Bioethics in Japan and iPS Cells*1

JMAJ 56(6): 448–457, 2013

Saku MACHINO*2

Abstract

iPS cells, developed by Dr. Yamanaka, solved 2 problems that ES cells had been facing—infringement of human embryos in the establishment, and the obstacle of immunological rejection in human application. This discovery has greatly helped resolve the bioethics confusion in Japan regarding human stem cells. This report examines the future of bioethics in Japan, while reviewing domestic debates, laws, and ethical guidelines.

There are three traditional characteristics in bioethics in Japan: 1) modesty of laws and superiority of administrative ethical guidelines, 2) ambiguity of ideas and concepts, and 3) emphasis on people's welfare and safety. I believe that Item 2 above is what has prevented the development of bioethics and medical/scientific research in Japan, and this must be resolved. In contrast, Item 3 is a good Japanese tradition. We should be aware of the emphasis on the right to self-determination in the Western world, but this tradition must be further maintained. The movement to create a new law to secure the safety of regenerative medicine coming from the viewpoint of protecting people's welfare and safety, and not from the viewpoint of protecting bioethical values, implies that Item 1 in the aforementioned tradition is being re-evaluated. This change in direction should be noted.

Key words Bioethics, iPS cells, ES cells, Regenerative medicine, Human embryos

My lecture addresses the impact that iPS cell development has had on bioethics in Japan. I will be examining this topic and comparing it with another problem, the genes.

iPS Cells and Genes

Transitions in the problems concerning genes

A new discovery that uncovers a range of potential, such as genes or iPS cells, always puts us in utter confusion. When variolation was developed in middle 19th Century in Japan, it was rumored that an inoculated person grows horns. A lot has happened with genetic problems, too. The confusion probably began with genetic engineering. As we all know, it gave rise to biohazard issues. Concerns for environmental laws were also raised, as it could upset the balance of ecosystems.

After these 2 concerns, attention shifted to gene therapy. Is gene therapy safe or not? Can it influence germ cells and disrupt a gene pool? What will happen to the future of mankind? Can we and should we use gene therapy for non-medical purposes such as the enhancement of humans? People began to discuss such ethical questions.

The problem we currently face involves the issue of genetic information, which is also the theme of today's symposium. The Act on the Protection of Personal Information in Japan provides rather vague definitions of "what constitutes personal information" and "what must be protected," but recommends "hiding when in doubt" to be on the safe side. It is true that personal information lies in the area of personal privacy, but it should be shared equally by everyone and used to benefit the human race as well as societies. Ridiculous as it may sound, the protection of personal information has been taken too far without such basic awareness.

*1 This article is based on the lecture originally presented in Japanese at the Japan Medical Association Research Institute Symposium on "Advanced Medicine and Gene Information—and the Future of Human Rights" held on February 15, 2013.

*2 Sophia University Institute of Bioethics, Tokyo, Japan (machino@sophia.ac.jp).

This is what has caused the very difficult problems we currently face.

Stem cell problem

On the other hand, we also have problems regarding stem cells. One issue is the question of medical safety. Next is the issue of obtaining informed consent from the person who provides somatic or stem cells (the provider). Another is the problem of protecting personal information. We need to be aware of these issues and carefully approach them, for they go beyond the stem cell problem in general or advanced life science technology.

ES cells

ES cells are created using surplus embryos. This very act is a violation of human life in the form of human embryos, and therefore, abandoning human life becomes an issue. Another issue is the creation of chimeric beings. Having a human liver in a pig's body is, in fact, a type of chimera. What if it were reversed: a pig liver in a human body? In short, the question here is how much of a chimera can be allowed. The Act on Regulation of Human Cloning Techniques in Japan separates the concept of humans from animals by distinguishing human-human chimeric embryos and animal-human chimeric embryos. However, some people argue that this distinction itself is arbitrary.

Stem cells derived from aborted fetus

Another problem, which once raised a controversy, concerns stem cells that are derived from an aborted fetus. Some researchers were once considering clinical research involving stem cells derived from aborted fetuses. However, the movement to lift the ban for such research was crushed. The major reason behind this was the case of Isezaki Clinic in 2004, in which an obstetrics-gynecology clinic threw away an aborted fetus as garbage along with other medical devices. Just as this news hit the media, a committee of the Ministry of Health, Labour and Welfare (MHLW) was discussing whether the use of aborted fetus should be allowed—and many people were opposed to the idea. Newspapers covered the story in a tone that questioned the respect for fetus, accusing the clinic for trashing them as garbage. I believe most newspapers shared this view.

In the end, the director of the clinic was convicted for violating the Waste Management and Public Cleansing Act, because he failed to follow the formal procedure for processing infectious wastes, and the case was concluded. We could say that this case ended in a very peculiar way—the public accused the clinic for throwing away the aborted fetus as garbage, but the court settled the case by accusing the clinic of throwing away the garbage in an improper manner. This case demonstrated that ways of thinking, or the issue of emotions, could not be ignored easily.

There are many debates regarding the protection of the aborted fetus and whether abortion is fair or unfair. However, an aborted fetus is obviously dead, so we cannot be certain *what* is being protected? In the course of discussion, I remember an occasion where a person said "aborted fetuses are alive," which surprised everyone. As I recall, a considerable number of people nevertheless pursued similar debate.

Autologous transplantation of somatic stem cells

Autologous transplantation of somatic stem cells has been actually performed for quite some time. Although there are various arguments, I believe it boils down to the question of safety.

iPS cells

The production of chimeric beings will probably be the only problem regarding iPS cells.

iPS Cells and ES Cells

ES cells pose a major issue for bioethics in Japan as well as overseas, and some people claim that iPS cells have resolved it all. Allow me to review the course of events involved.

Invention of iPS cells

As everyone is well aware, Dr. Yamanaka succeeded in creating the iPS cells using mice in 2006, and in humans in 2007. As a result, he received the Nobel Prize in Physiology or Medicine in 2012. The background of this research goes back to 1962 when Dr. John Gurdon produced a tadpole from the intestinal cells of *Xenopus laevis* using nuclear transfer technology. This meant that a cloned frog was produced, but the major achievement of this study was that it proved that somatic cells contain all the genes that design a body. The second significance was that it proved that a somatic cell can be reverted back to an embryo; that is, a somatic cell can

be initialized.

Years went by, and Sir Ian Wilmut created a cloned sheep, Dolly, in 1996. This is when the issues of reproductive cloning and therapeutic cloning, in which researchers create and study cloned human embryos (human somatic cell nuclear transfer embryos), emerged. Then, Dr. Thomson successfully established human ES cells in 1998. Dr. Yamanaka's research was born from these studies. When Dr. Gurdon was awarded the Nobel Prize along with Dr. Yamanaka, Dr. Gurdon reportedly called himself a grandfather of Dolly and a father of iPS cells.

Potential uses of iPS cells

What can we do with iPS cells? For starters, iPS cells solve 2 problems in regenerative medicine. We now potentially have the means of complementing the shortage of organs for transplantation. iPS cells solve the barrier of immunological rejection, which has been an obstacle for ES cells as well as organ transplants. iPS cells solved these 2 problems brilliantly at once, which deserves major recognition.

How can humans benefit most promptly from iPS cells? Many countries including Japan are in pursuit of becoming the "First in Man." A fabricated announcement of a successful myocardial transplant surgery using iPS cells came out when everyone was eagerly competing with one another. Clinical trials for treating age-related macular degeneration using retinal cell sheets have passed the ethics committee's review of the research institutions involved, and HMLW officially approved the trials in July 2013.

Another major contribution of iPS cells is in the area of pathological research. For example, we can create iPS cells from the somatic cells of patients who suffer from Parkinson's disease or amyotrophic lateral sclerosis, induce differentiation into nerve cells, and further manipulate them. Such a procedure will allow us to generate or reproduce a disease in nerve cells in a short period of time. It will help elucidate the cause of disease and develop new drugs for treatment as well. Moreover, iPS cells can be produced in large quantities, so iPS cells are greatly anticipated by many people, and various research efforts are in progress to enable very rapid practical application. For these reasons, iPS cells are said to revolutionize therapeutic chemistry.

Differences between iPS cells and ES cells

Problem of ES cells

How are ES cells different from iPS cells? One difference has been already mentioned earlier: ES cells are created at the loss of human life in the form of surplus embryos. There is also the problem of rejection. Organs using ES cells have not been created yet. However, if there were, such organs or tissues would likely cause rejection when transplanted.

Therapeutic cloning

Therapeutic cloning focuses on solving the latter problem, rejection. Rejection is not likely to occur if ES cells are created from cloned human embryos, which are embryos cloned using the somatic cells of the patient. However, the Guidelines on Handling Specific Embryos ban all specific embryos, including the cloned human embryos that were excluded in the Act on Regulation of Human Cloning Techniques. The laws allow it, but the administrative agency, which is supposed to observe the laws, has overruled it in its guidelines—this is beyond common sense. This ban on therapeutic cloning, the research used to create cloned human embryos, was lifted for the first time by the 2004 Report of the Council for Science and Technology Policy (CSTP). This report led to the revision of the Guidelines on Handling Specific Embryos, paved the road to create ES cells from cloned embryos, and the old guidelines on ES cells (officially the Guidelines on the Establishment and Use of Human ES Cells [2001]) were revised.

The obstacle of rejection can be overcome, but the problem of violation of human life still remains. True, the CSTP report has lifted the ban on creating cloned human embryos. As shown in the minutes of the CSTP meetings, many members shared the understanding that cloned human embryos are created differently from normal embryos and are different from human embryos. This probably goes against global common sense because we cannot say that a fertilized embryo is a human embryo but a cloned human embryo is not. Both have the potential to become a human. There are those who strongly oppose therapeutic cloning, especially in America, and one strong line of reasoning they use is that a human life in the form of a cloned human embryo is created only to be destroyed. However, iPS cells can overcome these obstacles.

Ethical problems in iPS cells

Ethical problems also exist with the use of iPS cells. One issue is that iPS cells can be used to create sperms or eggs for procreation. However, the same can be said of ES cells. Other ethical issues include the potential of creating chimeric beings using iPS cells derived from humans and animals, obtaining informed consent from the somatic cell providers, and the protection of personal information—just as in the case of ES cells. It is only natural to point out these issues. However, that does not mean that iPS cell research must not proceed; it means that these problems must be resolved before proceeding. If they cannot be resolved, then we cannot proceed. For example, if damaging or losing a human life can be never allowed, then, ES cell research will never be accepted—but many people would disagree. If you agree that iPS research should be explored further, then we can work on solving these problems.

Often, the media only reports the ethical issues involved with iPS cells. Personally, I believe that pointing out the problems without suggesting a possible solution is an unfair argument.

Ethics of Stem Cell Research

In general, ethical problems in stem cell research lies in 2 issues; the violation of human life, and the ethical questions involved in the use of stem cells. The question of human life violation, which has also been addressed in ES cell research, relates to the ethical status of human embryos.

Violation of human life

Ethical status of human embryos

As you know, the Catholic Church believes that a human life begins when an egg is fertilized and that the blessing of God is equally given from that very moment, and thus, a human embryo as in a fertilized embryo is equally considered a human. Ethically speaking, therefore, destroying a fertilized embryo is murder in their mind.

In the laws of Japan, on the other hand, one is considered a human only after he/she is born, even though human life may have started at the moment of fertilization. Still, the laws admit that fertilized embryos, or human embryos, must be respected as human life.

Now, Article 2 of the Supplementary Provisions of the Act on Regulation of Human Cloning Techniques states that fertilized human embryos are "plumules of human life," which is confusing. I will come back to this again later, but the Ministry of Education, Culture, Sports, Science and Technology (MEXT) translated these words as "emerging potential of human life" in English. That means that a human fertilized embryo is not yet a human life but will emerge as one. That implies that it is not yet a human life. If we start to think about the origin of human life, then, a sperm or egg also has "emerging potential." Since we can now create cloned human embryos, somatic cells themselves can be interpreted as "plumules of human life" as well.

Therefore, this discussion is completely meaningless. Those who wrote this clause in the act probably came up with this very Japanese expression, trying not to clearly state when a human life originates. However, once translated into English, the confusion is obvious. In short, a human embryo is a human life in semantics. Nevertheless, a human embryo had to be distinguished from a human life in the law, as an existence that can potentially emerge as a human.

Abuse of human embryos

Another problem in stem cell research is the abuse of human embryos. The serious issue here is that a human embryo is created with the intention of never allowing it to be born. In fact, the use of human embryos for research was banned in all countries except in the UK in the 1990s. Even now, the idea that creating a human embryo for research purposes must not be basically allowed is still quite strong. Therefore, as I mentioned earlier, creating a cloned human embryo for the purpose of establishing ES cells was thought to conflict with this taboo.

Another issue is whether the loss of a human embryo should be allowed. In my humble opinion, the problem of loss of life is not a concern with respect to iPS cells, and therefore, the only problem remaining pertains to how they are applied.

Unethical issues and safety in stem cell applications

One example of an unethical application of iPS cells would be the abusive use of the technology in reproductive medicine, such as the creation of chimeric humans or the improvement of the human species. Another issue is safety when

applied to humans. First, there is the problem of clinical application. Currently, clinical application is regulated by the Guidelines on Clinical Studies Using Human Stem Cells, which has not been legislated. Further debates are in progress in order to secure the safety of regenerative medicine by legislation.

One thing we need to note here is that medical service regulation in Japan basically addresses license systems, medical service providers, or facility regulations, but not the contents of medical services. People often ask, "What about organ transplant?" If you look up the law, you will see that the Act on Organ Transplantation actually addresses organ extraction. In fact, the act itself hardly touches on the extraction techniques.

Regulating regenerative medicine that uses stem cells by the government would mean regulating physicians and their services as well, and therefore, this is a major challenge. We are standing on a slippery slope, because allowing a single regulation of the content of medical service could lead the discussion of how far such regulations should extend. I myself am not against being regulated. However, there will be no end if we start regulating everything that needs to be regulated. We must approach this very carefully upon extensive discussion.

How Japan has addressed these new technologies in its laws and ethics

Regulations by ethical guidelines

How has Japan been addressing these newly emerged technologies in its laws and ethics? Mainly by regulating bioethics through ethical guidelines. The Act on Regulation of Human Cloning Techniques is quite exceptional among all such regulations. First, the Act on Regulation of Human Cloning Techniques was legislated, and then the Guidelines on Handling Specific Embryos followed it. Being governed by this Act, the Guidelines on Handling Specific Embryos also belongs to a category of mandates in legal terms. Because it is a legal standard promoted by the administrative agency, a penalty for violation can be instituted. Various conflicts arose in the course of preparing this Act on Regulation of Human Cloning Techniques. Some claimed that it should be regulated by guidelines only, not the law. On the other hand, there were those who insisted that all regulation should be through laws. Taking a halfway position between these completely opposite ideas, it was decided that acts that can lead to procreation, such as the production of clones, chimeras, and hybrid beings, are to be severely penalized by the law, whereas the studying of cloned embryos, chimeric embryos, and hybrid embryos are to be regulated by ethical guidelines. However, both the law and the guidelines are now considered as laws because these ethical guidelines have been stipulated in the law, and this has resulted in a situation in which the unapproved creation of cloned embryos is subject to penalty even if they are not created for the purpose of implantation.

The ES guidelines, on the other hand, are not stipulated in the law. Therefore, these are a set of administrative guidelines used for approving basic research only. For now, there are 2 guidelines for ES cell research; the Guidelines on the Establishment and Use of Human ES Cells (hereinafter referred to as the ES Establishment and Distribution Guidelines), and the Guidelines on the Use of Human ES Cells (hereinafter referred to as the ES Use Guidelines).

Effects of violating ethical guidelines

The violation of ethical guidelines involves refund claims of public research funding. This is not actually the direct effect of violation; it is the effect of research grants being revoked for failing to observe the terms for proper enforcement of research grants under the law. Ethical guidelines in Japan are said to be "soft" laws, but they are rather relentless for researchers. However, there is no legal penalty for violation.

Reasons that ethical guidelines become the center of regulation

Overseas, research on stem cells, ES cells, or iPS cells is regulated by the law, such as the Human Fertilization and Embryology Act (HFEA) in the UK, the *Embryonenschutzgesetz* [embryo protection law] in Germany, or the National Bioethics Law in South Korea. Researchers from overseas often ask me how Japan manages to regulate research with only guidelines, but answering them is quite challenging. The law in Japan is perhaps traditionally self-inhibitory toward research and medicine in Japan. Moreover, Japanese researchers obey the administration well, although they may complain at the regulations, and they do not easily break the law.

Another reason has to do with ES guidelines

that approve the use of surplus fertilized human embryos. Because it concerns the loss of life, many argued that such acts should be regulated by the law. However, we have the Maternal Protection Act in Japan, under which a fetus that is less than 22 weeks in gestation is not legally protected by the law. It will be quite awkward if we are to look the other way and protect embryos only in research. Therefore, relying on ethical guidelines is probably more appropriate than regulation by law.

Rules in Japan

There are some problems with the Japanese rules, so let me address these specifically. I believe many are familiar with this topic, so I will just list the problems.

Creating human embryos for non-procreational purpose

Creating a human embryo for non-procreational purposes is considered a taboo in the world, but many people in Japan are probably not fully aware of the seriousness of violating it.

This idea is believed to have come from Kant's *Der kategorische Imperativ* [Categorical Imperative], which states that humanity must not be treated as a means but as an end in itself.[1] Let us say that a researcher somewhere were to create human embryos because he wants to create ES cells for various studies. Then, it is for the sake of his research and not for the purpose of procreation, and therefore, it will most likely be considered a complete violation of this taboo. Most countries do not allow such acts in principle. When Germany legislated its *Embryonenschutzgesetz* in 1990, I thought that this law reflects the common sense of the world, for I am a person who is specialized in the Penal Code.

However, the fact is, the law legislated in the UK in the same year, the HFEA, approves the creation of human embryos for the purpose of reproductive medicine such as infertility treatment. I suppose many Japanese physicians thought this was normal. In Japan, the creation of human life for the purpose of stem cell research has been approved for quite a while.

In fact, Article 4 of the Act on Regulation of Human Cloning Techniques approves the creation of specific embryos without any restrictions on research purposes. Having said that, some people may have thought that specific embryos do not include human embryos. Actually, most specific embryos are human embryos, from which humans can be born. Therefore, the Act on Regulation of Human Cloning Techniques allows penalizing the offenders for producing individual beings. On the other hand, embryos, which are in the premature state, are being regulated by the guidelines. Thus, this results in approving the creation of embryos under the guidelines. Many people probably did not recognize that this point was in the violation of the taboo when this act was legislated.

At present, Article 2 of the Guidelines on Handling Specific Embryos limits the types of embryos that can be created. Animal-human chimeric embryos have been approved from the beginning, and cloned human embryos are now included. Any other types of embryos are still being prohibited. This probably goes against the law and therefore is an invalid measure, but that is how things stand now. Subsequently, ethical guidelines were established to approve the creation of human embryos for the purpose of reproductive medicine research—these ethical guidelines concern research in assisted reproductive technology, which creates fertilized human embryos. When preparing the guidelines, many people believed that this is a question best reserved for assisted reproductive technology research. In reality, it is more accurate to say that people were following the early ideas of the HFEA of the UK.

Violation of human embryos for the purpose of stem cell research

Currently, the ES guidelines allow the establishment of ES cells from surplus embryos and cloned human embryos, but they are separated into 2 categories. The ES Establishment and Distribution Guidelines categorizes ES cells established from surplus embryos as Class 1 Establishment, whereas those established from cloned human embryos are categorized as Class 2 Establishment. Again, the ES guidelines are not laws. Moreover, they are not a comprehensive set of regulations for human embryo protection. They obviously exist to balance the research use of human embryos with the operation of the Maternal Protection Act.

Application of stem cells

One of the restrictions on the applications of stem cells is that the creation of chimeric beings is prohibited. As I have repeatedly mentioned, Article 3 of the Act on Regulation of Human Cloning Techniques states that not only cloned human embryos but also human-animal hybrid embryos, human-animal cloned embryos, or human-animal chimeric embryos must not be transplanted into the womb. The purpose of this article is not to penalize any transplantation in the womb but to penalize implantation with the purpose of procreation. At least, that was the intention in the first draft. However, the wording with such a subjective purpose would resemble a clause in the Penal Code—for example, "any person who counterfeits documents for his/her own use shall be punished." Such wording would clearly imply that it is a penal code offense; therefore, it was re-stated in a more technical tone.

Because of the wording of the article, many people rush to think that implantation in the womb will be penalized and tend to jump to the idea that artificial implantation itself is wrong. The law prohibits implantation because it creates an individual being. The Guidelines on the Handling Specific Embryos prohibits the implantation of all specific embryos including any other types in order to take further steps in this direction.

Three main types of embryos are listed in Section 2, "Definition of the Terminology," of the Guidelines on Clinical Studies Using Human Stem Cells; namely, human somatic stem cells, human ES cells, and human iPS cells. Human ES cells and human iPS cells were not included initially, but the guidelines were revised in order to include them. In short, the revised guidelines approve the use of ES cells and iPS cells in humans. Now, the debate on whether or not a law should be legislated to secure the safety of regenerative medicine is in progress.

Future of Bioethics in Japan

I would like to discuss where the problems in regenerative medicine of Japan are likely to lead. Bioethics in Japan is quite confusing not only to foreigners but to Japanese people as well, especially lawyers. Moreover, researchers often do not understand why there is such regulation in this nation. Therefore, it is very true that bioethics in Japan lacks transparency for many people. Here, I would use the prospective applications of human stem cell research as the starting point and dare to foresee its future. In conclusion, I believe we must remove ambiguity from the area of bioethics, although it is considered to be a virtue in Japan. We also need to further emphasize the welfare and safety of people, even more than we have in the past.

Ethical issues of pluripotent stem cells

Production of human-animal chimeras

The most serious ethical problem involved in the use of pluripotent stem cells is the production of chimeras between humans and animals. The early discussion on pluripotency addressed this issue in depth. As I recall, Mr. Clinton sent a letter to the chairman of the President's Committee when ES cells were developed, saying "We will have chimeras now. You have to think of something." It has not been raised as a major problem since, but nevertheless, it is still a problem.

Other potentially ethical considerations

The old guidelines on ES cells regulated 3 aspects of human ES cells similarly in a set of guidelines; namely, its establishment, distribution, and use. Its preamble states that the establishment and use of human ES cells require careful consideration in view of bioethical problems, because they use human embryos that are plumules of human life and because they have the potential to differentiate into all types of cells. The statement that human ES cells "use human embryos that are plumules of human life" is understandable. Human embryos are destroyed to establish ES cells; therefore, this requires careful consideration.

However, I am not quite sure why the fact that human ES cells have the potential to differentiate into all types of cells requires ethical consideration. If there is any, it will be that they would enable the production of human-animal chimeras. When the ES guidelines were first created, a study involving the establishment and/or use of ES cells had to go through 2-step review: ethical review of the research institution involved as well as ethical review of the government. This drew much criticism.

It is understandable that destroying human fertilized embryos requires ethical consideration and thus needs to be reviewed by the govern-

ment. However, ES cells that are established from them are no longer human fertilized embryos but cells. Why should ES cells be treated differently from normal cells? Why should ES cell establishment be reviewed the same way as handling fertilized embryos? This is very strange. Hardly any other country does such a thing. For these reasons, the ES guidelines were divided into 2 separate sets of guidelines, leading to the birth of the ES Use Guidelines.

Ethical meaning of different origin or having pluripotency

The ES Use Guidelines, however, still state that there are bioethical problems with ES cells because they are established by destroying human embryos, and because they have the potential to differentiate into all types of cells. What does this really mean? One thing people often point out is that they have different origins.

Unlike normal cells or iPS cells, ES cells are derived from fertilized embryos. That is the difference, they claim. However, I fail to understand why that makes a difference. If a part of my body gives rise to another man, its origin is still a man. Should this person be given special consideration as given to cells? I do not believe so. The fact that this sort of incomprehensible argument is actually accepted is quite problematic. My teacher, Dr. Ryuichi Hirano, liked the word *yugami* [distortion]. He would probably say that "bioethics in Japan has a *yugami*." Another thing is what it ethically means to possess pluripotency. As mentioned earlier, there is a possibility of creating chimeras. However, I cannot quite understand why everyone thinks that cells with pluripotency deserve the same respect as fertilized embryos.

People perhaps have a notion that ES cells are the same as human embryos because ES cells allow us to touch the mystery of life. However, I believe that such an idea is in the world of Japanese-style animism. That is a good possibility, considering that some people claim that "aborted fetuses are alive."

Vague boundaries between life and death

We need to start the discussion at specific problems

As I have said many times in the past, the boundary between life and death has become very vague in Japan. Of course, the debate on human life is still insufficient, and we certainly need to carry on the discussion. It is also true that the problem of brain death has not been resolved yet, and this discussion also needs to continue.

So, where do we start? I believe that we need to start at specific problems, such as human embryo research or the fact that artificially induced abortion is practiced virtually freely. Some people say that human embryo research cannot be approved because it is questionable, has ethical problems, or goes against the respect for human embryos. Those people, however, look the other way with regard to the issue of induced abortion. I believe it is nothing other than deception. Moreover, it is unproductive to discuss what constitutes respect for human embryos or whether human embryos are humans or objects, and such a barren argument should not be pursued.

When I call such an argument barren, I am not being arbitrarily decisive; I say so based on my experience. When the CSTP report was being drafted, the members thought that the problem of human embryos must be discussed or else bioethics in Japan would be ill fated. I, however, said, "It won't get us anywhere"—and, as I anticipated, it only led to the question of what exactly human embryos were. Human embryos are not objects. Then, what constitutes "objects" to begin with? Objects are, for example, a pair of glasses or books such as the Statute Book. Then, there are human beings. Human embryos are neither objects nor humans, but somewhere in between. As foolish as it may sound, the interim report also includes such an expression. Therefore, a human embryo is in between a pair of glasses and a human? This is quite a surprise for both human embryos and humans.

We should start at specific problems in order to avoid such unproductive arguments. One starting point is to clarify the attitude and decision for each problem as the discussion proceeds. MEXT currently translates the wording in the ES guidelines, "plumules of human life," as "emerging potential." In the first draft, their translation was the "beginning of human life." Again, this translation was provided by MEXT, but the expression "beginning of human life" strongly suggests that human life has originated. However, the expression of "potential" suggests something else, something ambiguous. When the ES guidelines were drafted, many people

were very happy with the wording of fertilized human embryos being the "plumules of human life," thinking that it is a well-thought out expression. It felt a little questionable to me even back then—and now, I believe it was an unfortunate expression. Nevertheless, this wording is in the law, and we should not think too lightly of the law.

Dividing the bioethical problems into 3 aspects

Another problem is that there has been a strong trend in Japan to believe that the resolution of bioethical problems require social consensus or governance. When issues regarding the Act on Organ Transplantation were being discussed, many people argued that organ transplantation from brain-dead donors had not gained social consensus or that it had not taken root.

Apparently, Takeshi Kitano, the world famous movie director, actor, and comedian, once said, "Crossing a street against red traffic lights is not frightening as long as everyone does it." Dr. Ichiro Kato, who was the first chair of the Round Table Conference on Bioethics, quoted these words and criticized the social consensus argument, saying that it was much like this "red lights" phrase. Although his comment provoked tremendous antipathy among people, I personally believe he was right.

Recently, some people claim that governance is important, rather than social consensus. In short, some scholars in bioethics argue that the important point is that bioethics is being governed, and that is all it needs. However, we cannot substitute governance for bioethics since governance implies being governed by something. Dictatorship can be said to be the highest form of governance, but of course, this does not guarantee its ethics.

Therefore, I believe we need to divide the problems of bioethics into 3 aspects when discussing them. The first aspect is the ethics of the standards. These are basically the bioethical problems I have been addressing so far. The second aspect is social consensus. Establishing standards should proceed with public understanding, and seeking social consensus is necessary in this respect. However, having social consensus does not guarantee being ethical. This may be a radical example, but close to 90% of people supported the Nazis during its prime. Social consensus was definitely present. However, no one will now argue that the Nazis were just. Third is to actually implement standards. How do we maintain ethics when implementing the rules? This is where governance comes in.

Welfare, safety and security of the people

Emphasis on the right to medical care and welfare service

Lastly, I would like to discuss another tradition of Japan: ambiguity. Japanese people have a tradition of being vague. When Yasunari Kawabata won the Nobel Prize in Literature in 1968, he gave a lecture titled "Japan, the Beautiful, and Myself." Then, Kenzaburo Oe gave a lecture titled "Japan, The Ambiguous, and Myself," when he also won the Nobel Prize in Literature in 1994. In his lecture, Oe stated that Kawabata's title, "Japan, the Beautiful, and Myself," is rather confusing as to what it exactly means. Oe stated that Kawabata's title was "very beautiful and vague," for "it can imply 'myself as a part of beautiful Japan'" but "it can also imply 'beautiful Japan and myself,'" and said, "I cannot utter in unison with Kawabata the phrase 'Japan, the Beautiful and Myself.'" I very much agree with Oe.

People have traditionally emphasized the right to medical care and welfare services. In the area of mental healthcare, from which I entered the study of medical care and laws, this trend is especially pronounced. In 1918, Shuzo Kure, the pioneer of mental healthcare in Japan, stated in his report that mentally handicapped people in Japan were doubly unhappy—for suffering from mental disease, and for being born in this country. He also added that Japan must establish proper medical care systems, especially hospitals, and not leave such people unattended. This is what we now call the right to medical care. The provision of medical care was strongly emphasized and considered paternalistic. At the same time, however, the opposing view was also born from the standpoint of the patients' right to self-determination.

Nowadays, everyone admits that the right to medical care and welfare must be emphasized. It is also certainly true that self-determination alone cannot save patients. Japan is unique in that security is emphasized as much as safety is. The Science Council of Japan has issued the Report on Security and Safety several times. The original Japanese words for security and safety are *anzen* and *anshin*, respectably; however,

there is no exact translation for the word *anshin*. It is similar to "easy feeling" or "comfortableness," but I believe this semantic sense is probably unique to Japan. In a manner of speaking, the word *anshin* is ambiguous, and not quite a concrete enough concept to be the cornerstone.

From protection of human embryos to discussion of safety

It appears the emphasis in the discussion of bioethics in Japan is shifting from human embryos to safety. This probably owes a considerable amount to the advent of iPS cells. The revision of old ES guidelines to separate their establishment and use was also symbolic. Considering that the advent of iPS cells enables the creation of pluripotent stem cells without destroying either human fertilized embryos or cloned embryos, the center of discussion will increasingly shift to the safety issues associated with its application.

Legislation movement to promote regenerative medicine and ensure its safety

New legislation to promote regenerative medicine and secure its safety is in progress, especially with regard to stem cells. Some accidents have already occurred. In a case, a patient, who was referred by a medical institution based overseas, received stem cell treatment in Japan and died. Apparently, the patient came to Japan for treatment because pharmaceutical affairs laws in Korea prohibit autologous stem cell transplantation, but there is no regulation against it in Japan.

Normally in Japan, such a case would be considered professional negligence resulting in death under the law. Medical care is provided at the doctor's discretion, so basically it is to be provided freely. When the provided care fails, however, whether the physician in question is at fault becomes the question. Some time ago, many accidents resulted from the breast enlargement procedure in plastic surgery. Instead of completely banning the procedure for being risky, it was decided that the procedure can be performed but that it would be adjudged as professional negligence resulting in injury or death if an accident occurs.

However, this response cannot cover the aforementioned accident. The causality was difficult to prove, and the foreseeability was also questionable. It is extremely difficult to seek criminal charges in such cases. So, perhaps *ex ante* regulation should be enforced. In that case, the question is under which law it should be: the Pharmaceutical Affairs Act, or the Medical Care Act. The Pharmaceutical Affairs Act basically regulates the manufacture and sales of medical products. We must approach this carefully since this law does not really stipulate the use of medical products.

Ordinarily, Japanese regulatory practice is to regulate medical services. For example, what task requires which qualification is stipulated in laws, such as Medical Practitioners' Act, the Radiology Technicians Act, or the Act on Public Health Nurses, Midwives, and Nurses. A person will be punished for conducting unqualified tasks. However, ordinary regulation cannot cope with the current situation. This is where the idea of *ex ante* regulation comes in. Such regulation needs to step into the area of specific medical tasks, in which certain medical tasks will be regulated under a pre-approval system in several stages. This is the idea currently being debated. With regard to the amendment of the Pharmaceutical Affairs Act, some people are trying to create different systematic categories of stem cells that are unlike current standard medical products in order to regulate them in a different fashion. At the same time, they want to tie the current regulation of medical services to the approval system and incorporate it into the law.

In Japan, we have no choice but to place great emphasis on the ideas of safety. However, creating a new regulation under the law will unavoidably invite creating another regulation when something similar occurs, as I have repeatedly mentioned. What we need to do is to clarify where the difference lies and for what reason the regulation exists, as the discussion proceeds.

Reference

1. Guyer P. Kant, Immanuel. In: Craig E, ed. Routledge Encyclopedia of Philosophy. London: Routledge; 1998, 2004. http://www.rep.routledge.com/article/DB047SECT9. Accessed August 14, 2013.