danish government adopted a strategy of prohibiting marriages if both parties were carriers of a genetic disease.
Watson believed that it was the duty of scientists and physicians to ensure that genetics would never be used for eugenics again. Yet there is an intrinsic flaw to his logic, as most of the policies implemented by Hitler and the Nazi party were advocated and practiced by scientists and physicians at that time. Much of what the Nazi party did was promote propaganda in leading textbooks in use not only in Germany but in many other countries including America. Some intellectuals still advocate for the practice of eugenics as a way of improving society. They seek not to exterminate the individual, but the gene that causes the “imperfection.” According to Joseph Fletcher, proponent of the theory of situational ethics:

“...losers in the chromosomal lottery, which saddles us with four million Americans born with diabetes, of the two hundred fifty thousand children born in the United States with every year with genetic diseases, or the fifty million Americans whose I.Q.s are below ninety. Genetic engineering and fetal control will help enormously. The accusation that the new technology is trying to make a ‘master race’ is fair enough if it means that people with fewer defects and more control over crippling accidents of ‘nature’ are better able to master life’s ups and downs. Most of us would want to belong to the master race in this sense. Mastery in the sense of good health and inheritance is sanity.”

From a historical perspective, it would appear that science is not the best watchdog against eugenics.

**Gene Therapy**

The greatest issue facing genetic screening and genetic testing is the disparity between the number of tests available examining for the presence of genetic diseases, and the means by which to treat those diseases. This is a concern for individuals being tested for diseases such as Huntington’s because there are no treatments available if the individual receives a positive test result. This individual is now aware that he or she will die prematurely as a result of the effects this abnormal gene has on the body and there is
nothing that can be done. In this instance, individuals with Huntington’s and similar disorders often chose suicide as an alternative to losing control of their minds and bodies. As discussed earlier, expecting parents often chose to terminate a pregnancy when they receive positive results for genetic tests. If it was possibly to treat or cure a genetic disease then expecting parents might choose not to abort the fetus. Furthermore, those suffering from debilitating genetic disorders like Huntington’s would have hope for a healthy future. Treating and curing genetic disease is the goal of gene therapy.

According to Boylan and Brown, “The general aim of gene therapy is the introduction of a fully functional and expressed gene into a target cell resulting in the permanent correction of a specific genetic disease.” However, for that therapy to be successful the locations of both the structural sequence of the gene and the regulatory sequence controlling the transcription of that gene must be known. Before beginning a gene therapy there are some concerns that need to be resolved. Target cells, those cells intended for the delivery of the new gene, must be chosen. Most genes are only expressed in a subset of cell types. If the product of a mutation is only expressed in a few cell types then these cells would be the ideal target for the gene therapy. However it may not be possible to target these cells, or they might have such a fast turnover rate, like bold cells, that it is impractical to target them for therapy because it would not lead to a permanent cure against the disease. Instead it may be more practical to target stem cells which divide indefinitely or cells that possess a long half-life. Another factor to consider is the accessibility of the target cells. Some cells like bone marrow can be harvested, cultured, and manipulated ex vivo before being returned to the individual’s body. The normal (wild-
type) gene is inserted into the cell’s nuclei and then these cells are reinserted into the patient using a non-virulent virus enabling the new gene to enter a cell and be transcribed. However, not all tissues or cell types can be manipulated \textit{ex vivo} and in these cases all the manipulations must be performed \textit{in vivo}. This is often done by injecting the vector directly into the organ or the blood stream.

One must consider more than just the cell type and its accessibility before performing gene therapy. The goal of gene therapy is to introduce a wild-type gene that will produce the properly formed protein product. However, the overproduction of this protein may lead to a different disorder making it necessary to incorporate transcriptional factors to control the levels of protein product. One potential method to protect against overproduction of a protein product is to incorporate suicide genes into the vector delivering the genetic material. This allows for the transformed cells to be eliminated if there is too much protein produced or other adverse side effects. While overproduction may be a concern for future therapies, the current hindrance to genetic therapies is the lack of long term expression of the inserted gene in transformed cells. Furthermore, promoters and control sequences designed to regulate the amount of protein product being produced are not presently being incorporated into the vectors.

The mutation of the gene itself can also affect the method of treatment. That is to say, it is easier to treat a loss-of-function mutation than a gain-of-function mutation. Treating a loss-of-function mutation involves inserting a functional gene where there was never a functional gene. However, treating a gain-of-function mutation involves both
inserting the functional gene but also removing the mutated non-functional gene since it is the mutated gene’s new trait that are responsible for the disease.\textsuperscript{77} This is the challenge that faces researchers in trying to cure sickle-cell anemia. In this disease, the genes for hemoglobin proteins have mutated to give the proteins the new ability to stick to each other.

Gene therapy, if successful, introduces a gene that creates a product never before seen in that individual’s body. The immune system may recognize this new product as “foreign” and trigger an immune response destroying the cells manifesting that product.\textsuperscript{78} In 1998, an 18 year old undergoing gene therapy for a genetic kidney specific enzyme defect died four days after his treatment from a possible allergic reaction stimulated by the virus vector. This reaction shut down his lungs. Also, a study involving immune deficiency was halted when three of the participants developed leukemia-like symptoms.\textsuperscript{79}

A final consideration before beginning a gene therapy is the selection of the vector. Most vectors are engineered as modified viral vectors. Viruses are non-living, pathogenic, obligate parasites that use the host’s machinery to replicate and assemble new viruses. It is the viral vector that determines what types of cells can be infected with the desired gene since the vector can only infect its compatible cell types. Some viruses, specifically retroviruses, integrate the viral genome into the host’s cell genome. The vector’s ability to integrate is exploited by some therapies as it allows the genes to be present in all the cells derived from that initial transformed cell. Other viruses can infect non-dividing cells and transform them into “viral protein producing factories”. This is a strategy that gene
therapy uses to transform non-dividing cells to produce proteins of interest. While great care is taken to mutate the vector so that it is non-pathogenic, the potential remains for recombination with endogenous viral sequence in our genome or with the environment to produce a viable virulent virus. Studies are being conducted to look at insertion locations for viral vectors to prevent the possibility of a corrected gene being inserted into the coding region of another gene. Non-specific insertions could potentially lead to the creation of a new nonfunctional gene product. However for an individual with a life threatening condition, some physicians believe it is worth the risk of an inadvertent insertion, leading to a secondary mutation, if the fatal disease is treated.

There are two major categories of gene therapy currently performed depending on the nature of cell being transformed. The two different therapies are germ-line gene therapy and somatic gene therapy. Germ line therapy, sometimes called inheritable gene modifications or IGMs, targets the germ cells, sperm or egg. Any changes made to the germ line are permanent inheritable changes that will be passed to the offspring. This type of treatment has not yet been attempted in humans but is a routine procedure that has been performed on lab animals, especially mice, for decades. Somatic gene therapy, on the other hand, is used to correct a nonfunctioning or malfunctioning gene in either a monogenetic disease or a multifactor disorder. Unlike germ line therapies, these treatments will only affect the individual’s genome and cannot be inherited by the offspring.
Germ line therapy can be performed by modifying the parental germ cells, sperm, or by modifying the fertilized egg allowing for the new gene to be present in every cell of the developing individual’s body including his or her germ line allowing this correct gene to be transferred to following generations. A second method to perform germ line therapy is to modify the embryonic stem cells of an adult so that the adult’s body contains a high percentage of cells derived from this genetically altered line. Having the majority of the cells in an adult’s body transformed increases the probability of the new gene being present in that sperm or egg during a fertilization event. However since the new gene is not present in every cell, it is possible that a germ cell without the gene may be involved in a fertilization event. Therefore, this method of germ line therapy does not conclusively ensure that the desired gene will be inherited.

There is little question scientifically that germ line therapies could be performed in humans if desired. Furthermore, it is undeniable that there are certain advantages to germ line therapy. It has the potential to permanently cure genetic disorders from our population ridding by treating every individual with that disease thus ridding the human genome of lethal diseases. While this is an admirable goal, the issue that arises from germ line therapy is the notion of the “law” of unseen consequences. This concept reflects on the potential to create tremendous harm due to our ignorance. The current methods for genetic engineering are imprecise and there is the possibility of side effects to a treatment that the genetic engineers have not foreseen. Any changes or mistakes that may be made to that individual would be permanently incorporated into his or her lineage. With our current knowledge, any changes to the germ line involve too many possibilities for serious
and potentially fatal errors making this treatment simply unethical. Therefore, it will not be discussed further in this paper.

In clinical trials, human somatic gene therapy has been successfully shown as a method to treat some genetic diseases. One of the earliest successes for somatic therapy was in 1990 when several children were treated for a defective gene for the enzyme adenosine deaminase (ADA). ADA is normally expressed in T-cells, a cell type crucial to the body’s immune response. An individual with nonfunctional ADA suffers from a severe immunodeficiency, and even a common cold may be lethal. The children had samples of their own ADA-deficient immature lymphocytes and lymphocyte stem cells removed and cultured. A functioning ADA gene was inserted into a viral vector used to infect the cell culture, thus introducing the corrected gene into the cells. These transformed cells were then injected back into the patient. In the successful cases, the patient’s immune system began to function, although the children continued to undergo other medical treatment.

Somatic gene therapies are currently being investigated as a possible means to treat monogenetic or multifactor disorders. Monogenetic diseases are due to a non-functional protein as a result of a single gene mutation. The example of the ADA treatment is an illustration of this category. The goal of a monogenetic gene therapy is to cure the disease by either repairing the mutated gene or more commonly inserting a fully functional gene. The recent successes of monogenetic trial therapies have led some scientists to suggest treating monogenetic diseases in utero. By treating the fetus in utero, the disease would be controlled and corrected before complications could manifest. Gene therapy appears
more successful in fetuses due to the decreased risk of the fetus triggering an immune response to the new gene product. This is due to the fetus’ immune system not being fully developed and activated. However, in utero gene therapy poses a serious risk as it has an increased potential for an inadvertent insertion into or mutation of the fetus’ germ line.

In multifactor disorders, the diseases are not due to a single gene mutation but are the result of mutations in interacting genes often combined with environmental factors. Gene therapy designed to treat multifactor disorders, such as AIDS or cancer, may take the approach of adding genes to enhance the immune response. Genes may be inserted to protect healthy cells from effects of chemotherapy or to introduce suicide genes to killed targeted cells, a technique that is being explored as a way to destroy tumor cells. These therapies are designed to treat the disorder, but because there is not a single gene responsible for the disease that can be targeted these therapies will only treat but not cure the disease. Multifactor gene therapy is the most widely funded form of gene therapy currently being investigated. This is due in part to the difficulty of achieving long time expression of gene products in monogenetic treatments and the larger market for multifactor treatments. There is also interest in using genetic immunization through gene therapy to develop new vaccination strategies against infectious disease.

Through gene therapy, it may be possible to eliminate the eugenic practice of aborting genetically abnormal fetuses, but this does not mean that the issue of eugenics itself is solved. Gene therapy opens new avenues for eugenics. These new methods are more
insidious because it seeks not to eliminate those individuals that are different, but to “cure” them and society of these disorders. Speaking out against gene therapy Jeremy Rifkin has said:

“...There is no discernible line to be drawn between making inheritable repairs of genetic defects, and improving the species. Once we decide to begin the process of human genetic engineering, there is really no logical place to stop. If diabetes, sickle cell anemia, and cancer are to be cured by altering the genetic make-up of an individual, why not proceed to the other ‘disorders’: myopia, color blindness, left-handedness. Indeed what is to preclude a society from deciding that a certain skin color is a disorder?” 97

This idea of using gene therapy as a method to improve upon oneself is known as genetic enhancement. Genetic enhancements are morally unethical because it is fundamentally subjective, masking itself as an improvement to humanity while in actuality destabilizing that society. These enhancements are biologically, socially, and theologically detrimental to human life. Under no circumstances could a genetic enhancement be morally acceptable.

From a biological view point, the greatest harm that can result from a population wide genetic enhancement is the overall loss of genetic diversity. Diversity in a species, achieved through evolution, is critical for that species survival. Species that are diverse and have a wide range of genetic variability are in a better position to respond to environmental changes than a less diverse species. 98 Each change made through enhancement alters the differential fitness of genotypes or phenotypes available.99 Enhancement therapies carried out on large scale will inevitability reduce a population’s diversity. Without this diversity a species may not be able to adapt to the changes taking place in their environment. Therefore, any technique that compromises diversity on a population scale is disadvantageous for that species.
To some individuals, this warring against enhancements might seem overly cautious. After all, it seems rather strange to say that the survival of our species could be threatened by altering individuals’ eye color or skin color. Yet if these enhancement therapies were carried out there would be serious health consequences. Those with darker skin tones have historically been discriminated against, and a possible enhancement therapy might be to create lighter skin tones in the population. Skin color is control by the amount of melanin produced by the melanocytes skin cells. The more melanin produced, the darker the skin’s pigmentation. Melanin helps to protect the skin against the damaging effects of the sun which can cause skin cancers and premature aging. Individuals living in areas with higher sun exposure have evolved to have elevated levels of melanin present in their skin. In African American skin, the melanin level provides a sun protection factor (SPF) approximately equivalent to 13.4. This is compared to the levels of melanin that provide an SPF of approximately 3.4 in Americans of European decent. This decreased level of melanin in Caucasian individuals contributes to the increased prevalence of skin cancer in this population. However, the increased protection provided by greater amounts of melanin does not inhibit an African American from developing skin cancer.

The importance of diversity in traits can be illustrated in something as simple as our skin tone. If genetic enhancement were to be carried out on skin color then a significant proportion of our population would lose a genetic advantage. Furthermore, there is “no such thing as a good genotype. There is only a good genotype for a particular environment.” A further complication is that this rule also applies to genetic diseases that might be cured through gene therapies. One of the best understood examples of this phenomenon is the conservation of the sickle cell gene in malaria stricken areas. The mutated sickle hemoglobin, a gain-of-function
transformation, gets its name from the sickle shape the red blood cells assumed in oxygen poor conditions. Not only are the sickle cells cleared more rapidly from circulation than the normal blood cells leading to sickle cell anemia, but these sickle cells can aggregate together blocking blood vessels and organs, leading to extremely painful and life-threatening sickle cell crisis.\textsuperscript{102} This is especially true for homozygous carriers of the disease. However, this mutation is actually beneficial in regions of the world with a high prevalence of malaria. This is particularly true for individuals who are heterozygous for the sickle condition since they tend to experience less severe symptoms than their homozygous counterparts. The advantage to the sickle cell trait is that the malaria parasite cannot complete its life cycle in individuals with sickle cells; furthermore, the parasite’s proteins are released into the blood stream allowing for the immune system to mount a response.\textsuperscript{103} So in regions where there is malaria, those who are heterozygous for the sickle trait will have a selective advantage and be superior reproducers to those without the trait. Furthermore, the same genetic mutations that predispose individuals in the Western Hemisphere to allergens and asthma are advantageous in certain regions where parasites are a major health concern.\textsuperscript{104} A mutation in a gene for a specific molecule on a lymphocyte may normally be considered detrimental yet this mutation may offer protection from the HIV virus thus making it less likely that the individual will get AIDS.\textsuperscript{105}

There are social disadvantages to allowing population wide genetic enhancements, the most frightening drawback being the likelihood of eugenics. According to Feinberg, “without some ethical principal to prevent gene enhancement, the door will be opened for eugenics in its most extreme form, potentially totally redesigning the human genetic code in whatever way we want.”\textsuperscript{106} The very act of choosing a single standard as an example of perfection would by
necessity make all other possibilities defects or deformities. Extending this to its probable conclusion, Boylan and Brown would allow for “entire races, ethnic groups, and religions to be termed ‘defective’ by the standard makers and thus be targeted for discrimination until they are willing to undergo genetic enhancements.”

Also social diversity, like biological diversity, would decrease if gene enhancements were carried out over a long period of time on a large scale. The concern is that society might become so uniform that human freedom itself is jeopardized.

There are certain traits and characteristics that each society place great value in. In the United States, one of these characteristics held in high regard is intelligence. Due to the fact that a portion of our intelligence is related to genetics, it may one day be possible to augment our IQ through genetic enhancements. The apprehension involved with these types of enhancements is the possibility of the development of a genetic underclass: the genetic “haves” and the genetic “have-nots”.

As stated by Rifkin, “Those families that can afford to program ‘superior’ genetic traits into their fetus at conception could assure their offspring an even greater biological advantage, and thus a social and economic advantage as well.” Those in the genetic underclass would not be able to compete with wealthier individuals’ possessing the income to genetically enhance their intelligence or other traits. This would increase the gap between the rich and poor placing constraints on social justice and undermining the stability of society.

A final social concern with genetic enhancement is about who would be making the decision to enhance the individual. If the enhancement is being made in utero than the most
likely answer to this question is an individual’s parents. There is a fear that parents may begin
to design their children turning them into “commercial products with expected parameters of
normality and function.”¹¹¹ This production of desired children can be seen in the ability to
choose the sex of one’s child through preimplantation genetic diagnosis.¹¹² The standard of
what would be genetically desirable is most likely being chosen by that society’s economic and
political groups. Additionally, every society possesses its own set of norms and cultural
preferences, and enhancement therapy would allow for each individual in the society to meet
these preferences. However, allowing social preferences to dominate the selection of
individual traits can lead to serious disparity in that society. Case in point, China’s One Child
Policy as well as the Chinese cultural preference for boys lead to “the largest, the highest, and
the longest gender imbalance in the world.”¹¹³ It has been called a “gendercide” due to the
millions of parents that selectively choose to abort offspring lacking the Y chromosome. Thirty
years after this practice started, China is facing a serious social crisis due to the gender
inequality resulting from the 40 to 60 million women that were aborted.¹¹⁴ This policy and the
resulting gender imbalance will haunt China and affect its society for decades to come as the
country attempts to grapple with the lack of females.

Genetic enhancement of persons is detrimental theologically due to the nature of how
that individual is being treated. According to Eberhard Schockenhoff, to engineer someone
else’s genetic identity and want to multiply someone else’s traits due to the properties,
capacities, or characteristics of his or her genome, amounts to the clear recognizable
instrumentalization of humans.¹¹⁵ This idea is incompatible with human dignity since this treats
humans as only a means to an end. Genetic enhancements allow people to instill traits valued
for their functions into others. “Valuing is preferring; preferring is choosing”, according to Richard Stith.\textsuperscript{116} However, just because a trait is “desirable” at a specific moment does not ensure that it will remain “fashionable.” All valuations imply the possibility of an alternative to the thing being valued, and there is an intrinsic flaw to allowing value to be the deciding factor in genetic changes.

Stith states, “Valuing, by its very nature, is for a type. Value can only demand that a quantity or quality of life exists, not a specific individual.”\textsuperscript{117} If we can reduce human life to value, there could be no objection to substituting one enhanced individual for an ‘equally’ valuable enhanced individual.\textsuperscript{118} Yet most people would not be willing to substitute a friend or a loved one for someone of ‘equal’ value. Persons are appreciated for who they are as individuals.\textsuperscript{119} We would be unwilling to accept or exchange a substitute for that individual. If human life is revered, not valued, the unacceptability of genetic enhancements becomes clear. Reverence for life acknowledges that each human possesses sanctity not value. It seeks not to violate the object of its concern but rather let it be. The prime contrast between value and reverence is that the first seeks to preserve and control its object while the second does not.\textsuperscript{120} Genetic enhancement is incompatible with reverence for life because it seeks to dominate individuals on a molecular level.

German theologian, Helmut Thielicke, suggested that there are two ways to view individuals. They can be viewed in terms of their utility, or by their “infinite worth” due to their alien dignity. He argues that the “incommensurable, incalculable worth of human life is not due any imminent qualities of humans, but imparted on us by the love bestowed on man by
Human worth is an alien dignity that is integral to an individual, and because it is alien it does not have to be earned. Furthermore, it is not something that can be assigned nor can it be enhanced through genetic changes. This is because technical or utilitarian abilities do not define worth and even the loss of these traits cannot diminish that individuals’ worth. No one individual is worth more than another and two peoples’ worth cannot be compared. In this way “alien dignity equalizes all people”, yet acknowledges that no two people are the same. This is greatly different from genetic enhancement which seeks to equate individuals by making them genetically identical. Put simply, being made in the image and likeness of God meant that each person gained an alien dignity that stamped a fundamental worth on that person; a worth so central and ineradicable that nothing done by oneself or by others could ever remove it.

If we accept Rifkin’s premise then there is no distinct difference between gene therapies and genetic enhancements, and thus it would be morally unacceptable to treat disease with a gene therapy. Most scientists and medical professionals agree that treating a disease by inserting a correct wild-type gene for the mutated gene into a patient is not ethically different from using medicine to treat a disease. The issue here is that many conditions not normally considered diseases, like balding, are still treated by the medical community. It is tempting to question why treatments currently performed in a medical setting should also be available in a genetic therapy. Nevertheless for reasons mentioned earlier, genetic enhancement therapies cannot be allowed to be implemented. It is for this reason that strict ethical guidelines must be achieved before genetic therapies should be made available to the general populace.

**Conclusion**
Genetic engineering has touched all aspects of life. It has transformed and continues to transform medicine and the ways in which science is conducted. Curing debilitating and deathly diseases is the aim of these new genetic treatments. However, in the race to cure humanity, it is possible to lose sight of the most important factor in the treatment of disease: the individual. According to the Physicians’ Oath of the 1948 Declaration of Geneva, the health of the patient is the physician’s first consideration. It is the individual, not society, which the physician is treating. While it is true that the medical treatment of an individual may contribute to the betterment of society, the reverse is unacceptable. That is to say, the betterment of society should never be achieved through mass medical treatments on individuals.

It is a person’s uniqueness and personality that allows for an attainment of a sense of self, and part of this uniqueness is achieved through our individualized genome. Genetic techniques become unethical in medicine when the individual’s rights to diversity are ignored. The most extreme case of this abuse is the abortion of a fetus based solely upon the presence of abnormal characteristics and traits. As difficult as it may be to accept, an individual’s uniqueness is what allows for the presence of genetic abnormalities. Making it acceptable to eliminate a fetus with genetic abnormalities gives credence to the idea that it is permissible to purge society of any unique characteristic termed undesirable. This notion can allow for the practice of eugenics in its most extreme and terrifying form: mass extermination of specific groups of people. It is for this reason that it is unacceptable to abort fetuses exclusively on the presence of genetic abnormalities.
Gene therapy can be used to promote the health of the individual when it is used in the treatment of diseases. It is only ethical in situations where the distinctiveness of the person is being protected, and the possibility of the treatment being inherited is removed. Gene therapy or any medical treatment designed to create a more uniform population is immoral because it seeks to better society through the sacrifice of a person’s individuality. Furthermore, the loss of genetic diversity would correlate to a stagnant genome and a decrease in the ability to evolve. Genetic enhancements also deny individuals the protection provided by their alien dignity. It reaffirms that some people are worth more than others, and that these lesser individuals need to be “fixed”. This too is an idea that would lead to eugenic practices.

As our knowledge and genetic techniques improve, it is crucial to reaffirm the importance of the individual in medicine. We must remember that just because we have the tools to manipulate the genetic code does not necessarily give us the right to influence it. What makes us human is the overall identicalness of our genome, but what makes each of us special is our genetic uniqueness. The world we live in is a wonderfully diverse place and it should remain that way for future generations.


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48 Dyck, 26.
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