chapter 8

Human Gene Therapy

Human Gene Therapy

Routine use of gene therapy to treat genetic diseases is more remote than environmental applications of genetically altered organisms. The first successful use of human gene therapy—using genetic engineering to correct a genetic defect– has not yet occurred. Although the technology to correct specific single defects exists in animal systems, it has yet to be demonstrated in humans. Moreover, scientists have imposed regulatory constraints and rigorous review criteria for future testing. Despite these limitations, the potential exists for human gene therapy and genetic diagnostic technologies to create a medical revolution in treatment. In the next decade, gene therapy could be used in a few individuals to treat some fatal diseases that are currently untreatable. A wide variety of diagnostic tools have become available already.

Public perceptions of human applications of genetic manipulation will be affected by a number of factors. First, the benefits of human gene therapy are considerably different than for environmental applications. Second, human genetic manipulation raises issues of morality of a potentially different nature and magnitude than for environmental applications. Third, concern about human applications might focus as much on the acceptability of uses (i.e., therapeutic v. eugenic) as on the morality of the method. This chapter examines public perceptions of and beliefs about human genetic manipulation, as well as public acceptance of different uses of genetic manipulation in humans.

GENETIC DISEASES

The primary beneficiaries of human gene therapy will be persons and their families who have genetic diseases. At present, only a handful of genetic defects are considered potential candidates for human gene therapy. However, as scientific investigation continues to identify the causes of the vast array of single-gene defects, an increasing number of genetic disorders could be treated through genetic therapy.

As part of the inquiry into public perceptions of biotechnology and genetic engineering, OTA surveyed the self-reported incidence of genetic disorders in the American population. As noted earlier, the rate of acceptance of the various uses of biotechnology appears to vary with the likelihood of personal benefit. Thus, the demand for genetic applications to human disorders might be a function of the distribution and frequency, or perceived frequency, of the disorders in the population.

Over one-third of the American populace (37 percent) say that one or more immediate family members have (or have had) a genetic problem.

Nearly one in six families (16 percent) reports a member who has had a potentially fatal genetic disease. One in twenty families (5 percent) self-reports that a family member has been a carrier of a potentially fatal genetic disease. One in twelve families (8 percent) says a family member has a genetic proclivity to serious illness. Finally, 19 percent of Americans self-report they have immediate family members with other inherited health conditions and 8 percent report members with other birth defects. All together, the OTA survey found that 37 percent of adult respondents report they have (or had) one or more immediate family members with one or more genetic problems (table 50). Thus, the survey found a wide potential array of people who might perceive they would benefit from human applications of genetic therapy.

The profile of persons who report having family members with genetic problems shows little variation across the subgroups surveyed. The self-reported incidence of these problems does not differ across the three age groups under 65 years of age. The reported frequency is the same in the

Table 50.-Incidence of Genetic Problems in Immediate Family[a]

Question (F15):[b] Has anyone in your immediate family ever (READ ITEM)?

	Percent
Had a potentially fatal genetic disease	16
Been a carrier of a potentially fatal genetic disease	..
Had a genetic proclivity to serious illness	8
Had any other inherited health condition	19
Had any other birth defect	8
Net genetic problems	**37**

[a]Percentages are presented aa weighted sample estimates. The unweighed base from which the sampling variance can be calculated is 1,273.
[b]The code number of the question in the survey instrument (see app. B).

SOURCE: Office of Technology Assessment, 19S7.

central city and the suburbs, and the reported incidence is nearly the same in the East (35 percent), the South (36 percent), and the West (37 percent). The average incidence of genetic problems self-reported in the Midwest (4 I percent) is slightly higher than in other regions (table 51).

The frequency of self-reported genetic problems is higher among whites (39 percent) than among blacks (24 percent). The self-reported incidence of genetic disorders in the family increases from 32 percent of those without high school degrees, to 36 percent of high school graduates, to 41 percent of those who have attended college. Finally, women (41 percent) are more likely than men (32 percent) to report genetic defects in the family. Overall, however, the demographic differences are relatively small—resulting in a fairly uniform distribution of self-assessed genetic disorders in the American population.

Table 51.—Demographic Distribution of Self-Reported Genetic Problems

		Any genetic problems	
		Yes	No
Total	(1,27$"	37%	63%
Sex:			
Male	(606)	32	66
Female	(665)	41	59
Age:			
18 to 34	(546)	38	62
35 to 49.	(343)	38	62
50 to 64..	(252)	38	62
65 and over	(127)	32	66
Education:			
Less than high school	(165)	32	66
High school graduate	(456)	36	64
Some college	(300)	41	59
College graduate	(347)	41	59
income:			
$7,500 or less	(90)	35	65
7,501-15,000	(167)	40	
15,000-25,000	(240)	33	67
25,001-35,000	(286)	36	64
35,001-50,000	(227)	41	59
More than $50,000	(170)	42	56
Race:			
White	(140)	39	61
Black		24	76
Place:			
Central city	(363)	36	62
SMSA remainder	(583)	36	62
	(307)	33	67
Region:			
East	(316)	35	65
Midwest	(310)	41	59
South	(407)	36	64
West	(240)	37	63
Voters:	(935)	40	60

[a]Percentages are presented as weighted sample estimates, The unweighed sample base is presented in parentheses so that the sampling variance for these estimates can be calculated
[b]Standard Metropolitan Statistical Area.

SOURCE: Office of Technology Assessment, 1987,

MORALITY OF HUMAN GENE ALTERATION

The OTA survey indicates that Americans say they find human cell manipulation less acceptable -other things being equal—than the alteration of animal cells, plant cells, or bacteria. Does this mean, however, that the public views genetic alteration of human cells and human gene therapy as immoral?

According to the survey, a majority of the American people feels that genetic alteration of human cells is not morally wrong. Respondents were asked:

Some people believe that genetic alteration of human cells to treat disease is simply another form of medical treatment. Other people believe that changing the genetic makeup of human cells is morally wrong, regardless of the purpose. On balance, do you feel that changing the genetic make-up of human cells is morally wrong, or not?

The majority of Americans (52 percent) says that it is "not morally wrong" to change the makeup of human cells. However, a substantial minority (42 percent) feels it is "morally wrong." Another 6 percent of the public say they are "not sure" whether it is morally wrong (table 52).

Several factors appear to influence concern about the morality of human applications of genetic engineering. The belief that human genetic manipulation is morally wrong drops dramatically with education, from 49 percent of those without high school degrees, to 36 percent of those with some college, to 28 percent of college graduates. Conversely, the sense that human genetic alteration is morally wrong rises with religiousness, from 23 percent of those who are "not too religious" to 52 percent among the "very religious. " The perceived morality of human applications of

Table 52.—Morality of Human Cell Manipulation

Question (Q25):[a] Some people believe that genetic alteration of human cells to treat disease is simply another form of medical treatment. Other people believe that changing the genetic makeup of human cells is morally wrong, regardless of the purpose. On balance, do you feel that changing the genetic makeup of human cells is morally wrong, or not?

		Morally wrong	Not morally wrong	Not sure
Total.	(1,273)[b]	42°/0	520/o	6%
Education:				
Less than high school	(165)	49	43	8
High school graduate	(458)	46	48	6
Some college	(300)	36	59	5
College graduate	(347)	28	66	5
Religious:				
Very	(618)	52	40	8
Somewhat.	(437)	35	62	3
Not too/not at all	(208)	23	72	4
Heard *about genetic engineering:*				
A lot/fair amount	(514)	34	61	5
Relatively little.	(486)	43	51	7
Almost nothing	(257)	51	42	7
Effects of genetic engineering:				
Better.	(824)	36	60	4
Worse	(291)	63	31	6
Genetic problem in family:				
Yes.	(492)	40	56	4
No ,., .,., ,,. , ...	(781,)	43	50	7

[a]The code number of the question in the survey instrument (See app. B).
[b]Percentages are presented as weighted sample estimates, The unweighed sample base is presented in parentheses SO that the sampling variance for these estimates can be calculated

SOURCE" Office of Technology Assessment, 1987.

biotechnology varies directly with the amount of information about genetic engineering. Only a third (34 percent) of those who say they have heard "a fair amount" about genetic engineering think human applications are morally wrong compared to half (51 percent) of those who say they have heard "almost nothing."

The apparent widespread concern over the morality of human applications is potentially misleading. Responses to subsequent survey items discussed in the next section raise questions about the meaning and importance of this moral judgment. The question, however, does help to interpret the earlier finding about public perceptions of the benefits of genetic engineering. As noted earlier, public opinion about the effects of genetic engineering on the quality of life do not vary with the perceived risks. There is a clear relationship, however, between the perceived morality of human genetic alteration and the expected effects of genetic engineering on the quality of life. Sixty percent of those who think human applications are not morally wrong believe that genetic engineering will make life better. Sixty-three percent of those who think human applications are morally wrong believe that genetic engineering will make life worse. This suggests that either the public calculates morality on the basis of expected personal benefit or the perceived effects of technological innovation on the quality of life are strongly affected by the perceived rightness or wrongness of the action. The survey cannot discriminate between these two explanations.

SPECIFIC APPLICATIONS OF HUMAN GENE THERAPY

As noted in chapter 7, the objective of a biotechnology application is probably more important for public acceptance than the technique itself. Consequently, the survey respondents were asked to rate their approval of scientists changing the makeup of human cells for each of six purposes. The purposes ranged from curing fatal genetic diseases to eugenic goals. As in the previous chapter, the survey demonstrates that the acceptance of human genetic manipulation varies dramatically according to the objective. The findings also bring into question the meaning of the earlier survey result that 42 percent of the public believe human gene manipulation is morally wrong.

A large majority of the American public (84 percent) says it approves ("strongly" or "somewhat") changing the makeup of human cells to stop children from inheriting a usually fatal genetic disease. Similarly, 83 percent of the public say they approve the use of human cell manipulation to cure usually fatal genetic diseases. Over three-fourths of Americans state they approve of human genetic alteration to stop children from inheriting nonfatal birth defects (77 percent) or to reduce the risk of developing a fatal disease later in life (77 percent) (table 53). Each of these applications of human gene therapy receives approval both by majorities of those who consider human cell manipulation morally wrong, and by majorities who think it is not morally wrong. This suggests that the question of the morality of technological applications (discussed in the previous section) cannot be validly answered out of context, **A majority of Americans who think human gene manipulation is morally wrong in the abstract approve it when it is used to save lives and heal sick children. The majority of the public appears to be more concerned with the morality of the intent—the value of the application—rather than the inherent morality of the method.**

Only a minority of the public says it approves the use of human genetic manipulation for eugenic rather than therapeutic purposes. Nonetheless, support for nontherapeutic uses of genetic manipulation is high. Forty-four percent of the public report they approve ("strongly" or "somewhat") the use of genetic engineering to improve the intelligence level that children would inherit. An identical proportion (44 percent) says it approves of genetic manipulation to improve the physical characteristics that children would inherit (table 53).

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Table 53.—Opinions About Specific Applications of Human Ceii Manopuiation[a]

Question (Q26):[b] How do you feel about scientists changing the makeup of human cells to (READ ITEM) —would you strongly approve, somewhat approve, somewhat disapprove, or strongly disapprove?

	Strongiy approve	Somewhat approve	Somewhat disapprove	Strongly disapprove	Not sure
Stop children from inheriting a usually fatal genetic disease	51%	33%	80/0	7%	1%
Cure a usually fatal genetic disease	48	35	7	7	
Stop children from inheriting a nonfatal birth defect..	41	36	12	9	2
Reduce the risk of developing a fatal disease later in life	.39	38	12	9	2
Improve the intelligence level that children would inherit.	.18	26	22	31	2
Improve the physical characteristics that children would inherit	.16	28	23	31	3

[a]Percentages are presented as weighted sample estimates. The unweighted base from which the sampling variance can be calculated is 1,273,
[b]The code number of the question in the survey instrument (see app. B).

SOURCE: Office of Technology Assessment, 1987

Fifty-three percent of the public say they disapprove ("strongly" or "somewhat") of using gene therapy to improve the intelligence level that children would inherit. A majority (54 percent) also registers disapproval of genetic manipulation to improve the physical characteristics that children would inherit. In contrast, only 15 percent of Americans state they disapprove of gene therapy to stop children from inheriting a usually fatal genetic disease. And 14 percent say they disapprove applications of gene therapy that would cure a usually fatal disease (table **53).**

Thus, when faced with concrete uses of human genetic manipulation, the public approves of all the therapeutic uses presented. Human gene therapy gets a vote of confidence even from those who consider human genetic applications, in the abstract, morally wrong. Concerns exist, however, among a majority of the public about the morality and utility of eugenic uses of human genetic manipulation.

GERM LINE APPLICATIONS

At present, proposed uses of human gene therapy are restricted to somatic applications—i.e., clinical trials will only be approved to alter cells that do not affect inherited characteristics. The accepted uses of human gene therapy are restricted to correcting genetic instructions that cause genetic diseases in the individual, but not in a way that will affect diseases passed on to offspring. Such germ line applications are considered off limits in current proposals for human gene therapy.

The public was asked what it thought about the acceptability of somatic v. germ line applications of human genetic engineering. Since it was unlikely that much of the public would recognize the terms "somatic" and "germ line," the question

was put to survey respondents in the following way:

Suppose someone had a genetic defect that would cause usually fatal diseases in them and would likely be inherited by their children. Do you think that doctors should be allowed to correct only the gene affecting the disease in the patient, only the gene that would carry the disease to future generations, both genes, or neither gene?

The OTA survey results show that the public does not seem concerned with the somatic v. germ line distinction in human gene therapy—at least as answered by this question. Under the conditions described to them, 62 percent of the American public think doctors should be allowed to correct both the gene affecting the disease in the

Table 54.—Using Germ Line v. Somatic Cells in Human Gene Therapy

Question (Q27):[a] **Suppose someone had a genetic defect that would cause usually fatal diseases in them and would likely be inherited by their children. Do you think that doctors should be allowed to correct only the gene affecting the disease in the patient, only the gene that would carry the disease to future generations, both genes, or neither gene?**

	Both	Only affecting patient	Offspring	Neither	Not sure
Total ....(1,273)[b]	62%	8%	14%	11%	5%
Education:					
Less than high school .... (165)		11	15	11	5
High school graduate .... (458)	60		17	12	4
Some college .... (300)	69	6	11	9	5
College graduate .... (347)	65	, 9	10	10	5
Religious:					
Very . . . ., ...4...... (618)		10	14	14	6
Somewhat . . . .(437)	68	5	15	10	2
Not too/not at all ....(208)	68	8	12	5	7
Heard about genetic engineering:					
A lot/fair amount . . . .(5 1 4)	6 5	8	13	10	3
Relatively little .... (488)		7	17	10	
Almost nothing .... (206)	59	10	11	14	6

[a]The code number of the question in the survey instrument (see app. B).
[b]Percentages are presented as weighted sample estimates. The unweighed sample base is presented in parentheses so that the Sampling variance for these estimates can be calculated.

SOURCE: Office of Technology Assessment, 1987.

patient and the gene carrying the disease to future generations. Only 8 percent of the public believe doctors should be restricted to somatic applications. In fact, more people feel doctors should be restricted to gene therapy only for germ line applications (14 percent) than somatic applications (8 percent) (table 54). This could be another e$_x$-ample of the end objective being more important to the American public than the means, if respond-ents thought that germ line applications primarily could help future children.

Finally, 11 percent of the adult population of the United States feel that doctors should not be allowed to correct either gene. This is the segment of the population truly opposed to human gene therapy.

GENETIC TESTING

The use of genetic testing for some circumstances is not new, and nine of ten Americans say they approve making genetic testing available through doctors. Survey respondents were asked:

If there were genetic tests that would tell a person whether they or their children would be likely to have serious or fatal genetic diseases, would you approve or disapprove of making those tests available through a physician?

Making genetic testing available is overwhelmingly supported by the public. Eighty-nine percent of the American populace say they approve of mak-ing such tests available, compared to 9 percent who disapprove (table 55).

Additionally, greater than 8 of 10 Americans (83 percent) report they would take a test before having children, if such a test would tell them whether their children would probably inherit a fatal genetic disease (table 56). Religiousness has little effect on willingness to take a genetic test—81 percent of those describing themselves as very religious say they would take such tests.

Americans are less likely to take tests to determine their own proclivity to genetic diseases.

Table 55.—Availability of Genetic Tests From Physicians[a]

Question (Q28a):[b] If there were genetic tests that would tell a person whether they or their children would be likely to have serious or fatal genetic diseases, would you approve or disapprove of making those tests available through a physician?

	Percent
Approve	89
Disapprove	9
Not sure	2

[a]Percentages are presented as weighted sample estimates. The unweighted base from which the sampling variance can recalculated is 1,273.
[b]The code number of the question in the survey instrument (see app. B)

SOURCE Office of Technology Assessment, 1987.

Nevertheless, two-thirds of the public say they would take a test to determine if they are likely to develop a fatal disease later in life, if such a test becomes widely available. Religiousness does appear to have a minor influence on the likelihood of taking such a test. Sixty-three percent of the "very religious" say they would take such a test if it were available. Seventy-two percent of the "not too" or "not at all" religious report they would use a test (table 56).

Fetal testing might represent the most sensitive type of genetic testing. Nearly 7 of 10 Americans (69 percent), however, say that if genetic diseases could be detected in the early stages of pregnancy they would want such a test. This acceptance of fetal genetic testing is found across all levels of educational attainment, and a majority of the very religious (63 percent) say they would want such a test (table 57).

Table 56.—Comparison of Religiousness and Using Genetic Tests[a]

Question (Q28b):[b] If genetic tests become available that would indicate whether or not a person was likely to develop a fatal disease later in life, would you personally take such a test or not?

Question (Q29):[b] If genetic tests become available that would indicate whether or not it was likely that your children would inherit a fatal genetic disease, would you personally take such a test before having children or not?

		Religious		
	Total	Very	Somewhat	Not tool Not at all
Likelihood of developing fatal disease later in life:				
Would take test.	6 6 %	63%	70%	720/o
Would not take test	29	32	27	24
Not sure	4	5	2	4
Likelihood of children inheriting fatal genetic disease:				
Would take test.	83	81	86	84
Would not take test	15	16	12	12
Not sure	3	3	2	3

[a]Percentages are presented as weighted sample estimates. The unweighed base from which the sampling variance can be calculated is 1,273.
[b]The code number of the question in the survey instrument (see app. B).

SOURCE" Office of Technology Assessment, 1987

GENETIC THERAPY

Most Americans say they are prepared to undergo genetic therapy if genetic testing reveals a high risk for a serious genetic disease. Specifically, survey respondents were asked:

If tests showed that you were likely to get a seri- ous or fatal genetic disease later in life, how willing would you be to undergo therapy to have those genes corrected?

Nearly 8 of 10 Americans (78 percent) say they would be "very willing" or "somewhat willing" to undergo genetic therapy to correct a genetic proclivity to a serious or fatal disease (table 58).

Table 57.—Fetal Testing for Genetic Disease

Question (Q32):[a] Some genetic diseases can be detected in the fetus during the early stages of pregnancy. Would you want such a test during (your/your spouse's) pregnancy or not?

		Want a test	Don't want a test	Not sure
Total	(1,273)[b]	69%	27%	4%
Education:				
Less than high school	(165)	70	23	6
High school graduate	(458)	68	28	4
Some college	(300)	66	30	4
College graduate	(347)	71	24	4
Religious:				
Very	(618)	63	31	6
Somewhat	(437)	75	22	3
Not too/not at all	(208)	73	23	3
Heard about genetic engineering:				
A lot/fair amount	(514)	74	22	4
Relatively little	(486)	67	27	4
Almost nothing	(257)	63	32	5
Human cell alteration:				
Morally wrong	(484)	58	36	5
Not wrong	(715)	78	20	3

[a]The code number of the question in the survey instrument (see app. B).
[b]Percentages are presented as weighted sample estimates. The unweighted sample base is presented in parentheses so that the sampling variance for these estimates can be calculated.

SOURCE: Office of Technology Assessment, 1987.

Table 58.—Willingness To Undergo Genetic Therapy To Avoid Fatal Disease

Question (Q30):[a] If tests showed that you were likely to get a serious or fatal genetic disease later in life, how willing would you be to undergo therapy to have those genes corrected-very willing, somewhat willing, somewhat unwilling, very unwilling?

		Very willing	Somewhat willing	Somewhat unwilling	very unwilling	Not sure
total	(1,273)	35%	43%	12%	9%	2%
Education:						
Less than high school	(185)	42	38	10	9	
High school graduate	(458)	33	44	13	8	2
Some college	(300)		41	11	10	2
College graduate	(347)	31	47	11	9	1
Religious:						
very	(618)	34	40	12	12	2
Somewhat	(437)	35	47	11	5	
Not too/not at all	(208)	39	4 2	13	5	2
Heard about Genetic engieering:						
A lot/fair amount	(514)	40	41	9	9	
Relatively little	(488)	32	45	13	8	3
Almost nothing	(257)	32	43	14	10	2
Human cell alteration:						
Morally wrong	(484)	28	40	17	14	
Not wrong	(715)	41	45	7	4	2

[a]The code number of the question in the survey instrument (see app. B).
[b]Percentages are presented as weighted sample estimates. The unweighed sample base is presented in parentheses so that the sampling variance for these estimates can be calculated.

SOURCE: Office of Technology Assessment, 1987.

An even larger majority (86 percent) says if it had a child with a usually fatal genetic disease, it would be willing ("very" or "somewhat") to have that child undergo genetic therapy if needed; indeed, a majority says it is '(very willing" (51 percent). Religiousness has no effect on this opinion. If they had a child with a fatal genetic disease, the "very religious" (51 percent) say they are just as likely to be very willing to have the child undergo genetic therapy as the "somewhat religious" (51 percent) and the "not too religious" (52 percent) (table 59).

The bottom line on public perceptions of human gene therapy is that almost all Americans--regardless of age, race, education, religiousness, or even moral reservations about genetic engineering—say they approve and would be willing to use these therapies to save lives.

Table 59.—Willingness To Have Child Undergo Genetic Therapy To Correct Fatal Disease

Question (Q31):[a] **If you had a child with a usually fatal genetic disease, how willing would you be to have the child undergo therapy to have those genes corrected-very willing, somewhat willing, somewhat unwilling, very unwilling?**

		Very willing	Somewhat willing	Somewhat unwilling	Very unwilling	Not sure
Total.	(1,273)[b]	51%	35%	7%	4%	3%
Education:						
Less than high school	(165)	59	30	4	5	2
High school graduate	(456)	50		9		3
Some college	(300)	47	36		2	2
College graduate	(347)	46	36	9	6	4
Religious:						
Very	(618)	51	32	7	6	4
Somewhat	(437)		36	7	3	
Not too/not at all	(206)	52	37	7	2	2
Heard about genetic engineering:						
A lot/fair amount	(514)	52	34	6	5	2
Relatively little	(486)	50	35	8	3	4
Almost nothing	(257)	51	37	5	5	2
Human cell alteration:						
Morally wrong	(484)	44	35	10	8	3
Not wrong.	(715)	57	33	5	2	3

[a] The code number of the question in the survey instrument (see app. B).
[b] Percentages are presented as weighted sample estimates. The unweighted sample base is presented in parentheses so that the sampling variance for these estimates can be calculated.

SOURCE: Office of Technology Assessment, 1987.