Changing hopes and concerns about gene therapy in Japan

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Abstract

The attitudes that the public in Japan have to gene therapy were surveyed through the use of opinion surveys in 1991, 1993, 1995, 2000 and 2003. This paper presents the results of these surveys on different groups, and in particular examines the open comments that people made in response to being asked whether they would personally use gene therapy if they were suffering from a fatal disease. The optimism towards gene therapy among the public in Japan is similar in 2003 as it was in 1991, with over half agreeing to use gene therapy upon themselves if tests showed that they were likely to get a serious or fatal genetic disease later in life. The level of enthusiasm was also similar in national random surveys of natural scientists in 1991 and in 2000. The major reasons for this support were to save their own life, and a variety of other reasons are described. There is also a presentation of the titles and content analysis of articles on gene therapy published in *Asahi Shimbun* newspaper over the same period. The attitudes, policy and regulation are discussed.

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INTRODUCTION

One medical application of genetic engineering that has had extensive policy debates leading to elaborate regulatory schemes in a number of countries is gene therapy. There has been significant public and private investment into this technology, despite few positive clinical results. Gene therapy has also been widely discussed for several decades in a number of countries in public debates, even before the attempts at

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experimental therapy in clinical trials since 1990. Gene therapy is an interesting example of an application of science and technology because the ethical and social issues were discussed for many years before the first clinical trial in 1990.

The Japanese Society for Gene Therapy was established in 1995 and there have been regular annual meetings since where academics and researchers from government and company laboratories come together to discuss results. Also, in 1995, the government and seven pharmaceutical companies in Japan decided to work together to create gene vectors and other tools that could be used in gene therapy. This society was established following the establishment of regulatory systems that involve multiple committees and review, a system that was initially modelled upon the oversight mechanisms in the USA, and developed into the Japanese bureaucratic system, involving the Ministries of Education, Science, Culture and Sport (MEXT) and Ministry of Health and Welfare (MHW). A recent review of the attitudes of university and hospital ethics committees towards the system of ethical review found them significantly more positive towards the revised guidelines of 2002 compared to the initial 1994 guidelines.[1] This was partly due to increased information sharing and public involvement, which are concerns that had been detected among the public concerns in the data presented here. There was also support for a simpler line of control where the ultimate decision was required only from MHW, in addition to a clearer requirement for written informed consent and more diverse institutional review boards to consider the applications.

The fact that it is still not an effective cure for many diseases, although it has shown some promise, also makes it interesting as a model to examine public attitudes. We can ask questions about how long public expectations and hopes of a technology can be sustained over time when the media has generated such high public expectations of gene therapy as a 'miracle cure'. The attitudes that the public in Japan have to this therapy were surveyed through the use of opinion surveys in 1991, 1993, 1995, 2000 and 2003. This paper presents the results of these surveys and examines the open comments that people made in response to being asked whether they would personally use gene therapy if they were suffering from a fatal disease. The reasons behind people's attitudes have also been explored over time and allow us to see whether there is any shift in the way people view this technology compared to studies reported from surveys conducted in 1991[2] and 1993.[3] There is also a presentation of the results of a media analysis during the same period (1990–2003) of the surveys.

SAMPLE SELECTION AND SURVEYS

This paper presents data on the reasoning regarding gene therapy from different surveys and population groups. Comparisons to earlier surveys allow long-term comparisons as the key questions for examination had the same wording (in Japanese). The general public for the purpose of this paper is defined as those people who comprise the general society from a variety of occupations and social circumstances. In the 1991 (P1991),[2] 1993 (P1993)[3] and 2000 (P2000)[4] mail response surveys, anonymous letters were dropped into mail boxes without any contact with the householders to ensure they had few fears of invasion of privacy. The survey forms were lengthy, requiring a considerable amount of time as they included both fixed response and open questions. In the 2003 survey (P2003), the distributors personally asked randomly selected householders across Japan to complete the questionnaire leaving it with householders to complete and return.[5] The response rate in 2003 is thus higher than the 2000 survey at around 20 per cent and like the 1997 survey, responses were obtained from all of Japans 47 prefectures (sub-national jurisdictions; Table 1). In addition, a small sample obtained by national random telephone calling in 1995 is included, illustrating that the concerns that people may raise can be assessed in oral responses. For all public samples, sampling was done across all prefectures of Japan using random sampling methods with the cooperation of other persons. There is a mix of different sectors of the Japanese public (level

Table 1: Brief sample characteristics of surveys in Japan

%	P1991	P1993	P1995	P2000	P2003	S1991	S2000	Forum99	R1995	St91	St93
N	551	352	76	297	379	555	370	74	171	198	435
% female	47	48	50	38	48	10	11	23	28	47	33
Average age (yrs)	39.8	41.7	44	44.5	46.9	47.1	50	44.6	55.1	22	21.1
% married	66	66	71	71	71	86	93	72	77	2	1
% with children	65	60	68	35	70	82	85	65	68	0	0

Note: Abbreviations and references for surveys used in this paper are in the text.

Table 2: Optimism towards gene therapy (a) Q. 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 before symptoms appear? Why? (b) Q. 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? Why?

%	P1991	P1993	P1995*	P2000	P2003	S1991	S2000	Forum99	R1995	St91	St93
(a)											
Strongly agree	25.0	42.0	—	23.6	25.3	25.4	27.5	40.8	28.1	19.7	44.4
Agree	29.0	24.0	51	24.3	32.1	28.1	25.6	32.4	28.1	31.8	29.5
Disagree	18.0	15.0	16	22	20.3	15.6	14.2	5.6	11.1	26.8	11.2
Strongly disagree	12.0	6.0	—	15.8	5.8	13.6	24.4	15.5	20.5	9.6	4.5
Don't know	16.0	13.0	33	14.3	16.5	17.3	8.3	5.6	12.3	12.1	10.5
%	P1991	P1993	P1995*	S1991	R1995	St91	St93				
(b)											
Strongly agree	36.9	53	—	32.1	36	28.4	51				
Agree	29.3	21	55	30.1	29	37.6	25				
Disagree	11.2	10	8	9.7	9	11.3	7				
Strongly disagree	7.0	1	—	7.6	10	5.2	2				
Don't know	15.6	15	37	20.5	16	17.5	15				

*The 1995 telephone survey of the public had only three replies, Yes, No or Don't know.

of education, occupation (not shown) and rural and urban populations). Over 90 per cent of respondents had no direct involvement with research. We estimate sample error at ±5 per cent and the limitations of not being able to reach the non-responders to surveys in the society are acknowledged.

For comparison, the surveys conducted in 1991 (S1991)[2] and 2000 (S2000)[4] among natural scientists are also included, both of these also being national random mail response surveys. There are also results of surveys in biology students in 1991 (St91);[2] a sample that was comprised of medical students from each of six years of medical studies in University of Tsukuba conducted in 1993 (St93)[6]; a survey of all members (academics) of the Japan Association of Bioethics in 1995 (R1995)[7] and participants at a Novartis Life Science Forum conducted in 1999 (Forum99).[4] Several key sample characteristics compared are given in Table 1 to allow comparisons between the surveys.

The results of the key questions on gene therapy are given along with the question phrases in Tables 2 and 3 and examples of the comments for each category are also given below. The reasons that the respondents gave for their attitudes in the open spaces on the surveys for the open questions were categorised on the basis of the keywords and concepts that were expressed into a total of 20 categories following the methods of Macer.[2,3] Each comment was categorised into up to two concept categories to describe the ideas in the answer. A summary of the reasoning across the different samples is given in Table 4, and to standardise all the comments were categorised and checked by the authors of this paper.

ATTITUDES TOWARDS GENE THERAPY

There was generally high support for use of human gene therapy as shown in the results to the question 'If tests showed that

Table 3: Acceptance of gene therapy in specific cases

	P1993 (%)	P2000 (%)	P2003 (%)	S2000 (%)
Q. How do you feel about scientists changing the genetic makeup of human cells to:				
(*a*) *Cure a usually fatal disease, such as cancer*				
Definitely agree	42.0	38.3	39.2	40.1
Agree	41.0	34.8	43.4	40.6
Disagree	3.0	12.9	5.0	10.1
Definitely disagree	2.0	4.3	2.2	5.6
Don't know	12.0	9.8	10.2	3.6
(*b*) *Reduce the risk of developing a fatal disease later in life*				
Definitely agree	35.0	28.1	40.4	30.5
Agree	40.0	35.2	40.4	40.9
Disagree	5.0	17.2	4.1	15.4
Definitely disagree	1.0	5.5	2.2	5
Don't know	9.0	14.1	12.8	8.1
(*c*) *Prevent children from inheriting a usually fatal disease*				
Definitely agree	37.0	29.8	—	27.7
Agree	43.0	36.2	—	32.5
Disagree	3.0	16.3	—	19.8
Definitely disagree	1.0	5.7	—	8.5
Don't know	16.0	12.1	—	11.6
(*d*) *Prevent children from inheriting a non-fatal disease, such as diabetes*				
Definitely agree	25.0	20.3	—	17.7
Agree	37.0	31.7	—	27.4
Disagree	15.0	23.8	—	30.6
Definitely disagree	2.0	7.1	—	11.4
Don't know	21.0	17.1	—	12.9
(e) *Improve the physical characteristics that children would inherit*				
Definitely agree	12.0	11.7	11.3	3.4
Agree	16.0	12.9	17.4	6.4
Disagree	35.0	43.4	34.8	47.1
Definitely disagree	16.0	18.8	14.4	31.7
Don't know	21.0	13.3	22.1	11.5
(*f*) *Improve the intelligence level that children would inherit*				
Definitely agree	13.0	10.5	10.3	3.4
Agree	13.0	10.2	16.8	5.3
Disagree	35.0	46.1	34.1	45
Definitely disagree	49.0	20.7	15.6	33.8
Don't know	20.0	12.5	23.2	12.6
(*g*) *Make people more ethical*				
Definitely agree	14.0	11.4	10.6	3.4
Agree	10.0	8.3	13.6	3.7
Disagree	32.0	33.9	32.8	38.5
Definitely disagree	21.0	28.7	17.5	39.4
Don't know	23.0	17.7	25.6	15

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 before symptoms appear? Why' (Table 2). The results in 2000 and 2003 were more similar to 1991 than to the 1993 sample, suggesting a decrease in public acceptance since the peak in 1993. In 2003 when asked whether they knew someone with a genetic disease, 72 per cent said that they did know someone (Q19), very similar to 68 per cent who said so in 1993.[5]

A comparison of the researchers in the R95 sample with the other groups shows that they are less willing to support gene therapy than the public in 1993. The results from a small telephone survey ($N=74$) conducted in 1995 by Macer (P1995) also find less people agreeing and more people say that they do not know. The P1995 survey was conducted from the end of 1994 to early 1995, when

there was discussion in the media of the eminent approval of the Hokkaido University gene therapy trial; however, that trial did not commence until August 1995. Therefore the differences were not due to the results of the trial but could be due to the intense discussion of the trial and release of regulations, which may have made people believe that there was something dangerous about gene therapy. There was generally no statistically significant difference with demographic characteristics; however, in the R1995 sample there was a significant difference in the acceptance of gene therapy with religiosity. There were more serious religious believers among members of Japan Association of Bioethics (R1995) than other samples in Japan. By using the scale 1 = very willing, 2 = somewhat willing, 3 = somewhat unwilling and 4 = very unwilling, the average values for the respondents who answered that religion was very important, somewhat important, not too important or not at all important, for personal use was 2.72, 2.12, 2.11 and 2.00, and for child's use, 2.29, 1.90, 1.89 and 1.24, respectively. The difference between those who said religion was not at all important and very important was significantly different ($p < 0.01$).

In the 2000 survey, there is little difference between the public (P2000) and scientists (S2000) in attitudes to gene therapy (Table 2), as also seen in another question presenting a range of cases for gene therapy (Table 3). Scientists in 2000 were twice as likely to say 'very unwilling' compared to 1991. The most remarkable feature of the survey results is that the approval is not dependent upon the educational level of the sample; however, the similar rise in approval in 1993 is seen in all samples conducted in that year. This would be consistent with there being a widespread euphoria over gene therapy at that time.

REASONING BEHIND THE ATTITUDES TOWARDS GENE THERAPY

In order to examine the concerns that people had, the reasons given for each of the responses to the general question (Table 2) were analysed. We examine comments resulting from this analysis and see whether the concerns have changed over time. In 1991, respondents were not asked to give a reason for their answer. Also we should note that the proportion of respondents who did not state their reason was highest in 2003 (45 per cent) with 31 per cent in 1993 and 2000 not giving a reason. The data in Table 4 are presented not as a proportion of those giving reasons but rather as a proportion of those who answered the attitudinal question. If the numbers were given as a proportion of those who gave comments, they would be significantly more than the proportions indicated here. The overall results find that the most common reason given to support gene therapy was saving life, and the most common response for disapproving were that it is unnatural or that it presented risks to health (Table 4). There were similar reasons given in response to the question regarding use of gene therapy on children.

In the 1995 telephone survey respondents were also asked to give reasons: 'Considering the gene therapy that is done now, how do you think about gene therapy in the future in Japan?', and the responses were: 13 per cent Not stated, 3 per cent Don't know; Benefits: 0.4 per cent for family benefit, 12 per cent save life, 1 per cent healthcare is right, 1 per cent improve quality of life, 4 per cent right to choose such medicine and 8 per cent another benefit; Concerns: 4 per cent need ethics committees, 6 per cent need to be open to public, 11 per cent said it depends on situation, 4 per cent ethics, 2 per cent play God/unnatural, 2 per cent economy, 2 per cent misuse, 0.4 per cent eugenics and 15 per cent had health concerns, while 10 per cent mentioned another harm.

REASONS SUPPORTING GENE THERAPY

A breakdown of the reasons people gave to support gene therapy is presented below. The proportion of conditional answers, under 'Depends on the Situation' represents some moderated judgment in the acceptance of technology, and remained at about one-eighth of the respondents.

Table 4: Reasons for personal acceptance of gene therapy

	P1993	P2000	P2003	S2000	Forum99	R1995	St93
N	335	285	387	364	71	171	421
	%	%	%	%	%	%	%
Save life	26.0	20.4	29.0	21.7	31	30.4	38.8
Right to chose	2.1	1.4	0.8	1.9	2.8	1.2	0
Save family	3.3	2.5	5.6	1.4	0	1.8	0.2
Personal	4.2	0.7	0.3	0.3	1.4	1.2	0
Technology benefits	—	0.7	0.8	1.4	2.8	—	—
Social reasons	3.6	1.1	0.3	1.1	4.2	0.6	1.2
Improves genes	5.4	2.1	2.2	0.3	0	3.5	1.9
Improve QOL	6.0	4.9	2.7	2.7	0	4.1	3.4
Other benefit	1.5	0.4	1.3	0.5	0	1.2	2.4
Depends	9.0	18.6	11.7	17.6	5.6	21.1	10.7
Economy	2.4	1.4	1.1	2.5	1.4	1.2	0.5
Ethics	0.3	0.7	0.5	1.1	0	1.2	1.0
Playing god	5.1	17.5	7.2	23.1	9.9	12.3	5.3
Misuse	0.9	0	0.5	0.3	0	0	1.5
Eugenics	0.9	2.1	0.5	2.1	0	0	0.2
Health bad/risk	5.7	9.5	7.7	11.5	0	12.3	10.2
Other harm	3.6	3.5	3.2	5.5	1.4	3.5	2.4
Not stated	31.5	30.5	45.1	24.2	36.6	24	28.5
Don't know	0	1.4	0.3	0.3	2.8	1.2	3.4

Saving life

Inside this broad category are a number of types of comments that were subdivided into the following types of comment:

(i) *To live long a long time*

Many people stated 'I want to live long'. Most people wrote only that, some people wrote that they have something to do in future. In addition to these reasons, there were some opinions that it is natural as a human to want to live long. For example:

> I want to carry out my purpose by living long.
> Health becomes important. Everyone in their 40s or 50s hopes to live long.
> It is human egoism, but I want to have it if it is established as a perfect technology. (+Safety)
> I want to love my life to live a happy future.

(ii) *To prevent falling ill*

This reason seems to be connected with the reason to want to live long and to improve Quality of Life (QOL). For example:

> It's the same as taking an antibiotic when one catches a cold.
> I cannot decide whether to change my fate for my own convenience. But I think it seems that I will have the cure. I'm afraid of this thinking.
> I want life if I know it's curable.

(iii) *Live out allotted span of life*

This reason suggests that there is 'an appropriate life span'. Perhaps they think it is right to die of old age. This is an interesting thought, and related to a type of Taoist thinking that has also been found in interview research on senior persons attitudes towards life.[8] Some respondents who were negative to gene therapy also wrote this reason. There is a difference in the interpretation of the word 'allotted span of life' between those who gave positive reasons and those who were negative. Maybe negative respondents who used the word as the reason understand it as something like fate, whereas in a positive comment it reflects a similar idea to wanting to live as long as is 'natural'. For example:

> I want to live out my allotted span of life given by God.
> I hope it if I can live out my allotted span of life by it. But I don't want to go so far as to have immortality.

Improve QOL

(i) *To avoid pain*

There was reference to the idea of avoiding painful diseases such as cancer. For example:

> If the disease is cured, one will be liberated from unnecessary pain.
> I will accept the disease and wait for death at a hospice, but I will have every treatment for

the purpose of avoiding inheritance to my children because I feel painful when I think that my children will suffer from pain. There will be thought that I don't know how apologize to my children.

(ii) *To be healthy*
These reasons regarded how should they live highly more than the length of the life. For example:

I want to think by my brain, speak, write, and live by my will. If in the situation one can't do that, it's a living dead. The situation that there is no value to live is painful for me. And, I want to live long in a good condition if I could.
The therapy is a prevention just like vitamin C before catching a cold.

(iii) *To avoid troubling my family or to save my family*
Respondents who wrote about troubling their family seemed to worry about the burden to their family more than the matter of themselves. 'I don't mind the matters of myself, but I don't want to trouble my family to take care of me. So I want to have the treatment', they said. For example:

I'm anxious about my bereaved children if I become sick now. I want to have it for my family.
To avoid troubling society.
I will accept my own destiny although I let my child undergo the therapy.

Improves genes
For example:

If 'serious' and 'fatal' is real, I want to make the next generation healthy by stopping the inheritance.
It's a problem of myself and my posterity, so I want to discover the possibility to solve it. Because it's becoming clear how genes works.
Basically I want to complete my life with having it, but I don't want to leave the gene type which should normally die earlier to coming generations.
The offspring is pitiful if a bad gene remains. I want to try the therapy because a bad gene can be removed.
I want to undergo the therapy in order to give my child a good gene.

Technological benefits
There were several respondents who said that they would participate in trials as a benefit to research and technology, for example:

I don't stick to prolonging my personal life, but it is needed to increase the case of experiment.

CONCERNS EXPRESSED ABOUT GENE THERAPY
Respondents seem to have many unclear matters about gene therapy. They have doubts about the effectiveness, and bad influences especially about influences to their posterity. The major reasons were as described below.

Playing God or interfering with nature
This was not only seen among the public, but also among scientists. Comments from two scientists in 2000 included this type of argumentation:

I want to leave it to nature.
I leave it to God's will.
Creatures must die when they should die.
'Disease' is one of the phenomena of creature's selection, it goes against 'bioethics' to control this.
Because I accept hereditary things as my fate.
I will leave my 'life' to God standing on the recognition of 'natural selection'.

Other comments for example:

I don't want to live by using the means that will produce regrets after ages because God created us like that. We'll die sooner or later whether we use it or not.
I don't want to manipulate my body which is given by my parents.
I accept my fate as the divine punishment for my sins.
I'm coming not to know my thought when I read the similar questions again and again.
Immortal humans, or humans who never become ill, don't need to be human. Then I think where human came from. In my current thinking, I don't want to let the

organisms that grew up by using odd weed killer which kills only weeds but doesn't kill vegetables grow thickly in this world. It's wrong that organisms which humans eat are safe but others die through they are the same plants. I think humans themselves will be improved. And unknown diseases will be produced one after another. I'm not negative about academic research, but I'm positive for public use.

Health risks

This included not only to oneself but also to future generations. For example:

It's good if there is no problem about side effects, after effects, costs and so on.
I don't know because it's not clear what is the risk of modifying genes. I will have treatment if it is absolutely safe.
I can't be a guinea pig.
I'm afraid of the side effects and bad influences to posterity even if the disease itself has been cured.
I'm afraid of the bad influences to other parts by modifying the problem gene.
It's possible that the gene controls other functions.
(Maybe I can say like this because I'm not in such a situation) There's no assurance to be cured even if the gene was modified, and one may have more serious disease on the contrary. (+Depends on situation)

Economics

Few respondents gave comments relating to companies or commercial issues, despite the views expressed in other questions in the survey that were generally suspicious of the safety comments made by companies (and government). There were some concerns about the expense of gene therapy, for example:

I may use it if the cost is low and it's easy to use, but I don't think I want to use it spending much money.
I will have it, if I was required to think personally, not socially. But if I am really in that situation, it's strongly possible to think that it won't pay and stop it considering the cost (money, loss of time, interruption of my social duty, and so on) which the treatment requires.

Eugenics or fear of germline change

A few persons gave their concerns about misuse in eugenics, or stated that it should not be applied for reproduction. For example:

I think it's not a problem basically if it is not a reproductive cell.
I don't want to live life like that personally.
I think it's acceptable to use generally unless leaving the gene to the descendants.

Other concerns

There were a few other comments of mixed idea, for example:

It's nonsense to bother to help the dying person.
Because it is needed to die according to one's life span for the lasting of the species which one belongs to.

PRAGMATIC RESPONSES

There were a significant number of people who chose 'Neither' as an option. This was more often because of the difficulty in balancing the positive and negative aspects than because of them being less aware of the technology. These types of comments illustrate mixed reasoning, following a case-by-case approach to deciding whether to use gene therapy. These were also seen in those selecting 'agree' or 'disagree' as an option.

Situation-based responses

Many people stated 'It depends on the situation'. Their concerns were mainly focused on the 'possibility (to be cured)', the 'reliability (of the treatment)', 'side effects' and 'costs'. Respondents who are positive still have some doubts or chose 'Don't know'. For example:

I don't know because I'm normal.
I want to get well by applying the most advanced therapy. But I'm not going to do so if there is pain.
Because it's not my aim of life to live long. (Those who want to live long should take it.)

> It's acceptable if the modification is on a single gene or simple (AD Deficiency, for example).
> It's O.K. unless I don't hand over to my descendant. It's acceptable if the cure for my body doesn't invade others' rights. But I will investigate about costs. I will consider whether my life is worth such or not.
> My answer is 'disagree', but good informed consent will change my mind.

Personal

Several people had specific individual reasons behind their responses, such as their family history of genetic disease. For example:

> Because many people in my family have genetic disease.
> I want to undergo the therapy because I have to bring up my children. But, if I do not have such responsibility, I will not do so because the therapy is in the experimental status.

MEDIA COVERAGE OF GENE THERAPY IN JAPAN

The results above present a picture of the way that different groups in Japanese society consider the use of gene therapy. Given that only a handful of people in Japan have been involved in clinical trials of gene therapy, the major source of information is through the media, which includes newspapers, television and specialised journals such as science magazines. The surveys showed that newspapers were the most common source of information.[5] In order to examine whether there were any trends in the positive or negative reporting over time, a search was made between 1990 and 2003 for every article about gene therapy in the *Asahi Shimbun* newspaper (the largest selling mainstream newspaper in Japan). The results of this analysis are presented in Table 5, and a translation of all the article headings and subheadings is in Appendix 1.

The peak of media coverage in the newspaper was in 1995 with 15 articles. Articles covered many of the key events in gene therapy in Japan and internationally. The allocation of articles into more positive or negative was based on the words such as risk or benefit that were presented in the article, and reflects the overall tone of the article. Overall, the newspaper has published more positive than negative articles about gene therapy.

CONCLUSIONS

Optimism towards gene therapy among the public in Japan was as similar in 2003 as it was in 1991, with 54 per cent (P1991) to 57 per cent (P2003) agreeing to undergo gene therapy themselves if tests showed that they were likely to get a serious or fatal genetic disease later in life. There was also strong support for use of gene therapy to treat children. There was a period of public euphoria over gene therapy, which was associated with the commencement over the

Table 5: Frequency of articles about gene therapy in the *Asahi Shimbun* newspaper (1990–June 2003)

Year	Total	Positive	Supportive	Concerns	Negative
1990	4	2		2	
1991	4	1			3
1992	1	1			
1993	6	4		2	
1994	6	3	1	1	1
1995	15	11		4	
1996	6	3		3	
1997	5	3		1	1
1998	6	4	1		1
1999	8	1	6		1
2000	9		5		4
2001	11	6	3	1	1
2002	8	3	3		2
2003 Q1–2	0				

The articles were graded on a four-point scale based upon their content from very positive, supportive, some concerns, to very negative.

first trials in Japan and was observed in the 1993 public opinion survey when 66 per cent said they would use gene therapy in that case (Table 2). The level of enthusiasm was similar in national random surveys of natural scientists in 1991 (54 per cent) and in 2000 (53 per cent). The major reasons for this support were the chance to save their own life or that of a family member and to limit the burden they would place on their families should they get seriously ill in the future (Table 3). This suggests the promotion of gene therapy can continue to build upon the common desire to cure disease.

While there is a greater optimism seen among those with some technical training in the field of medicine (medical students) or biotechnology (Forum99) (Table 2), there is still a residual group of 15–25 per cent of people who say that they would not use gene therapy themselves. Interestingly however, when asked in a different question about the modification of human cells by gene therapy to treat fatal cancer, only 12 per cent say that they disagree. The major reasons for disagreement are potential health risks followed by concerns that it is unnatural to change one's fate by using genetic therapies (Table 4). There were a significant proportion of scientists who also gave reasons that gene therapy was interfering with nature, suggesting that higher education did not lessen the concerns about the use of technology to modify genes.

The reasons for a decline in public opinion since 1993 cannot be found in the comments of the survey respondents but could be attributed to a variety of events including the establishment of regulations to govern gene therapy, media reporting or a loss of trust in science and technology. The drop in support for gene therapy seen in 1995 was, however, not seen for science and technology in general, despite widely reported events including the Aum Shinrikyo cult Tokyo subway Sarin gas terrorist attack in 1995, the ongoing AIDS crisis and the BSE crisis in the UK in 1997. It could be simply that the euphoria in 1993 over gene therapy led to widespread approval for gene therapy, suggesting a significant power of the media in both the public and scientists in Japan. The general attitudes to science and technology in these surveys remained similar over the period 1991–2003, but the reason for the optimism in 1993 cannot be directly attributed to a difference in the newspaper coverage of gene therapy between the early 1990s and subsequent years. There were a number of articles discussing the regulations that Japan established, especially in 1995.[9] Over this period, the public also had television as a source of information about gene therapy, and the completion of the Human Genome Project may have countered the negative coverage associated with the case of US 18-year-old Jesse Gelsinger who died during a gene therapy clinical trial after suffering a massive immune response to the viral vector used to transport the gene into his cells. Overall, the newspaper in Japan tends to publish articles on a number of bioethical issues.[10]

Overall, the results suggest that people in Japan will embrace human gene therapy as a medical treatment when it is safe and available. While health risks and concerns have remained relatively constant (1993 (6 per cent), 2000 (10 per cent) and 2003 (8 per cent)), the peak of the 'playing God' concern was in 2000. It may be that the euphoria associated with science and technology is making people think more simply of the benefits of saving their own life, treating disease and not restricting their access to life-saving medicine even if by genetics.[5] There has been a healthy media and social discussion of the issues it raises, and importantly groups within society supporting, questioning and rejecting the technology are present. There were a range of comments suggesting bioethical maturity in Japanese society. While opinion surveys continue to find mixed opinions about gene therapy in Japan,[11] it is only natural that there will be mixed opinions about the acceptance of new technology. Meeting the concerns of surveys regarding a technology is a challenge for policy makers, and in the case of gene therapy we can see considerable discussion and policy development prior to its clinical use. The increasing satisfaction observed among those familiar with the details of the ethical committees and oversight process that governs gene therapy suggests progress in governance

of the technology; however, there is still room seen for increased community involvement.[1,6]

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Appendix 1

Headlines in the *Asahi Shimbun* Newspaper about Gene Therapy 1990–2003

List of articles over 37 lines in length

28/7/90 (News) Gene therapy is approved; On the condition that reproductive cells are excluded

28/7/90 (Interpretive article) Problems are left yet in safety and ethics

4/8/90 (News) Gene therapy is going to be started with the approval by the US advisory committee; The first case is blood cell with little impression that it is 'body remodelling'; For cancer or enzyme deficiency; The ethical discussion is not finished yet in Japan

7/8/90 (Interpretive article) Gene therapy is going to be 'opened'; Medical ethics will be required in 'the era with too much knowledge'; There is a fear that the prediction of disease will cause confusion; The discussion about the 'influence' to descendant is going to start from now on

1/4/91 (Interview) Medicine is at a turning point; Gene therapy; The main target is metabolic disorders; The brakes not to let medicine have its own way are needed

20/8/91 (News) Gene therapy on cancer is approved; NIH, for 30 people

10/9/91 (Interview) A year has passed from the start of 'gene therapy'; 'We will decide by comparing disease with risk of treatment'; The fear of side effects is not zero; Explaining is done for some weeks until the agreement of the patient

3/12/91 (Special report) Looking at the gene technology in Germany; Being careful looking back at the Nazi era; They have prohibited therapy on reproductive cells in law

22/6/92 (News) The research on gene therapy will be promoted; Interim opinion by the Ministry of Health and Welfare; They have also suggested strict safety measures

23/1/93 (News) Gene therapy is going to be researched in earnest; The Ministry of Health and Welfare will do it from next year; Discussion about ethical problems will also done

16/4/93 (News) Guidelines of gene therapy; National examination has vanished; There are problems on checking and publication

4/10/93 (News) Examination organisation for gene therapy; The Ministry of Health and Welfare will establish it in a month for clinical application

28/12/93 (News) Gene therapy is going on clinical research; The Ministry of Health and Welfare will help with expenses; 100m yen for AIDS and so on

28/12/93 (Interpretive article) There are many problems in application; Social consent or confirmation of safety

26/1/94 (News) Clinical application of 'gene therapy'/It was approved at Niigata University; There also is opinion demanding careful reaction

8/2/94 (News) Government also checks gene therapy; Conference with jurists and moral philosophers

13/4/94 (Special report) Strategies of gene therapy are expanding; It's efficient for congenital immune deficiency; There is a hope that it cures cancer or AIDS

24/6/94 (Interview) Be careful about gene therapy

30/6/94 (News) Gene therapy evaluating committee; It decided publication as a general rule

30/6/94 (Interpreting article) The first step to breakthrough secrecy

19/7/94 (News) Hokkaido University approved gene therapy; The first case of clinical application in Japan

19/7/94 (Interpreting article) The processing need is confirmation of safety

2/2/95 (News) Gene therapy was approved first/The group of Hokkaido University applied

The special Committee in the Scientific Council stated 'It fulfills safety'; Council in the Ministry of Health and Welfare is left

2/2/95 (Interpreting article) The processing need is developing the structure of government; Gene therapy was approved first, but unknown part of safety is left

7/2/95 (News) Gene therapy will be done next month at the earliest; The plan of Hokkaido University is approved by the council in the Ministry of Health and Welfare too

7/2/95 (Interpreting article) Verify the 'consent' of the patient

7/2/95 (News) Explanation to the family is 'not enough yet'; Opinions in the committee were divided about the approval of gene therapy

3/31/95 (News) Gene therapy on HIV patient; The first case in Japan, University of Kumamoto approved the plan

15/7/95 (News) United States permitted exportation of gene 'vector'; Hokkaido University will start therapy in the last ten days of this month

20/7/95 (News, Top priority on the front page) Gene therapy will start from 1st next month; Hokkaido University uses for the four-year-old child who has immune deficiency; The first case in Japan

1/8/95 (News, Top priority on the front page) Human's hands get into 'blueprint of life'; Hokkaido University started the first gene therapy in Japan; For the boy who has immune deficiency

1/8/95 (Interpreting article) Problems still remain in efficiency and safety

1/8/95 (News, Top priority on the general news page) 150 times injection into muscle, without playing outside; Fight against his disease for three and half years, he bet his 'life' on gene therapy; The four-year-old child bore a long period for drawing blood; Develop it carefully, anxiety is spreading little by little

8/8/95 (News) Hokkaido University returned the lymphocytes which introduced genes into the boy's body

6/10/95 (Special report) Controlling cancer by apoptosis; It opens up the possibility of gene therapy; Papers are read one after another in the academic meeting

10/11/95 (News) Gene therapy for HIV patient; Kumamoto University applied to government

10/11/95 (News) The progress of gene therapy in Hokkaido University is good; The enzyme is produced normally in lymphocyte in the body

3/6/96 (News) There may be problem in gene therapy with adeno virus; Disorder in a brain was found in the animal experiment

7/8/96 (News) Gene therapy for cancer; Committee in Tokyo University approved for the first time

7/8/96 (Interpreting article) The efficiency is still unknown; Solidifying the basis is important

29/10/96 (News) Gene therapy for HIV infection is basically approved; The joint committee of the Ministry of Health and Welfare and the Ministry of Education, Science and Culture will conclude next year

29/10/96 (Interpreting article) The efficiency is still unknown; Accumulate data

15/3/97 (News) The first gene therapy has got result and may be finished; Hokkaido University's case, the boy will enter elementary school next month

15/3/97 (Interpreting article) The processing need is promoting basic research

2/6/97 (Special report) Gene therapy will start in earnest in Japan, but there are opinions that it needs to be reconsidered in United States; Kumamoto University gave green light following Hokkaido University; Tokyo University and Okayama University have also started examination; The effect of therapy is not seen clearly; The American authority says 'Great importance should be placed on basic research'

5/8/97 (News) The first gene therapy is 'effective'; Hokkaido University research team said, they will observe the progress from now on

26/1/98 (News) Midori-Juji corporation gave up gene therapy for AIDS; The effectiveness of American medicine was not confirmed; Approval inspection by government is problematic

30/1/98 (Special report) Citizens speak about gene therapy; University professors started conference; Discussing about high-technology together; Clone sheep interested them; The risk is… the allergy is

27/3/98 (News) Introduce patients' viewpoint to gene therapy; The citizens made opinion paper

30/9/98 (News) Gene therapy on cancer is going to be carried out; Tokyo University will do for the kidney cancer patient, for the first time in Japan

5/10/98 (News) Cancer tissue was extracted in Tokyo University medical science research institute; 'The first step' to gene therapy

9/11/98 (News) Plans of cancer gene therapy is being presented one after another; Strengthening immune power and decreasing side effects; The problem is Japanese original development capacity

9/2/99 (News) Gene therapy will also be applied for chronic diseases; The special committee in the Ministry of Education, Science and culture decided

24/5/99 (Special report) Can we break the barrier? 1 – A guardian deity; Accumulating data by treatment for cancer

31/5/99 (Special report) Can we break the barrier? 2 – A commander; Remodeling cells and suppressing metastasis

7/6/99 (Special report) Can we break the barrier? 3 – A decoy; Cover on the gene of heart disease

14/6/99 (Special report) Can we break the barrier? 4 – An antidote; Carrying gene with HIV

21/6/99 (Special report) Can we break the barrier? 5 – Support; Preparation for the environment of test decide the future

27/10/99 (Interview) An introduction to the 21st century; Gene therapy can strengthen immune reaction and beat cancer

14/11/99 (News) Gene therapy influences descendants; American researcher confirmed with rat

29/1/00 (News) Gene therapy for severe heart disease; Tokyo University professors and others succeeded with hamster

2/3/00 (News) Liver cancer suppressing gene was discovered; Medical science institute of Tokyo University; Possibility of treatment in future arose

20/4/00 (Special report) Gene therapy is still in clinical trial; Surveillance and evaluation are needed.

20/4/00 (Special report) Vector is a key to success for gene therapy

7/6/00 (Interview) Prevention and early finding of cancer are key to overcome the disease

31/10/00 (News) Synthesised DNA will be insert to a boy to treat Muscular Dystrophy next month

7/1/01 (News) Clinical application of a drug for cell reproduction starts, which accelerates gene therapy

13/4/01 (News) First gene therapy for breast cancer starts in Japan

1/7/01 (News) Keio Univ. to plan new type gene therapy using recombinant gene of a virus

27/8/01 (News) Kyushu Univ. to plan gene therapy using a virus vector made in Japan

5/11/01 (News) Hokkaido Univ. to plan new type gene therapy for the boy received gene therapy in 1995

9/3/02 (Interpreting article) American study group succeeds in an animal experiment

using a cloning technology that a part of gene therapy

5/10/02 (News) French government commanded that gene therapy had to be stopped because of fear of leukemia. Tohoku Univ. also decided on postponing gene therapy

Articles less than 37 lines (excluding headline and subheading) 2000–2003

10/5/00 (Interpreting article) FDA advises Tafutu University to improve the internal guideline on gene therapy

25/5/00 (Interpreting article) University of Pennsylvania quits gene therapies for human

26/9/00 (News) A patient died midway through gene therapy at Nagoya University

27/9/00 (News) Family of the dead patient charges Institutional Bioethics Board of the University of Pennsylvania

19/12/00 (News) Chiba California will implement gene therapy for cancer of the esophagus

18/4/01 (Interpreting article) Gene therapy for reproduction of brain nerves system starts in University of California

25/4/01 (News) Institute of Medical Science in the University of Tokyo to plan gene therapy for pediatric cancer

11/5/01 (Interview) Dr Kamatani investigates a gene that is useful for the treatment of brain ischemia

21/6/01 (News) IRB in Osaka University approves gene therapy using HGF gene

26/6/01 (News) Osaka University to starts gene therapy using HGF gene

29/6/01 (News) University of Tsukuba to plan gene therapy for leukemia

28/8/01 (News) IRB of the Institute of Medical Science in the University of Tokyo to approve gene therapy for pediatric cancer

12/12/01 (News) The patient received gene therapy with HGF gene lost three fingers

28/12/01 (News) Osaka Univ. – The patient received gene therapy with HGF gene is recovering

1/2/02 (News) 'Gene therapy for pediatric cancer by the University of Tokyo is no problem,' said Committee consisted of MOHLW and MOECSST

6/3/02 (News) Japanese government accelerates the review of gene therapy

18/4/02 (News) Osaka University – Insulin-producing cells are in Mice by inserting related gene

17/5/02 (News) MOHLW will approve two plans of gene therapy to Hokkaido University and Tohoku University

15/8/02 (News) Osaka University asked an NPO to check the process of gene therapy

2003 *No article in first six months.*

