

New Perspectives in Japanese Bioethics

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Edited by

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INTRODUCTION

C.D. HERRERA

Authors in bioethics must make decisions, some theoretical, some very practical, about context when they write. Things are even more complicated when context itself is the topic. These decisions about what is supposed to matter to readers can then be understood in a number of ways, subject to the author's interpretation of the context. Supply too much context, and readers will have trouble understanding what the discussion is supposed to mean to them. When the conversation concerns potentially better or worse ways to act, such ambiguity can itself have ethical significance. Yet if an author does not supply enough context, readers can rightly object that once more *those* philosophers seem to have missed the forest and fixated on trees (trees that don't resemble anything in the reader's experience).

These concerns are not unique to bioethics discussions, of course, but I do think that in our field there are especially interesting questions about what we should pack and what we should leave behind each time that we enter the conversation. Even the notion that there could be only one conversation is controversial. We can ask common-sense questions about who should be able to take part in a discussion of informed consent, for instance, or which voices should dominate. We can ask more complicated questions that have to do with what it would mean to understand the concepts or terms within that conversation, and what obligation an author has to bring everyone else up to speed. And who gets to decide what speed is optimum?

Again, while it is not only bioethicists who can encounter these troubling questions, to the degree that our discussions aim to reflect or challenge laws and policies, such as those governing human experimentation, it would be odd to dismiss the questions as being only of general academic interest. Doctors and patients are, to take another example, going to continue interacting, and the outcome can have a dramatic effect on a general quality of life. But their interaction will take place within a specific context, so it makes sense that bioethicists would continue to find something problematic in questions about how we are to understand such

relationships, and that we would continue to believe that much will depend on how we are able to talk about it.

There might seem to be some promise in trying to simplify a few of the contextual judgments by narrowing our focus to local interests. In that respect, we would not worry so much, in our discussions about the allocation of scarce medical resources, whether the bioethicists in Scandinavian countries agree with what the bioethicists in Japan seem to be saying. But would adopting that approach really amount to progress? Since it is becoming increasingly common to define *culture* in broad terms, we should expect that nearly any discussion of ethics worth having will be cross-cultural in some sense. After all, there is youth culture, senior culture, institutional culture, academic culture, and so on. I suppose that we could decide that, for our purposes, or for just this instance, the only context that matters is one that Japanese bioethicists would want to claim as their own. Yet that would surely strike many readers as a cop-out.

The trouble with narrowing the context is that authors can then seem to have evaded many of the problems which emerge when scholars set out to discuss a particular issue, or set of issues. Maybe it makes sense to think that authors should be compelled to first establish their context, and defend the judgments that went into that. A reader expecting a discussion of Informed Consent, for example, would then know to be ready for, or have interest in, a view of Informed Consent in Japan. Likewise, a scholar of Japanese views on assisted-suicide might not expect too much in the way of knowing how to adapt the discussion so that it has relevance to scholars that are more used to discussing that topic in another context. Again, the challenge is in knowing how much context to build into the discussion of bioethics, and how much to relegate to footnotes, if one decides that the details are even that important. And for any question about how much one would have to know to appreciate a cross-cultural question in bioethics, the follow-on question would be how much one should care.

Then there is that forest. The more that considerations of context seem to intrude into the discussion, the more likely it is that the relevance of the underlying topic (what many will think of as the "real" topic anyway) will be lost on readers. Could the solution be to assume that too much context is better than not enough? As authors, we might be careful not to overestimate the bearing that cultural and contextual distance can have on understanding. We might also take it as part of our mission to reduce that distance, so that we write as if what happens in Scandinavian countries should interest all bioethicists, and that the arguments of Japanese bioethicists are more informed than we realize by contexts which are taken for granted in our attempt to understand them all.

Ideally, we should be able to discuss bioethics in a way that the conversation will not stall, or prove uninteresting, as everyone awaits a verdict on which assumptions about context a listener or reader will need to hold. That ideal could take effect not in a simplistic claim that we can all learn from each other, although there is reason to think that we might. The suggestion could be that one is not really writing bioethics if there are not accompanying value judgments about what counts as relevant and what does not. I would like to think that bioethicists are especially qualified to elaborate on those judgments. I would also tend to believe that such judgments are as much a part of our ethical arguments as the more substantive claims about something like assisted-suicide are, to put it another way.

In the end, even if we could be sure that a roomful of scholars will be familiar with the peculiarities, and preoccupations, associated with Japanese views on the allocation of scarce healthcare resources, it would still seem important to entertain questions about context. Would each of those scholars be equally familiar with the needs of elderly patients? What about the different needs between male and female patients? This is the problem of cultures within cultures that I mentioned earlier. When we face such problems, it does not seem that we have the luxury of being able to retreat to the familiar, and gripe that the trouble with context is that there is always too much and not enough of it, at the same time.

Alexandra Perry (my co-editor) and I asked authors to submit papers that would address one or two bioethics issues in a way that would draw on their own understanding of the origin and nature of *Japanese* bioethics. We began with the assumption that there are good reasons to think that we should try to understand the history of bioethics, and to see how it has developed in what at first seem to be different contexts. Authors were also told to feel free to question the idea that there is a bioethics canon, for instance, or even a unitary concept of *bioethics*. I think that the papers that we ultimately accepted for this volume can make good on a promise to provide fresh perspectives on what are hardly new problems, and that the authors each provide interesting evidence of what "Japanese bioethics" might mean, and what it might aspire to.

That might be optimistic, but it does not seem to be a cop-out. At worst, each of us would be wrong to think that there is a "Japanese bioethics." But that would mean that there would still be something to learn in the different directions that our errors have taken us. And if we are right to think that we can establish some boundaries around this area of bioethics, we can discuss the relevance of cultural details, including those concerning Japan and its own history, as well as our attempt to assess the

specific ethical claims. Those who would describe themselves as Japanese bioethicists seem to also need to be able to discuss that relevance, and I think that the authors in this volume do a good job at that.

CHAPTER ONE

A JUST HEALTHCARE SYSTEM FOR CENTENARIANS

ATSUSHI ASAI

Introduction: Issues Surrounding Centenarians are Relevant to All

The time when centenarians are prevalent in society has nearly arrived. An investigation by the Ministry of Health, Labor and Welfare in 2012 identified 51,376 people who were 100 years or older. The investigation noted that this was the highest number of centenarians in history, and numbered 3,620 more than the previous year [1]. In Japan, it is often said that “life is 50 years long,” but more recently, this phrase has changed to “life is 80 years long.” In the very near future, this may yet change to “life is 100 years long.” As those in a period that follows senescence, the centenarian generation will add a new population layer to the conventional human society.

This prediction is not pie in the sky. With improvements in national public sanitation, enhanced nutritional levels, and rapid advances in modern medicine such as regenerative medicine and genetic engineering technology, the arrival of the centenarian generation is highly likely, at least in Japan, but also possible in several developed countries where the population includes those defined as ‘super old.’

Safe and effective medical interventions are now available for those over 90 years old, and major surgical operations have become rather common among patients in their 90s (2). For example, in 2012, a 109-year-old woman underwent an emergency surgical operation for peritonitis due to appendicitis, and reportedly left the hospital in fairly good condition (3). Increasing numbers of elderly people desire to continue vigorous social activity for as long as possible, and are willing to accept medical interventions for lifesaving and health maintenance purposes. At the same

time, more and more bedridden elderly or patients with dementia will also elect for life-prolonging treatment.

Issues pertaining to the arrival of the centenarian generation do not only concern the elderly and policymakers. If the current youth do not die young, they too will become elderly at some point, and the possibility of centenarianism will be even higher for them than it is for elderly now, due to better circumstances overall. Thus, these issues are important and applicable to all of us.

The arrival of the centenarian generation will significantly influence social awareness of what it means to live to be 100 years old. Current knowledge of this matter would dictate that becoming a centenarian is a very rare, happy, and wonderful occurrence, and one typically receives a blessing from his or her family and community that may even involve a local celebration. However, these favorable social attitudes toward centenarians would change if the total number in the communities was to increase explosively. The sense of rarity and respect that is currently associated with being a “sage” and “elder” would diminish gradually, and these positive concepts would likely be replaced by negative ones such as “nuisance” and “burden.”

I fear that our society is not prepared to face the inevitable increase in centenarians, and that in many ways, we ourselves are not prepared to live as human beings for longer than 100 years. In a society where many centenarians commonly and casually go about their daily lives among other younger generations, how is it possible to ensure the appropriate operation of social security services such as healthcare, employment, and benefits? Even now, the Japanese society is seemingly unable to cope with diverse issues related to the aging population, and frequent and sometimes arbitrary changes continue to be made in healthcare policies as the result of trial-and-error management strategies. Different governments have different policies on this matter. Arguably, the healthcare system and medical ethics have been unfit to resolve problems brought about by a rapidly growing super old generation, and I am uncertain that a solution to address these difficulties is likely to materialize any time soon.

Given the situations mentioned above, I wish to consider a just healthcare system for centenarians from a bioethical perspective. What would comprise medical care and healthcare delivery system that would be appropriate for centenarians as well as the rest of the population? What principles and values demand our respect and protection in the coming years for centenarians? While I have not reached a definitive conclusion, I present some thoughts and key concepts underlying healthcare and social systems in the age of centenarians.

Issues and Thoughts Regarding Healthcare for Centenarians

What comprises just healthcare for centenarians? Some would affirm that obviously, the chronological age of the individual should not affect the medical care available to him or her, first of all because vast physical and physiological differences exist even among people of the same age, but also because of the universal right to life, and because healthcare should be claimed as a fundamental human right available to every human being, regardless of one's age. In contrast, others might assert that the only option appropriate for centenarians is a peaceful death with no medical interventions, as they have lived a long enough life already. Still others would say that it is case-dependent.

If a 101-year-old long-distance runner suffered sudden cardiopulmonary arrest during a race, what would most of the spectators do? Would I perform cardiopulmonary resuscitation without delay or hesitation, or just leave the old person unattended? I wonder what Confucius, one of the most influential thinkers in Eastern philosophy and a representative of Eastern culture (4), might say. What would the saying, "Do not inflict on others what you yourself would not wish done to you," lead us to do for the centenarian (5)? It may be beyond our imaginative capacity to know what we would or would not want to have done for ourselves if we were 100 years old. Even Confucius might say that it depends on the individual case.

Centenarians may have diverse preferences for the medical care provided for them. Whether or not they would desire a particular medical intervention to keep them alive would naturally depend on their physical situation and human relationships at the time. Those who have continued to live actively in society may desire medical care that would allow them to survive and maintain the same level of activity and quality of life. However, some may feel that they have lived long enough and that they are ready to die, satisfied with the full life they have lived.

One Japanese writer who became famous in his late sixties, and who is now in his nineties, wrote that he has had multiple operations to survive and continue working for as long as possible, and is still on the active list as a writer in Japan. However, he has reported that other famous Japanese writers, many of whom he knew well, accepted death calmly, refusing invasive interventions (6). In 2012, a 94-year-old man ran for the Lower House election (7). A famous centenarian doctor is an opinion leader in the Japanese society and in its medical communities. Some centenarians suffering from pain and agony and those who despair or grow tired of their

lives may desire euthanasia. Those with consciousness disturbance and advanced dementia may not have any desires at all. Advance directives can arguably be used in these situations, but these are rarely written. Moreover, even if they were available, the likelihood that people would respect the directive and follow through would largely depend on the preferences and intentions embraced by others such as the patient's family and healthcare professionals in charge.

The Japanese phrase, "Mo Toshi Dakara" ("I'm old enough" or "He or she is old enough"), requires close scrutiny. "Mo Toshi Dakara" usually implies that because of one's old age, it is very natural for one to die by accepting that fate. Of course, decisions based on the sentiment of "Mo Toshi Dakara" do not have reliable scientific grounds, but rather have been strongly informed by our instincts, deep thoughts, and clinical experiences cultivated over many years. In fact, I have actually heard that many Japanese physicians and patient families use this term at the bedside of elderly patients. The effect of the "Mo Toshi Dakara" sentiment is not always trivial, either. I would assert that sometimes it is necessary to tell a patient's family that the patient will die because of his or her old age. Many medical professionals are also likely to turn to the "Mo Toshi Dakara" sentiment, as it convinces them that it is very natural for very old individuals to die, and allows them to justify not using medical interventions when they are taking care of very old patients. Patient families are also known to share this sentiment, and some might say, "There is no need for further interventions. My mother is old enough to die."

Anyone, regardless of whether they are medical professionals or not, can easily warm up to ideas and technologies such as organ transplant from brain-dead persons or assisted reproductive technology if they are exposed to them for a sufficient length of time. In a similar manner, repeated or perhaps daily exposure to very old patients including centenarians in clinical settings may diminish the sense of surprise and discomfort in medical professionals. At the end of the day, these medical professionals may start to feel that it would be very natural to treat these very old patients aggressively. Japan has been an aging society already now for several decades, and patients in their 90s are already quite common in the clinical setting. It is highly probable that many healthcare professionals will soon come to believe that active care for patients over 100 years old is rather natural, and not extraordinary. When that happens, medical professionals are likely to slowly lose their sense of "Mo Toshi Dakara," and treat old patients including the centenarians at an increasing

frequency, rather than declining treatment with the reasoning that they are too old for it or that they are old enough to die.

My assumption is that many medical professionals would tend to refrain from performing cardiopulmonary resuscitation for a 90-year-old patient, solely due to the patient's age; in fact, they would likely reason that it is rather futile. However, in the near future, a considerable portion of Japanese physicians might naturally come to the conclusion that they should treat centenarian patients aggressively using even intensive care or major surgical operations. With increasing numbers of centenarians in clinical settings and in society, medical professionals as well as the general public will also have an increased awareness and acceptance of centenarians as commonplace. In addition, fewer and fewer people will think that medical care for them should be withheld or withdrawn simply because they are 'old enough' or because it is futile.

Let us consider the viewpoints of the families of the centenarian patients. From my own clinical experiences as a physician studying clinical ethics, I would speculate that some people with centenarian patients would desperately ask medical professionals in charge to do everything possible to keep their parents alive as long as possible, regardless of their physical and mental conditions. From a third-party standpoint, death at the age of 100 years is quite natural and constitutes a good, peaceful death that everyone hopes for, at least at present.

However, for some relatives such as spouses, children, or even grandchildren, the death of the centenarian would not seem natural at all and thus difficult to accept. Regardless of patient age, for the blood kin, a centenarian spouse, sibling, or parent remains such from their subjective and personal perspectives. Their love for the centenarian patient would likely lead them to request all possible interventions to extend the life of their loved one. From the family's perspective, the centenarian will never be just another very old dying patient.

Socially speaking, however, increasing medical costs for the aged would be a huge burden on the younger generations, and the already growing difference in financial status between generations would only increase further. Japan is already facing some staggering issues regarding decreased social security services such as pensions, medical and welfare costs, the younger generation's burden of caring for the elderly, and debates about how quality healthcare should be maintained (8).

In an argument known as the "fair inning argument (FIA)," it is suggested that those who have not yet reached a normal life expectancy should have a stronger claim on medical resources than those who have (9). This is often asserted by those who wish to limit the medical care for

the elderly. However, we must focus not only on the duration of their lives, but also on what they received during their lives. No one knows the exact normal life expectancy that should be applied to individuals, and these only represent statistics. Hughes suggests that individuals need to be treated respectively. In the same manner that those with lower incomes should not be excluded simply because they, as a group, are statistically less likely to contribute to the whole, groups of older people should also not be excluded simply because they are old. In any case, the FIA requires consideration of a qualitative component, as individual innings cannot be fairly judged solely on the basis of their length. This type of consideration of the elderly and who they are, as well as the topic of ageism, leads us to one conclusion: older people form a heterogeneous group, and if we are to do the right thing for them, we must treat them individually (10).

I would also assert that we cannot blame the centenarians for their longevity. In fact, it is not their “fault” at all, no matter what living conditions they would end up as a centenarian. No one reaches 100 years old solely by self-determination or self-control. General social circumstances, available medical interventions, and one’s inherent personalities, together with destiny and chance significantly contribute to their health, well-being, and lifespan. Thus, we should not punish them for what they have not done by depriving them of desired and necessary medical interventions.

We have always attempted to advance medical science and healthcare for better health and longer life. New technology and novel findings in medicine have always been received enthusiastically, and drugs for anti-aging or longevity are always welcomed, because long and healthy life is the most valued prize among people in our society. This trend is unlikely to end, and no one is likely to even try to slow down the progress. Thus, if too many centenarians existed in our community as a consequence of general societal intentions, desires, and activities, then those who should be blamed for difficult problems related to the aging society are not the elderly, but the whole society. Human life is fragile, so we should not deprive others the chance to live. I therefore cannot support the position of those who argue for withholding medical interventions from centenarians due to the assumption that the younger generations will be better off by limiting their healthcare offerings for the elderly.

Ethical Principles and Values Relevant to a Just Healthcare System for Centenarians

Particularly in the context of the healthcare system, situations and problems related to the advent of centenarians in our society have been

reviewed from personal, medical, and social dimensions. What principles or values should be respected and protected in order to enact a just healthcare system for centenarians in our society? Currently existing valuable concepts in ethics and rights will be tested soon. Would ethical principles such as autonomy, beneficence, non-maleficence, and justice effectively resolve difficult dilemmas caused by the newly arriving centenarian generation? In the context of disputes over the appropriateness of life-sustaining treatment for super old patients, what might be clarified by a consideration of human rights? Will we need a novel groundbreaking value to cope with super-aging societies? Could the concept of “kizuna” (human ties, human bonds, or solidarity), a recently popularized concept that attracted much attention after the 3.11 earthquake disaster in Japan, serve this very purpose?

Given the vast diversity in mental and physical conditions and human relationships among centenarians, the subjective nature of their quality-of-life perception, and inconsistent social attitudes towards centenarians, a clear respect for autonomy and self-determination may be the most useful tool to guide us in making just decisions regarding what to do for centenarian patients. In many cases, however, the decision-making capacity of a centenarian would be considerably compromised. As mentioned above, the use of advance directives have been less effective with regard to the objective of respecting patient autonomy. In addition, from the social standpoint, situations might arise in which we could not accept an individual’s medical decisions if they negatively affected other’s welfare or basic rights.

For example, respecting a centenarian’s decision to use every possible medical resource to live as long as possible might deprive younger patients of necessary medical care or put an unacceptably heavy burden on other people. On the other hand, if the centenarian decided to die with dignity without any medical interventions, society might interpret this as the patient stating that centenarians should readily accept one’s death because they live long enough and are old enough to die “naturally.” As such, unconditional acceptance of centenarian autonomy could be harmful.

I find it difficult to believe that we could all come to a consensus regarding the definition of common and essential qualities that compose human dignity. The composition of human dignity varies widely by individual, culture, religion, society, and time period. In cases that involve sick centenarians, the best interest of the patient is not always clear, and what constitutes harm, especially when a patient is only partially conscious, severely demented or comatose, can be ambiguous. The decisional power of the concepts including a peaceful death, nature, senility, and “being

human,” is questionable in clinical judgments, especially in life-and-death situations and different people would have different interpretations and find diverse meaning in them. This is also the case for the sentiment of “Mo Toshi Dakara.” While human ties are undoubtedly regarded as highly precious and important in present-day Japan, one question that needs to be addressed concerns whether centenarians are considered part of those ‘ties’ or not. Newly arriving centenarians could be perceived as aliens.

An unprecedented new ethical principle or novel normative concept may be necessary to help our society confront these issues raised by the arrival of a number of healthy centenarians as well as sick ones. Unfortunately, I have yet to identify either of these, and it would suffice to say that no others have succeeded in this either. As such, I would like to ruminate on the concept of a just healthcare system for centenarians from a different viewpoint, i.e., the standpoint of human happiness. I hope to propose a solution that would allow for the happiness of the individual, one’s family, and the community.

Regardless of what we are currently, we may be the centenarians of the future, and thus we must create a society in which centenarians can live happily. To this end, it would be helpful to identify what factors make the life of a centenarian unhappy. Pain, physical suffering and limitations, and dependence on others are all medical factors contributing to the unhappiness of centenarians, while loneliness, worthlessness, uselessness, emptiness, boredom, and the feeling that one is unloved or not needed would also make centenarians very unhappy.

Francois Lelord, a French psychiatrist and writer, once explained that to be happy, it is important to be able to live with people you love, and that there is no point to living for 100 years if you are all alone (11). He also asserted that persons you love should also be able to lead a decent life safely and without any significant lack: we would be unhappy if our loved ones were not happy. In addition, it is important to have something for which we live as well as the feeling that we are important to others and to ourselves. In addition, living environments should be comfortable to a certain extent. Centenarians may have difficulty achieving their happiness in a society where so much money is poured into healthcare but so little is invested in the other living environments (11).

Thus, living in a society in which descendant generations can live peacefully and safely would also make centenarians happy. To that end, no one should be cut off from healthcare arbitrarily, discrimination and special treatment should be prevented, and deprivation of anyone’s future and dreams, regardless of their age, should be avoided. Nobody should be sacrificed, and even the most vulnerable should be able to live.

Discrimination against the elderly and neglect of our youth are equally unacceptable.

Unfortunately, healthcare resources are clearly limited, and a certain capacity exists for Japan as well as the earth as a whole. Suppose that we are passengers of a boat named "Nippon (Japan)-Maru." She is about to sink any minute, due to the weight of the passengers. Imagine that 10 passengers are on board, one from each decade ranging from the teens to 100s. All passengers will drown unless one is thrown into the sea. What should be done? Frankly, sound ethical judgments employing actual problem-solving techniques are quite impossible in situations such as this one. In fact, it is likely that a strong person or several strong persons would forcibly throw the weakest from the boat. Thus, our best efforts should be made in advance to avoid such a situation altogether.

While this does not constitute a bright or novel idea at all, all societal members including the centenarians should display mild altruism for one's own benefits, i.e., to be happy and make mutual concessions to make others happy. A give-and-take relationship is more important now more than ever. As mentioned earlier, most human beings are not happy when they are all alone. Most of us are not saintly and cannot be completely unselfish. Thus, a wise policy to affect happiness for all would be to share each other's pain and inconvenience. At the very least, a healthcare policy to keep centenarians from using expensive medical interventions, to put them in hospices automatically, or to force them to pay 100% of their medical fees is unacceptable. In the same vein, "granny dumping" (abandonment of the elderly) should also be forbidden.

Abusive and unwise use of medical treatments (e.g., antibiotics for simple viral infections, fluid replacement for fatigue due to excessive workload, or inpatient care for social reasons) must stop. In addition, patients in all age groups must work to prevent moral hazards (e.g., ambulance use for non-critical or non-urgent case, or using the emergency room to obtain a non-emergent medication). Self-pay rates could be increased according to patient income, which could help maintain a strong healthcare system. The national insurance policy may have to focus and limit its coverage for cases involving high medical risk (8), so self-help efforts put forth by patients in every age group are critical. Everyone must endure some inconvenience and share each other's pain as we live together in a society. It is necessary to have medical cost paid to some extent by the elderly including the centenarians working well, and it may be necessary to increase co-payment depending on the income of the elderly. The principle of human ties may underlie this type of thinking. However, my

position is primarily concerned with individual happiness, rather than the intrinsic value of “Kizuna,” or human ties.

What should we do if, despite our best efforts, measures and policies noted above, the “Nippon-Marū” begins to sink due to the weight of the 10 passengers? There is no good ethical answer. However, I would imagine that a sage, centenarian passenger in the boat may demonstrate the virtue of compassionate concession by leaving the boat for the future happiness of the youth, regardless of whether his or her descendants were among the younger people on the boat. If I were the centenarian in the sinking boat, I would feel obliged to do so. However, without strong convictions such as “I have already lived long enough,” “I have no remorse or regret,” “it is time to go,” “Thank you for everything,” or “it is worth more to have all of you live instead of me,” no one would be willing to sacrifice their life.

Finally, it is extremely important to mention the healthcare-related issues for centenarians whose cognitive function is impaired. I would argue that it is completely useless to prolong the life of those who lack any ability to appreciate happiness or unhappiness in the absence of others who desire their survival. Furthermore, if the patient’s family or others suffered and became unhappy due to the burden of care for their unconscious family member, it would be acceptable for us to terminate life support for the centenarians with no higher brain function, as the lack of this function determines whether we are happy or unhappy.

CHAPTER TWO

AN ETHICAL VIEW ON THE FIRST CLINICAL IMPLEMENTATION OF NEW STYLE PREIMPLANTATION GENETIC DIAGNOSIS OF EMBRYOS IN JAPAN: BIOETHICAL RESEARCH REGARDING THE STATE-OF-THE-ART ASSISTED REPRODUCTIVE MEDICINE

MASAYUKI KODAMA

Foreword

Preimplantation Genetic Diagnosis (PGD) is a state-of-the-art reproductive technology aimed at the prevention of the tragic reality of abortion following prenatal diagnosis. In Japan, where since 1998 the clinical implementation of PGD has been strictly regulated, the Japan Society of Obstetrics and Gynecology (JSOG) commenced the augmentation of the clinical implementation of PGD through the publishing of its June 2010 report, *Opinions on Preimplantation Genetic Diagnosis*. However, on July 11, 2012, the Yomiuri newspaper published an article on the unauthorized implementation of new style PGD that used comparative genomic hybridization (CGH) in numerical chromosomal abnormality examinations for preventing abortion by Dr. Tetsuo Otani, president of Otani Ladies Clinic, which was not endorsed by the JSOG. Following this article, on July 27, the JSOG released the Declaration of the Japan Society of Obstetrics and Gynecology Regarding 'PGD Media Coverage'. Since that time, the JSOG has been thrown willy-nilly into a debate on the augmentation of PGD implementation. In this article, I will identify the new state of affairs brought about by Dr. Otani's new and effective cure

for miscarriage thought to be caused by numerical chromosomal abnormalities, as well as a bioethical bottleneck in the case of new style PGD implementation that needs to be solved (1), and I will submit that bottleneck to an ethical examination (2).

The New State of Affairs Brought about as a Result of the Publication of the Clinical Implementation of New Style PGD in Japan, and a Bioethical Bottleneck in the Implementation of New Style PGD

The Development of PGD and its Clinical Implementation Abroad

The first successful clinical implementation of PGD on a patient suffering from a critical hereditary condition (the world's first cases of gender diagnosis and PGD by Polymerase Chain Reaction (PCR)) for the prevention of the tragic reality of abortion following prenatal diagnosis was performed in 1989 at Hammersmith Hospital in Great Britain. Thereafter, whereas German-speaking countries and countries such as Italy are passive in the clinical implementation of PGD, English-speaking countries, in particular the US, have been active in the clinical implementation of PGD. PGD was first performed at Cornell University's medical center in 1993 on a patient in danger of chromosomal abnormalities-caused miscarriage (the world's first case of preimplantation genetic screening (PGS)), and since achieving pregnancy in this first case, clinical implementation of PGD has been augmented focusing on patients with critical hereditary conditions and those in danger of chromosomal abnormalities-caused miscarriage. In 2008, remarkable treatment results were reported at Dr. Santiago Munné's US facility, where new style PGD (comprehensive analysis of all chromosomes possible) has been implemented for preventing abortion instead of the PGD that had been used previous to this time (only limited chromosome analysis possible).

The Current State of Affairs in Clinical PGD Implementation in Japan and the JSOG's Response

The JSOG, in battle with the ethical issues related to reproduction, while being presented with concerns from disability groups in Japan concomitant with the clinical implementation of PGD (concerns that PGD could lead to the selection of life and the denial of the existence of people

with disabilities), limited PGD implementation in its 1998 regulations to people with ‘critical hereditary conditions’. The JSOG then added a comment to the effect that the diagnosis of genetic disorders should be seen as basis for PGD. In short, it was made clear that gender diagnosis and PGS as something different from genetic disorder diagnosis could not be approved, so there was no margin for making the causal factor in abortion of ‘chromosomal abnormality (structural abnormality and numerical abnormality)’ a reason for PGD implementation.

However, in its 2006 regulations, the JSOG decided to expand PGD implementation to include ‘chromosomal translocations (reciprocal translocation and Robertsonian translocation)’ among its listed number of ‘structural chromosomal abnormalities’. Following this augmentation, the JSOG newly added the following as approved reasons for clinical PGD implementation: Duchenne muscular dystrophy (DMD); myotonic dystrophy (MD); adrenoleukodystrophy (ALD); Ornithine transcarbamylase deficiency (OTC deficiency); Leigh disease, and ‘chromosomal translocation-caused habitual abortion’. Furthermore, in its regulations issued in 2010, the JSOG decided to add to its 2006 regulation list not only ‘critical hereditary conditions’ but also ‘structural chromosomal abnormality-caused habitual abortion (including recurrent abortion)’ as a reason for PGD implementation.

Then, on July 11, 2012, it was made public in the Yomiuri newspaper that Dr. Tetsuo Otani had on his own initiative, without approval from the JSOG, implemented new style PGD in numerical chromosomal abnormality tests for the prevention of abortion (97 cases from February 2011 until May 2012). Dr. Otani’s PGD treatment results were revolutionary (e.g. of 97 frequent miscarriage patients with an average age of 39.1, 53 patients had successful fertilized egg cell womb implantation, of whom 39 became pregnant and 16 gave birth. In comparison with the 25% pregnancy rate in the common IVF-ET transplantation procedure, the 74% pregnancy rate among successful fertilized egg cell womb implantation patients with an average age of 39 is 3 times as high). However, his violation of JSOG regulations (guiding principles) is without argument. JSOG chairman and Kyoto University professor, Ikuo Konishi, who dealt with the media coverage over this violation, published in the same newspaper on the same day the following opinion on the augmentation of PGD implementation, “There are members of national disability groups who are opposed to the technology, so we must widely and purposely debate the problem of implementation of new style PGD within our society in order to gain consensus. We cannot allow technology to take the lead.” Following this statement, on July 27, 2012, the JSOG clearly showed its stance with the

release of the Declaration of the Japan Society of Obstetrics and Gynecology Regarding Media Coverage Concerning 'Preimplantation Genetic Diagnosis' under the signatures of JSOG chairman Ikuo Konishi, and Ethical Committee chairman Kazunori Ochiai. Two points were made in this release.

In relation to cases of unauthorized performance (of, author's note: PGS) other than those cases deemed as suitable by this Society, we clearly state that this conduct will never be approved.

We express our concerns that through media coverage inappropriate information concerning this problem has been widely dispersed within society.

In support of this second point, the JSOG stated that: there is insufficient scientific evidence to just assert that new style PGD (PGS by CGH) entails 'a rise in the pregnancy rate' and that it is 'good news for infertility' (July 11, 2012 Yomiuri newspaper article), 'and that there is a possibility that people will gain too much hope and have misunderstandings'. 'A meta-analysis (an analysis of a multitude of published scientific papers) has made it clear that the performance of PGS (author's note: new style PGD) does not contribute to the rise in the pregnancy and child birth rates'. 'In 2010, ESHRE also released a declaration stating that, because of the fact that a scientific basis cannot be found for the value of PGS (author's note: new style PGD) in cases of recurrent miscarriage, implantation failure and with women of advanced age, a Randomized Controlled Test (RTC) involving several facilities is required'.

The New State of Affairs Brought about by Dr. Tetsuo Otani's Clinical New Style PGD Implementation and a Bottleneck in the Implementation of New Style PGD

Even though, at this stage, the JSOG does not approve the implementation of new style PGD (PGS by CGH) on numerical chromosomal abnormality patients, it can be predicted without difficulty that, as a result of the publication of the revolutionary results gained by the implementation of new style PGD on numerical chromosomal abnormality patients, circumstances will arise in which not only 'structural chromosomal abnormality carriers (including translocation chromosomal abnormality carriers)', but also the JSOG non-endorsed numerical chromosomal abnormality patients (chromosomal abnormality patients in general), can unanimously hope to receive new style PGD treatment at the Otani Ladies Clinic. In proof of this, Dr. Otani has relayed the fact that since the July 11, 2012 Yomiuri article, the number of infertility patients applying for

new style PGD treatment at the Otani Ladies Clinic has witnessed a sudden increase by a factor of 10.

How will the JSOG respond to the foreseen new state of affairs? If the treatment results of new style PGD implementation were the only problem, it would also have been possible for the JSOG, once their stance had been clarified in their [Declaration] of July 27, 2012, to observe how the situation would develop and to tacitly permit new style PGD implementation with miscarriage patients visiting the Otani Ladies Clinic. However, things are not as simple as this.

In Japan, due to such factors as the rising age for first pregnancies as a consequence of greater participation of women in society, the number of people suffering from infertility is increasing. Many gynecologists taking the side of infertility patients would like to implement new style PGD, the 'good news for infertility', with older women. However, there exists a bottleneck in this case consisting of 'concerns that new style PGD may lead to the selection of life and the denial of the existence of people with disabilities'. With these concerns in mind, the JSOG has stated in its July 27, 2012 Declaration that CGH, 'on the one hand, entails the possibility of gaining useful information for future treatment, but its application should be treated with the utmost care'. In my opinion, the Gordian Knot, the most important bioethical issue, must be cut. Not only the JSOG, but also scholars of bioethics, whether pro or con, should rapidly construct a tightly knit code of conduct.

Considering How to Solve the Bioethical Bottleneck

As stated above, the evidence behind the reason that the careful position of the JSOG in the clinical implementation of new style PGD (PGS by CGH) does not break down can be found in a recent meta-analysis that has been published in the *2010 ESHRE (European Society of Human Reproduction and Embryology) Declaration*, that includes the *Opinion of the American College of Obstetrics and Gynecology (ACOG) Committee* promulgated in March 2009 (Harper, 2010; Harton, 2011; ACOG 2009).

The other side of the story is, that not only Dr. Munné and Dr. Otani, but also many recent international papers, publish highly favorable results for new style PGD clinical treatment. For example, Yang's paper shows the results from a prospectively randomized pilot study, claiming a 41.7% to 69.1% increase in the continued pregnancy rate with new style PGD, when single blastocyst transfer was performed on patients under 35 years of age (Yang, 2012). Hodes-Wertz's paper shows the result of a decrease

in miscarriages to 6.9% with new style PGD in patients unable to carry to full term without a clear cause (Hodes-Wertz, 2012). Forman's paper shows an increase from 41.8% to 55.0% in the continued pregnancy rate with new style PGD using single blastocyst transfer (Forman, 2012). The pregnancy rate even increased in the older group (average age of 37.3) who received PGD, when compared with the group (average age of 34.2) who did not receive PGD. Al-Asmar's paper recommends PGD, old and new style, for patients who have had a miscarriage caused by aneuploidy, as the proportion of fertilized egg cells with aneuploidy in aneuploidy miscarriage patients was almost twice as high as the proportion in non-aneuploidy miscarriage patients (2012). Concretely speaking, whereas in patients without experience with miscarriage caused by aneuploidy the rate of fertilized egg cells with aneuploidy was 34.0%, this rate was 67.8% in patients whose previous miscarriage caused by aneuploidy took place after natural impregnation, and the rate was 65.8% in patients whose previous miscarriage caused by aneuploidy took place after IVF impregnation. Scott's conference summary shows the results of a prospective randomized controlled trial claiming the effectiveness of comprehensive chromosomal PGS on blastocysts using a different method called SNP array (2010). Treff's conference summary clarifies that an important reason for not being able to establish PGS effectiveness is that the fertilized egg cell implantation capability in case of blastomere biopsy decreases whereas the implantation capability shows almost no decrease in case of blastocyst biopsy (2011).

Why should there be such huge discrepancies of opinion between the cautious JSOG camp and the advancement camp of Dr. Otani regarding the effectiveness of new style PGD in the face of so many numerical chromosomal abnormality-caused miscarriage patients?

In the following section, we will consider the background reasons that are troubling the JSOG, that is to say, the ethical bottleneck of 'concerns that new style PGD may lead to the selection of life and the denial of the existence of disability patients', after first confirming the usefulness of the advanced medical technology of new style PGD.

The Usefulness of New-Style PGD

One weak point of the FISH (fluorescence *in situ* hybridization) method, that has been used so far to date is that it only permits the analysis of genetic information from a limited number of chromosomes, allowing for a maximum of 12 chromosomes to be analyzed at once. Furthermore, because the limit for segmentation without compaction is 1/8 embryo

(fertilized egg cell) in case of PGD and PGS by FISH, it is necessary to perform 1 or 2 embryo biopsy on 4-8 week old embryo blastomeres. However, since the implantation rate will decrease to a certain extent by performing a biopsy, this decrease was compensated by removing fertilized egg cells with a chromosome abnormality. The miscarriage rate will certainly go down when fertilized egg cells with a chromosomal abnormality are removed, but the situation is such that an increase in the implantation rate of IVF fertilized egg cells after biopsy cannot be achieved. When the above facts are taken into account, it stands to reason that with old style PGD, i.e. PGD and PGS by FISH, which require biopsy, clumsy physicians could end up damaging fertilized egg cells and, as a result, a 'pregnancy rate increase' shall not be witnessed.

Furthermore, the data being held by the JSOG for their own scientific evidence for the reasons for their unrelenting cautious attitude towards clinical implementation of new style PGD (PGS by CGH, SNP array and quantitative PCR) are old, whether they are those from the *March 2009 ACOG Committee Opinion No. 430*, or those from the *2010 ESHRE Declaration*. The data from both these publications are based on treatment results from old style PGD (PGS by FISH). Since Dr. Santiago Munné's publication at the 2008 US Conference on Reproductive Treatment on the effectiveness of achieving pregnancy through CGH implementation in the comprehensive genome DNA analysis of all chromosomes using trophectoderm cells obtained by performing a blastocyst biopsy, CGH has come to be implemented for the highly accurate selection of fertilized egg cells without aneuploidy, necessary in order to elevate the implantation rate in infertile women with fertilized egg cell implantation failure caused by frequent aneuploidy (Munné, 2008). PGS by CGH (new style PGD) has been attracting attention ever since as an alternative method for PGS by FISH (old style PGD). Given that the JSOG extols scientific evidence for its own opinions, it should also take data from treatment results of new style PGD, that has spread as the technological alternative for old style PGD since 2009, as the foundation for its argument. It can be expected that, from now onward, Randomized Controlled Tests showing the effectiveness of new style PGS will come out one after the other.

On the other hand, in addition to the fact that new style PGD allows for the analysis of all chromosomes at once, it has almost no influence on the implantation rate, since only 2 or 3 trophectoderm cells will be collected from the several tens to approximately 100 cells that are obtained by performing a blastocyst biopsy. And because even clumsy physicians will not cause much damage to the embryo here, the merits of removing fertilized egg cells with chromosomal abnormalities should be clearly

apparent. Regarding it rationally, it could be expected that new style PGD, i.e. PGS by CGH, allowing for the comprehensive analysis of all chromosomes, will achieve greater infertility treatment results more than possible with IVF-ET, in which embryos with a visually appealing form are selected.

If this is true, we are forced to consider that there must be a different and even larger issue than the advanced reproductive technology scientific evidence problem that lies hidden behind the assessment of the JSOG top echelon regulation of new style PGD implementation.

The Pretexts that are Troubling the JSOG, i.e. the Bioethical Bottleneck Consisting of the ‘Concerns that New Style PGD may lead to the Selection of Life and the Denial of the Existence of Disability Patients

The assertion of Dr. Otani and the reputation of former JSOG president and Keio University professor Yasunori Yoshimura were published in the August 6, 2012 issue of *AERA* magazine (Asahi Shinbun, 2012). With this article as a lead, the following is a consideration of the ‘concerns that new style PGD may lead to the selection of life and the denial of the existence of disability patients’.

When the *AERA* journalist who wrote this article straightforwardly began his inquiry by stating, “there are voices who say that PGD touches on the selection of life,” Dr. Otani responded in the following manner.

I do not think that what I do is selection. Preimplantation fertilized egg cells cannot be legally seen as life. I think of new style PGD as a technology for the creation of life. A ‘natural screening process’ inside the uterus weeds out most egg cells with numerical chromosomal abnormalities. All I am doing is to avoid the danger of these fateful fertilized egg cells beforehand.

Furthermore, Dr. Otani stated his belief that PGD of preimplantation fertilized egg cells was preferable to the prenatal diagnosis of the fetus. The reason that he gave was as follows:

In case an abnormality of the fetus is found after prenatal diagnosis and, in the end, it is decided to interrupt the pregnancy; the woman’s body and mind are shattered to pieces. I believe preimplantation fertilized egg cell diagnosis performing the process of selection at the fertilized egg cell stage to be more desirable than prenatal diagnosis entailing the possibility of a miscarriage, something tragic to both the mother and the child.

Former JSOG president and Keio University professor Yasunori Yoshimura refuted the above assertion as follows: