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IFFS SURVEILLANCE 07

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IAN COOKE, AND ROGER KEMPERS

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IFFS Surveillance 07

General Editors: Howard W. Jones, Jr., Jean Cohen, Ian Cooke, and Roger Kempers

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Statement of general purpose

Howard W. Jones, Jr., M.D., and Jean Cohen, M.D.

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Internationally, there is a wide divergence in views on the methods and the content of surveillance of assisted reproductive technologies (ART). This was clearly brought out by "IFFS [International Federation of Fertility Societies] Surveillance 98," published in *Fertility and Sterility* 1999;71(Suppl 2) and "IFFS Surveillance 01," published in *Fertility and Sterility* 2001;76 (Suppl 2), as well as by "IFFS Surveillance 04," published in *Fertility and Sterility* 2004;81(Suppl 4).

The 1998 data were presented to the national delegates who had participated in the 1998 survey at the IFFS meeting in San Francisco, California, in October 1998 in the hope that at least some of the discrepancies brought out by the survey could be resolved. This effort had limited success, because the delegates were concerned that they were not empowered to authorize a deviation from the situation as revealed by the survey. Thus, consensus on the various issues remains elusive.

Because of the experience in trying to get consensus for the 1998 survey, this effort was not repeated with the data collected and published in "IFFS Surveillance 01" and in "IFFS Surveillance 04." An effort was made simply to record the situation as it existed. Indeed, that will probably be the fate of "IFFS Surveillance 07," which will be presented to the delegates at the IFFS meeting in 2007.

The divergence of views on various issues makes it appear likely that the exact purpose of surveillance is elusive. Historically, surveillance was initiated in response to public concern about a new technology that dealt with the mysterious origins of the human being. Thus, the details may be unimportant as long as the public believes that some type of surveillance is in place. However, one hopes that the scientific community would strive for a higher goal. Indeed, the current discussions about multiple pregnancies and the number to transfer are evidence of this scientific aspiration.

In the final analysis, the purpose of this survey, "IFFS Surveillance 07", is to document the current status of the various issues in hopes of further steps along the road to a scientifically based consensus.

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Preface (2004)

Howard W. Jones, Jr., M.D., and Jean Cohen, M.D.

Eastern Virginia Medical School, The Howard and Georgeanna Jones Institute for Reproductive Medicine, Norfolk, Virginia; and Rue de Marignan, Paris, France

The development of in vitro fertilization (IVF) and its subsequent variations and extensions, all now included under the umbrella of ART, appears to have generated more interest and concern among religious leaders, bioethicists, and the general public than any other medical procedure. Not only the ethicists and moral theologians but also consumer advocate groups have expressed dissatisfaction with one or more aspects of their treatment or lack of access thereto. This widespread interest and concern has attracted the attention of, or was called to the attention of, the political process.

As a result of these events, many committees and commissions, some governmental, some not, have examined the ethical, legal, religious, medical, and public policy aspects of ART, resulting in the establishment of unofficial guidelines and/or government regulations in many sovereign states wherein ART is practiced. For the purpose of this discussion, the word *guideline* is used to designate sets of rules to be followed voluntarily, generally proposed by unofficial organizations such as an infertility society or a society of obstetrics and gynecology. The word *regulation* is used to designate sets of rules adopted by legislative action, with assigned penalties for violations.

It is to be noted that there are several political entities—Canada, for example—wherein there are neither regulations nor guidelines. It is of interest that the practice of ART in these entities without either guidelines or regulations conform in general to the practices in those entities where guidelines or regulations are in force.

Such guidelines or regulations have taken various forms. They often not only express a particular medical perspective but sometimes reflect the social and religious mores of the particular sovereign state. Some of the guidelines or regulations have been formulated to accommodate special-interest groups. Furthermore, surveillance of compliance with guidelines or regulations ranges from none at all to the issuance of a license by a governing body after designated requirements are fulfilled, often including periodic follow-up inspections.

The specific purposes of this project are as follows:

- Tabulating the practices of sovereign nations or political subdivisions thereof with respect to the adoption of guidelines or regulations;
- Tabulating the methods of surveillance, if any, of such guidelines or regulations;
- Tabulating the similarities and differences of the guidelines or regulations themselves concerning the various procedures under the umbrella of ART, especially in view of identifying within the guidelines or regulations any that may be medically naïve, contradictory, or not supportive of the best interests of the patients, their families, and society in general; and
- Highlighting the changes between this survey, "Surveillance 04," and the previous two surveillances sponsored by IFFS.

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Preface (2007)

Howard W. Jones, Jr., M.D., and Jean Cohen, M.D.

An e-mail survey was developed and one or more individuals from the principal sovereign nations were invited to respond. Answers were obtained from 57 countries, but not all questions were answered in all responses. This explains why in some of the tables that follow some information is not given. The number of centers is an estimate and should not be taken as fact. The coordinators (Natalia van Houten and Keith Gordon) prepared the tables under the various subheadings matched to the questionnaire. The analysis of the survey was prepared by the editors Jean Cohen, M.D., Howard Jones, Jr., M.D., Ian Cooke, M.D., and Roger Kempers, M.D.

This report, "IFFS Surveillance 07," summarizes the various laws, regulations, and/or guidelines established by 57 nations to regulate and oversee the medical practice of ART.

The most striking finding is the great diversity in these laws and guidelines.

The following two questions immediately arise:

1. Why does society wish to oversee ART as opposed to other specific medical procedures?
2. What exactly does society wish to oversee?

An answer to both questions may arise principally from a single source. Historically, there was great objection to the work of the pioneers in IVF. This protest was from a variety of organizations, all under the umbrella of the religious right. Although objections took various forms, the essence of the complaints was that IVF resulted in the destruction of some fertilized eggs, which were considered by the objectors to have the moral status of a human already in being, in other words, of a human being.

It must also be said and emphasized that many religious organizations of various persuasions, as well as a large segment of the population, take the position that the developing human conceptus does not deserve protection by society during early development, which is the situation in the clinical application of IVF.

The divergent views concerning the moral status of the developing embryo are likely the chief cause of the divergent rules and guidelines, because pressure is exerted by adversary groups and individuals on those responsible for enacting such laws or guidelines.

The very fact that it has been necessary to adopt laws or guidelines probably is itself an expression of the tension arising from the various points of view about moral status.

If this analysis is correct, it appears that a consensus on the necessity for and the method of surveillance of ART is unlikely in the foreseeable future. Even physicians and scientists can reflect the societal influences and thought that surround them.

Meanwhile, one hopes that "IFFS Surveillance 07" will prove to be a source of information about these matters and will stimulate more discussion of why and what society is trying to achieve by its monitoring of ART.

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CHAPTER 1: Number of centers

"Surveillance 07" has obtained information from 57 countries (Table 1.1).

For some countries, information sent by different correspondents was identical. For some others, there were differences in the reported number of centers, explained by the absence of an official national registry, or the existence of several small centers with no activity. We compared our list with that of the World Collaborative report on IVF for the year 2000, authored by the International Committee for Monitoring ART (ICMART) (1). Most of the answers, although not identical, are comparable, except in the cases of Brazil (this survey found 200 centers, whereas ICMART reported 38), Egypt (50 vs. 18), Italy (315 vs. 115), and Japan (520 vs. 590).

In June 2006, Lancaster (2) published data on world variations in ART treatment cycle. Among the selected countries, there was up to a fivefold difference in the use of ART clinical services. The highest treatment ratios were in Denmark (1,251 treatment cycles per 100,000 women aged 25–44 y), Finland (1,080 cycles per 100,000), and Australia (954 per 100,000). The lowest treatment ratios were in the United States (237 cycles per 100,000 women aged 25–44 y), New Zealand (328 per 100,000), and the United Kingdom (396 per 100,000). Other European countries such as Belgium (794 per 100,000 women aged 25–44 y), France (667 per 100,000), the Netherlands (612 per 100,000), and Germany (515 per 100,000) had intermediate treatment ratios. Sweden (772 per 100,000 women aged 25–44 y) had a lower treatment ratio than did its Nordic neighbors. Among those countries with high overall treatment ratios, the ratio for women <35 years of age was considerably higher in Denmark (1,567 treatment cycles per 100,000) than in Finland (1,196 per 100,000) or Australia (893 per 100,000) and was almost double that seen in Sweden (772 per 100,000).

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2. Lancaster P. Worldwide variations in the use of ART services. Hum Reprod 2006;21(Suppl 1). Abstr O-061, i23.

TABLE 1.1

Number of centers.

Country	n
Argentina	20–26
Australia	75
Austria	25
Belgium	18
Brazil	105–200
Bulgaria	14
Canada	16
Chile	8
China	178
Colombia	17–18
Croatia	6
Czech Republic	23
Denmark	18–23
Ecuador	6
Egypt	50–51
Finland	18
France	93–100
Germany	120
Greece	50
Hong Kong	7
Hungary	11
India	100–200
Ireland	7
Israel	24–27
Italy	315
Japan	520–590
Jordan	16
Korea	122
Latvia	4

Cohen. Number of centers. Fertil Steril 2007.

TABLE 1.1

Continued.

Country	n
Lithuania	3
Malaysia	23
Mexico	40
Morocco	14–16
Netherlands	13
New Zealand	3–6
Norway	10–11
Peru	4
Philippines	3
Portugal	20–23
Romania	15
Russia	51
Saudi Arabia	23
Singapore	8
Slovenia	3
South Africa	15
Spain	203
Sweden	13–15
Switzerland	25
Taiwan	66
Thailand	33
Tunisia	5
Turkey	68
United Kingdom	80–119
United States	399–450
Uruguay	4
Venezuela	5–12
Vietnam	6

Cohen. Number of centers. Fertil Steril 2007.

CHAPTER 2: Legislation and guidelines

ANALYSIS OF SURVEY

Since "Surveillance 04," we have obtained information on 12 new countries, specifically, Colombia, Croatia, India, Latvia, Lithuania, Malaysia, New Zealand, Peru, Philippines, Russia, Thailand, and Vietnam. Despite many attempts, we could not get reliable full information from Bangladesh, China, El Salvador, Saudi Arabia, or Poland.

We continue to classify countries according to the technique of surveillance as follows:

- Countries with national legislation that provide laws covering the practice of ART;
- Countries that have guidelines only, usually provided by a national medical group, and for which there is therefore no legal enforcement, although there may be surveillance, as noted in Sovereign Nations or Political Entities With Voluntary Guidelines; and
- Countries that have neither legislation nor voluntary guidelines.

New laws were enacted in Portugal, Finland, and Spain late in 2006 after this survey was completed and are not reflected in this report.

Table 2.1 shows the number of nations according to the above categories. Figures 2.1 and 2.2 further break down the method of surveillance according to the country. It may be concluded that roughly two thirds of the world population can be accounted for by the survey. It needs to be understood, of course, that access to ART in various countries varies widely.

In some situations, the classification is admittedly arbitrary in that some part of an ART program may be subject to national legislation, whereas other parts and perhaps the major part are covered by guidelines. The United States may be cited as an example. There is no national law covering the clinical practice of IVF. However, the embryological laboratories are often subject to state laboratory regulations, and indeed the federal Food and Drug Administration, which is a national organization, levies severe penalties for violating the transplant of tissue from a donor to a recipient. Thus, programs that use donor eggs or sperm are subject to Food and Drug Administration regulations covering the laws that concern testing of the donors for certain transmissible diseases.

India may be cited as another example of a guideline country, and yet the state accrediting authority has the power to order a clinic to be closed for violation of the guidelines. Indeed, the state authority may delegate the power to levy a fine in the event of any violation. Australia may also be listed as a somewhat special situation in that there is no federal law controlling the clinical practice of IVF; however, some of its provinces, for example, Victoria, have laws that strictly regulate the practice of ART.

In all, 57 nations have been surveyed. It may be noted that the United Nations comprises 198 sovereign states, but it also needs to be noted that many of these can be classified as undeveloped and rather small in population.

Since "Surveillance 04," many countries have changed their legislation or their guidelines. Such is the case with Australia, Austria, Belgium, Canada, the Czech Republic, France, Greece, Hungary, Italy, Korea, New Zealand, Norway, Russia, Singapore, Spain, Sweden, Switzerland, Thailand, Turkey, the United Kingdom, and Vietnam. Most of these countries have considered the changes to be an improvement.

The two most important improvements have been in Belgium and in Greece. In Belgium, a law passed in 2003 on research on embryos in vitro accepted all types of research directed at therapeutic purposes and at increased medical knowledge. This included research for germ-line somatic gene therapy, therapeutic cloning, and the development of embryonic stem cell lines. Because this presupposes the creation of embryos for research, this too is allowed. Other goals such as sex selection for nonmedical reasons, eugenic practices, and reproductive cloning are prohibited. In general, the law expresses a belief in the importance of freedom of research and the acceptance of ethical pluralism in society.

In Greece in 2005, a law was passed referring specifically to married couples and to unmarried women who were either single or living as part of a heterosexual couple. Although lesbian couples are not specifically precluded, legal scholars supported the notion that they are not prohibited by the law. Sperm, oocyte, and embryo donation, as well as surrogacy and preimplantation genetic diagnosis, are allowed. Donations must be anonymous.

In Australia, Italy, Norway, and the United Kingdom, the update was considered to be retrogressive. The major change has been in Italy, where, since 2004, access to ART has been restricted to adult heterosexual couples who are married or living together and who are both alive and in the reproductive period of their lives. Single persons and homosexuals are prohibited from ART. Couples requesting medically assisted procreation or ART must produce a medical certificate confirming a sterile or infertile condition for which no other solution is possible. A maximum of three oocytes can be fertilized, and every embryo has to be replaced, regardless of its quality and the age of the future mother. Cryopreservation or the donation of embryos is not allowed. In Norway, the

TABLE 2.1

How is the use of ART governed in your country?

Country	Statutes or law	Guidelines	Neither statutes nor guidelines
Argentina		Guidelines	
Australia		Guidelines	
Austria	Statute		
Belgium	Statute		
Brazil		Guidelines	
Bulgaria	Statute		
Canada	Statute		
Chile		Guidelines	
China		Guidelines	
Colombia			None
Croatia		Guidelines	
Czech Republic	Statute		
Denmark	Statute		
Ecuador			None
Egypt		Guidelines	
Finland			None
France	Statute		
Germany	Statute		
Greece	Statute		
Hong Kong	Statute		
Hungary	Statute		
India		Guidelines	
Ireland		Guidelines	
Israel	Statute		
Italy	Statute		
Japan		Guidelines	
Jordan			None
Korea	Statute		
Latvia	Statute		
Lithuania		Guidelines	
Malaysia			None
Mexico		Guidelines	
Morocco		Guidelines	
Netherlands	Statute		
New Zealand	Statute		
Norway	Statute		
Peru			None
Philippines		Guidelines	
Portugal			None
Romania			None
Russia	Statute		
Saudi Arabia	Statute		
Singapore		Guidelines	
Slovenia	Statute		
South Africa		Guidelines	
Spain	Statute		
Sweden	Statute		
Switzerland	Statute		
Taiwan	Statute		
Thailand		Guidelines	
Tunisia	Statute		
Turkey	Statute		
United Kingdom	Statute		
Uruguay			None
United States		Guidelines	
Venezuela			None
Vietnam	Statute		

Cohen. Legislation and guidelines. Fertil Steril 2007.

FIGURE 2.1

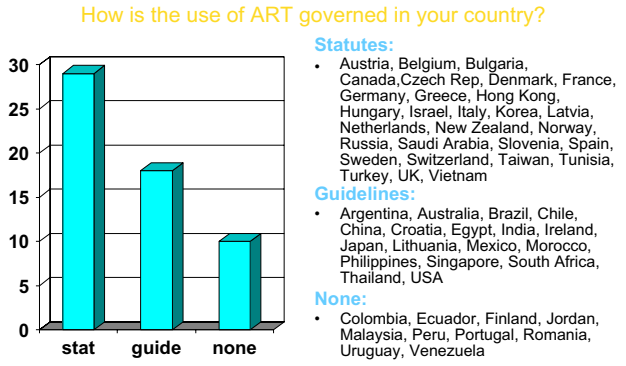

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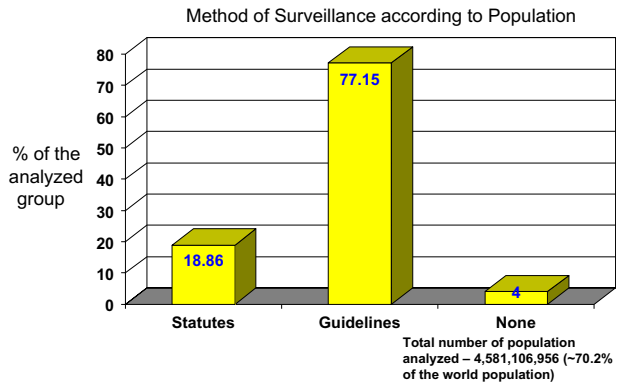
FIGURE 2.2



Cohen. Legislation and guidelines. Fertil Steril 2007.

use of anonymous donors for AID is not allowed. In the United Kingdom, anonymous gamete donation has been ended. This has been considered an improvement by some and a retrogression by others.

Nations or States With Laws and Statutes

For the most part, surveillance is performed by the requirement of the submission of a periodic report, although many nations, for instance, Greece, the Netherlands, New Zealand, Russia, Solvenia, and so on, also have a method of on-site inspection, which many times is unannounced. There are severe penalties for violation of the statutes with regard to clinical practice, and fines are very common, but it further is possible to withdraw licenses in many instances, such as in the United Kingdom or Hong Kong, and, indeed, imprisonment may occur, as for instance in New Zealand, where imprisonment may be for $\leq$5 years or a fine of $>$$200,000 may be imposed in the event of a violation.

Sovereign Nations or Political Entities With Voluntary Guidelines

Guideline countries also resort to a periodic report or on-site visits. The guideline report may be submitted to a quasigovernment agency or to an agency that is quite independent. For example, Japan reports to a group organized by the Japan Society for Obstetrics and Gynecology; the Philippines, likewise. However, in Singapore, the report, although voluntary, is to the Director of Medical Services of the Ministry of Health. In the United States, the report traditionally has been to the Society for Assisted Reproductive Technology subgroup of the American Society for Reproductive Medicine, although that may be changing in the very near future. The Centers for Disease Control and Prevention, which is a US federal agency, issues the report on data collected by a private agency. By definition, there are really no penalties in the guideline countries for violation of the guidelines; that is, there are no fines or imprisonment. However, adverse publicity may be the penalty that is imposed by the accrediting groups in the guideline countries. Guideline countries that approve clinics can withdraw that approval, but of course, this has no official role in controlling the ability of a particular clinic to practice or not to practice.

Entities Operating Without Guidelines or Regulations

There are 11 surveyed nations without any guidelines or regulations of ART. It is notable that practices in these national entities do not differ greatly from those in nations with legislation or voluntary guidelines.

Licensing Body

Among the 29 countries with legislation, 21 have a licensing body (Table 2.2). The composition of the licensing body is quite variable. Details can be seen on the IFFS Website (1). The clinical surveillance of centers is performed in different ways (for details, please refer to the IFFS Website). There are various penalties designed for violation of statutes with regard to clinical practice in 23 countries (Table 2.2). Details of these penalties are quite variable and may also be seen on the IFFS Website. The embryological laboratory surveillance is performed in different ways, and there is laboratory accreditation in 14 countries (1). There are penalties designated for violation of statutes with regard to laboratory procedures in 19 countries (1). Among the 15 countries with guidelines, clinical surveillance is performed in 10 (1). Embryological laboratory surveillance is performed in 8 countries (1).

In the period 2003–2006, there has been more publicity given to violations in Austria, Canada, the Czech Republic, Hungary, Slovenia, and Thailand.

DISCUSSION

Since the IFFS surveillance report of 2004, there have been more countries that have adopted laws. For instance, in the 2004 report, there were 13 surveyed nations without guidelines or regulations, and this time there were only 11. However, some countries with legislation have severely tightened legislation regarding what can be done with the

TABLE 2.2

Countries with statutes or laws.

Country	Is there a licensing body?	How is clinical surveillance carried out?	Are penalties designated for violation of statutes with regard to clinical practice?	What are these penalties?
Austria	Yes	Periodic report	Yes	Fines
Belgium	No	Periodic report	No	
Bulgaria	No	Periodic report	No	
Canada	Yes	other	Yes	Fines or imprisonment, or both (laid out in the Act)
Czech Republic	No	other	No	
Denmark	No	Periodic report	Yes	Fines
France	Yes	Periodic report	Yes	Same as previous law
Germany	Yes	Periodic report	No	
Greece	Yes	Periodic report. On-site inspection	Yes	Criminal and civil penalties include fines, license suspension, and imprisonment.
Hong Kong	No	Periodic report. On-site inspection	Yes	Refer to section 39 of HRTO, p. A1751
Hungary	Yes	On-site inspection	Yes	In serious case, withdrawal of license
Israel	Yes	Periodic report	No	
Italy	No	Periodic report	Yes	600,000 euros and cancellation of license are some of the penalties for doctors. No penalties for patients
Korea	Yes	Periodic report. On-site inspection	Yes	Cancellation of license Suspension of business Fine Imprisonment
Latvia	No	Periodic report	No	
Netherlands	Yes	Periodic report. On-site inspection	Yes	Loss of license
New Zealand	No	On-site inspection	Yes	Penalties depend on the section of the Act. The most severe are 5-y imprisonment and/or a fine of $200,000.
Norway	Yes	Periodic report	Yes	Fines, $\leq$3 mo in jail, and withdrawal of license to practice ART

Cohen. Legislation and guidelines. Fertil Steril 2007.

(*Continued on next page*)

TABLE 2.2

Continued.

Country	Is there a licensing body?	How is clinical surveillance carried out?	Are penalties designated for violation of statutes with regard to clinical practice?	What are these penalties?
Russia	Yes	Periodic report. On-site inspection	Yes	Withdrawal of license.
Saudi Arabia	Yes	No response	No response	No response
Slovenia	Yes	Periodic report. On-site inspection	Yes	From 209 to 20,920 euros
Spain	Yes	Periodic report	Yes	See IFFS Website for details
Sweden	Yes	Periodic report	Yes	Loss of license to perform IVF
Switzerland	Yes	Periodic report. On-site inspection	Yes	Fine or prison sentence.
Taiwan	Yes	Periodic report. On-site inspection	Yes	Suspension of license for ART practice
Tunisia	Yes	periodic	Yes	6-mo imprisonment and/or penalty of 5,000 Tunisian dinars
Turkey	Yes	Periodic report	Yes	Closure of the ART center for a period of time, as issued by a committee in the Ministry of Health
United Kingdom	Yes	On-site inspection	Yes	Depends on problem; center can be closed down. Reproductive cloning is criminal offense. Revocation of license that prevents the continuation of practice. Lesser penalties are conditions placed on the license.
Vietnam	Yes	Periodic report	Yes	Fines for violations

Cohen. Legislation and guidelines. Fertil Steril 2007.

clinical practice. Italy would be a primary example; since the last report, their laws have been tightened to eliminate the fertilization of more eggs than are expected to be transferred and to eliminate cryopreservation. Penalties for violation have been very severe. This has led to a certain amount of fertility tourism by patients from one country to another, in search of a location that permits procedures that cannot be performed in the home country.

It is interesting to note that of the legislative countries in which severe penalties are imposed for violation of the code, all penalties apply to the practitioner and to the clinic, and there appears to be no country with legislation that penalizes the patient for being involved in a procedure that is not covered by the legislation.

It is difficult to document to what degree guidelines are followed. Abundant anecdotal evidence suggests that violation of some aspects may be widespread. For example, in the United States, there is some evidence that the number of embryos to be transferred (as provided by the guidelines) is being exceeded, because there continues to be a very high rate of reported multiple pregnancies. It needs to be mentioned at this point that there is at least one country in the world, Costa Rica, where the restriction against ART is so severe that ART cannot be practiced. The constitutional court

of Costa Rica has held that IVF violates the national constitution in that the constitution provides that personhood begins with fertilization; thus, in view of the fact that IVF may destroy life, it is therefore unlawful to practice it.

SUMMARY

In general, there appears to have been further legislation in additional countries in regard to the practice of ART. Furthermore, in some countries of the world, for example in Italy, legislation has become much more restrictive. Italy has passed very restrictive legislation, specifically that ART must be practiced in couples with a stable relationship; that there is no donor insemination, no surrogacy, no preimplantation genetic diagnosis, and no freezing; that no more than three embryos may be created; and that all created embryos must be transferred. In addition, it needs to be mentioned that in at least one country—Costa Rica—ART cannot be practiced because it is considered to violate the constitutional law that defines the beginning of personhood at fertilization. Countries with voluntary guidelines appear to enjoy public confidence, and public pressure for a change appears to be very minimal in those countries where guidelines are in vogue. As noted in the third paragraph of this chapter, either legislation or guidelines cover approximately two thirds of the world's population.

REFERENCE

1. International Federation of Fertility Societies. Available at: http://www.iffs-reproduction.org/.

CHAPTER 3: Insurance coverage

Third-party payment for clinical ART is subject to great variation from nation to nation (Table 3.1). Of the respondent entities, essentially half have no third-party reimbursement by any national health plan or private insurance companies. The countries without coverage may be seen in Table 3.1. It is interesting and perhaps significant that many of these countries are from areas in the world, especially such as South America, in which Roman Catholicism is dominant, a persuasion that discourages individuals from resorting to IVF.

The United States appears to be the only nation in which the only insurance available is through private sources. In the 2004 report, Turkey was in that category, but Turkey now has a national health plan that provides partial support for ART.

There are six countries that have a national health plan that gives complete coverage. These are Belgium, France, Greece, Israel, Solvenia, and Sweden.

Of particular note is the Belgian plan, which has now been in operation for a sufficient time for the initial results to be available. This plan, which was initiated in the latter part of 2003, provides for six cycles of ART for women <42 years of age, provided that strict criteria are met, as follows: if the patient is <35 years of age for the first cycle, she is limited to a single-embryo transfer; for the second cycle, she may have a one- or two-embryo transfer; for the third through the sixth cycles, she may have two-maximum embryo transfers. If she is between the ages of 35 and 39 years, for the first and second cycles, no more than two embryos may be transferred, and for the third cycle, no more than three. All patients, regardless of age, can have no more than two frozen embryos transferred. Furthermore, no patient is eligible for insurance if she is ≥ 42 years of age. Between the ages of 39 and 42 years, there are no maximum embryo transfer numbers. It is interesting that as of 2005, the initial results from this insurance program had become available, and it is perfectly clear that the number of multiple pregnancies has been greatly reduced; not eliminated, but reduced from a percentage in the 30s to a figure around 10%. It would be anticipated that with further application of this program, the reduction would be even greater. The Belgian program appears to be a great success and could serve as a model for other countries that are interested in controlling the number of embryos transferred and therefore in eliminating the problem of multiple pregnancies.

Israel provides for as many cycles as required, but coverage ceases after the birth of two children to any given couple. In Hungary, the medication cost must be partially paid by the patient. In the United States, insurance coverage is mandated in some 16 states, with variable restrictions from state to state.

DISCUSSION

It is clear that third-party payment for ART is subject to wide variation. At one extreme, there are countries such as Belgium and France, where coverage is essentially unlimited but, as in the case of Belgium, is tied to good clinical practice. At the other extreme are possibly one half of all reporting countries, which have neither private nor public coverage.

SUMMARY

There is no international consensus on insurance coverage for ART. Approximately one half of the surveyed entities had neither public nor private insurance. However, a few countries, for instance Belgium and France, offer very sophisticated coverage to the public sector. Interestingly enough, in Belgium, this coverage is tied to good clinical practice, which may only be possible if the insurance is of a governmental nature.

TABLE 3.1

Is ART covered or reimbursed?

How ART is governed		How is ART covered?		
		National health plan	Private insurance	No coverage
Covered by statutes	Austria	+/Partial		
	Belgium	+/Complete		
	Bulgaria	+/Partial		
	Canada			+
	Czech Republic	+/Partial		
	Denmark	+/Partial		
	France	+/Complete		
	Germany	+/Partial		
	Greece	+/Complete		
	Hong Kong			+
	Hungary	+/Partial		
	Israel	+/Complete		
	Italy	+/Partial		
	Korea			+
	Latvia			+
	Netherlands	+/Partial		
	New Zealand	+/Partial		
	Norway	+/Partial		
	Russia			+
	Saudi Arabia			No data
	Slovenia	+/Complete		
	Spain	+/Partial		
	Sweden	+/Complete?		
	Switzerland			+
	Taiwan			+
	Tunisia	+/Partial		
	Turkey	+/Partial		
	United Kingdom	+/Partial		
	Vietnam			+
Covered by guidelines	Argentina			+
	Australia	+		
	Brazil			+
	Chile			+
	China			+
	Croatia	+		
	Egypt			+
	India			+
	Ireland			+
	Japan	+/?		?
	Lithuania			+
	Mexico			+
	Morocco			+
	Philippines			+
	Singapore			+
	South Africa			+
	Thailand			+
	United States		+	

Jones. Insurance coverage. Fertil Steril 2007.

(*Continued on next page*)

TABLE 3.1

Continued.

How ART is governed		How is ART covered?		
		National health plan	Private insurance	No coverage
None	Colombia			+
	Ecuador			+
	Finland	+/Partial		
	Jordan			+
	Malaysia			+
	Peru			+
	Portugal	+/Partial		
	Romania			+
	Uruguay			+
	Venezuela			+

Jones. Insurance coverage. Fertil Steril 2007.

CHAPTER 4: Marital status

Views about marital status and ART show considerable divergence. Table 4.1 indicates the restrictions on couples by country. Some nations appear to have no requirements, including Australia, Belgium, Brazil, Bulgaria, Canada, Korea, Latvia, Mexico, the Netherlands, New Zealand, South Africa, Spain, Thailand, the United Kingdom, and the United States.

In some nations with requirements, it is possible for single women to be treated, including in Chile, Greece, Hungary, India, Israel, Peru, Russia, and Vietnam. Lesbian couples may be treated in countries with no restrictions and in Israel.

DISCUSSION

Proof of a stable relationship differs. In France, unmarried couples must have a certificate of life in common; in Sweden, a minimum of cohabitation for 2 years is asked. Our survey results show that the majority of societies, either as expressed through legislation or as influenced by religious or cultural issues, appear to prefer a traditional heterosexual family (marriage or stable relationship) and hesitate to provide full access to alternative groups. In Slovenia, there was a referendum on whether to provide service to singles; the result was no, 80% and yes, 20%.

However, more legislation has been passed to recognize homosexual couples in recent years.

There is undoubtedly some demand for ART from single women or lesbian couples. In countries where legislation or guidelines do not provide ART access for alternative groups, there is fertility tourism toward countries where it is permitted (e.g., Belgium, Finland, Greece, and Spain).

Very few studies have been performed on the children of relationships other than heterosexual. Such studies concern essentially donor-insemination children. Brewaeys et al. (1) compared 30 lesbian-mother families with the heterosexual-parent families of 38 donor-insemination children and 30 naturally conceived children. The development of the children was found to be similar. Vanfraussen et al. (2) studied 41 children (7 to 17 y of age) of lesbian parents; 46% of the children wanted to meet their donor. Perry et al. (3) compared 38 lesbian mother families, 73 heterosexual families, and 58 single-, heterosexual-mother families. The findings indicated positive mother–child relationships and well-adjusted children.

SUMMARY

In most countries, ART is supposed to be performed only for heterosexual couples, those either married or in a stable relationship. However, other groups, such as single women and those in homosexual relationships, have gained access to ART in many countries. Follow-up studies in these alternative groups are currently in progress.

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TABLE 4.1

Couple requirements for ART.

How ART is governed	Country	Couple restrictions[a]
Covered by statutes	Austria	Marriage or stable relationship.
	Belgium	No requirements. Permitted for single women and lesbian couples.
	Bulgaria	No requirements.
	Canada	No requirements. Permitted for single women and lesbian couples.
	Czech Republic	Marriage or stable relationship.
	Denmark	Marriage or stable relationship.
	France	Marriage or stable relationship.
	Germany	Marriage or stable relationship.
	Greece	Marriage or stable relationship. Permitted for single women.
	Hong Kong	Marriage.
	Hungary	Marriage or stable relationship. Permitted for single women.
	Israel	Marriage or stable relationship. Permitted for single women and lesbian couples.
	Italy	Stable relationship.
	Korea	No requirements.
	Latvia	No requirements. Permitted for single women.
	Netherlands	No requirements. Permitted for single women and lesbian couples.
	New Zealand	No requirements. Permitted for single women and lesbian couples.
	Norway	Stable relationship.
	Russia	Marriage or stable relationship. Permitted for single women.
	Saudi Arabia	No information
	Slovenia	Stable relationship.
	Spain	No requirements. Permitted for single women.
	Sweden	Stable relationship.
	Switzerland	Stable relationship.
	Taiwan	Marriage.
	Tunisia	Marriage.
	Turkey	Marriage.
	United Kingdom	No requirements. Permitted for single women and lesbian couples.
	Vietnam	Marriage. Permitted for single women.
Covered by guidelines	Argentina	Stable relationship.
	Australia	No requirements. Permitted for single women and lesbian couples.
	Brazil	No requirements. Permitted for single women and lesbian couples.
	Chile	Stable relationship. Permitted for single women.
	China	Marriage.
	Croatia	Marriage or stable relationship.
	Egypt	Marriage.
	India	Marriage or stable relationship. Permitted for single women.
	Ireland	Stable relationship.
	Japan	Marriage.
	Lithuania	Marriage.
	Mexico	No requirements.
	Morocco	Marriage.
	Philippines	Marriage.
	Singapore	Marriage.
	South Africa	No requirements. Permitted for single women and lesbian couples.
	Thailand	No requirements.
	United States	No requirements. Permitted for single women and lesbian couples.
None	Colombia	Stable relationship.
	Ecuador	Stable relationship.
	Finland	Not an issue.
	Jordan	Marriage.
	Malaysia	Marriage.
	Peru	Permitted for single women.
	Portugal	Stable relationship.
	Romania	Not an issue.
	Uruguay	Stable relationship.
	Venezuela	Not an issue.

[a] Formal restrictions or as customary.

Cohen. Marital status. Fertil Steril 2007.

CHAPTER 5: Number of embryos for transfer in ART

ANALYSIS OF SURVEY

Multiple gestations are recognized as a major problem associated with ART. This survey only deals with IVF and was not able to register intrauterine insemination in association with ovulation induction or ovulation enhancement.

According to Nygren (European IVF Monitoring), in Europe in 2003 (1), there was still a 22% rate of twin births, 1.1% rate of triplets, and 0.08% rate of quadruplets (after embryo reduction during pregnancy). Triplet delivery rates were 4.4% in Hungary; 4.3% in Macedonia; and 3.1% in Italy, Portugal, and Bulgaria.

In "Surveillance 04", we observed a general worldwide decrease of the limit in the number of embryos to transfer, from three to four to two to three, regardless of the legislative situation (2). Since the publication of "Surveillance 04", we have observed a further decrease, from two to three to one to two. In the following 26 countries, there has been some implementation of the laws or the guidelines concerning the number of embryos to transfer: Argentina, Australia, Belgium, Croatia, the Czech Republic, Denmark, Greece, Hong Kong, Hungary, India, Israel, Italy, Japan, Latvia, Mexico, Morocco, Norway, Philippines, Singapore, Slovenia, Spain, Sweden, Switzerland, Thailand, the United Kingdom, and the United States. The data summarized in Table 5.1 can be further categorized as follows.

- There are countries in which it is possible to transfer more than three embryos (usually only in older women or those that have previously failed): Greece, Hong Kong, Hungary, Croatia, India, Japan, Singapore, and the United States;
- There are countries in which three embryos is a maximum: Argentina, Belgium, the Czech Republic, Italy, Germany, Latvia, Slovenia, and Spain; and
- There are countries in which two embryos is the rule (with occasional exceptions): Australia, Denmark, Israel, Norway, New Zealand, and the United Kingdom.

Single-embryo transfer is proposed in Nordic countries and imposed in Belgium. Since 2004, Belgian law has allowed funding for the two first IVF cycles if elective single-embryo transfer (eSET) is practiced on women aged <36 years. If it fails, cycles three to six can become two-embryo transfers. For women 36–39 years of age, the first two cycles can involve up to two embryos being transferred, or up to three embryos for patients >39 years of age.

DISCUSSION

Two-embryo transfer, or double-embryo transfer (DET), has become established as the standard of practice in a number of countries, with the expected marked reduction in triplet pregnancies without a reduction in twin rates. Nevertheless, risks also exist for twin pregnancies. The risk of a mother's death is multiplied by threefold, whereas the risk of morbidity increases, due mostly to hypertension and postpartum hemorrhage. The risk of premature delivery increases ninefold. The twin rate is still 30.4% in Korea, 22.8% in Greece, 33.7% in Chile, 30.3% in Canada, and 31.1% in the United States, according to the World Collaborative Report on IVF 2000 (3). In relation to such consequences on the babies' health, the mother's psychology, and the economy of the health system, it has been proposed that only one good-quality embryo should be transferred. This solution was advised by Gerris et al. (4), who showed, over the course of a 4-year program lasting between 1998 and 2002, that eSET would result in a 37% rate of developing pregnancies, with a rate of 1.1% twin pregnancies in case of embryos of good quality. Lesser-quality embryos produced a 20.5% rate of developing pregnancies, with a 4.2% rate of twins. In case of DET, pregnancy rates (PRs) were 35.1%, including 30% twins.

Articles originating from Belgium (5), Sweden (6), and Finland (7) have shown increases in the proportion of eSET in these countries, accompanied by a major decrease in the twinning rate. Bergh (6) reported a live-birth rate of 37.4% with eSET and of 36.6% with DET. The twinning rate was $<2\%$ with eSET.

However, van Montfoort et al. (8) has shown in a randomized controlled trial involving 308 unselected patients that the ongoing PR after eSET was significantly lower as compared with after DET (21.4 vs. 40.3%). However, the twin rate was reduced from 21.0% after DET to 0 after eSET. If the transfer of cryopreserved embryos was included in the results, the probability of a pregnancy after the first ovum pickup would have increased but would not reach the PR of DET.

Many factors explain the resistance to eSET. We know that there are differences in PRs between countries and between centers in the same country. If clinical PRs are $>30\%$ in a fresh cycle and $>15\%$ in a frozen-thawed cycle, it may appear easier to propose eSET than when these rates are lower, taking into consideration the competition arising between centers, especially when ART is not reimbursed. The age of women patients is linked to the expected PR, as is the duration of infertility (the longer the infertility, the worse the results). Laboratory expertise is of vital importance as well. The material means available, themselves derived from the cost of attempts, are also a factor. In countries where the state reimburses IVF at a fixed price, the average success rates of

TABLE 5.1

How many pre-embryos can be transferred, and are there any exceptions?

How ART is governed, by country	Country	Limits on numbers of pre-embryos that can be transferred and any exceptions
Covered by statutes	Austria	Not specified.
	Belgium	Patients aged <36 y: a maximum of 1 in cycles 1 and 2; in cycles 3–6, a maximum of 2. Patients aged 36–39 y: a maximum of 2 in cycles 1 and 2; in cycles 3–6, a maximum of 3. Patients aged 40–42 y: no limits; in cryo cycles, a maximum of 2 always.
	Bulgaria	Not specified.
	Canada	Not specified.
	Czech Republic	3
	Denmark	2–3
	France	Not specified.
	Germany	3
	Greece	≤3–4 depending on age of woman and special conditions determined by the authority.
	Hong Kong	3, women ≤34 y: no more than 3; women >34 y, >3 'E' transfer.
	Hungary	3 or even 4 if the patient is >35 y of age or she has had unsuccessful IVF treatment(s).
	Israel	Not specified
	Italy	All the embryos produced after a maximum of 3 oocytes fertilized. Exceptions only when there are maternal risks in transferring embryos.
	Korea	Not specified.
	Latvia	3
	Netherlands	Not specified.
	New Zealand	Not specified. But an SET policy is in place for public treatment, meaning 90% of cycles in women ≤35 y have SET. Similar SET rates are occurring among private patients voluntarily. Uptake of SET is growing in older women. The policy is not legally enforceable but is considered good practice.
	Norway	3
	Russia	No response
	Saudi Arabia	No response
	Slovenia	3
	Spain	3
	Sweden	1–2 (2 in older women)
	Switzerland	3
	Taiwan	Not specified.
	Tunisia	Not specified.
	Turkey	Not specified.
	United Kingdom	2
	Vietnam	Not specified.
Covered by guidelines	Argentina	Women ≤35 y with appropriate response to stimulation, ≤2 advised, of good quality. More can be transferred if of poor quality according to medical criteria and considering age of patient.

Cohen. Number of embryos for transfer in ART. Fertil Steril 2007.

TABLE 5.1

Continued.

How ART is governed, by country	Country	Limits on numbers of pre-embryos that can be transferred and any exceptions
	Australia	Limit is 2 for women <40 y. RTAC recommends ≤1 fresh embryo be transferred in the first attempt if woman is <35 y.
	Brazil	Not specified.
	Chile	Not specified.
	China	Not specified.
	Croatia	3, exceptions are for women >40 y or who have previously already failed IVF attempts.
	Egypt	Not specified.
	India	2 in normal responders. 3 in poor responders or older women. ≤3 except in poor-prognosis group.
	Ireland	Not specified.
	Japan	3 generally, but >3 depending on quality stage of embryos, maternal age, and other conditions.
	Lithuania	Not specified.
	Mexico	3
	Morocco	2 for good responders.
	Philippines	No more than 3. Preferably 1–2.
	Singapore	No more than 3 under usual conditions. ≤4 if the following 3 conditions are met: [1] all children conceived as a result of procedure will be delivered and cared for in a hospital that has a level 3 neonatal intensive care unit, [2] the woman has undergone >2 previous stimulated ART cycles that were unsuccessful, and [3] patient age is >35 y.
	South Africa	Not specified.
	Thailand	New guidance (under revision by RTCOG) will specify only 2 embryos, except in old-aged couples and those with recurrent implantation failure (not to exceed 3).
	United States	Varies by age and quality of embryos. <35 y: 2 or 1 with good morphology, 35–37 y: 2, 38–40 y: 4, >40 y: 5.
None	Colombia	No. Customarily, 2–3, even 4.
	Ecuador	No. Customarily, maximum 2
	Finland	No. Customarily, maximum 1–2 (exceptionally 3).
	Jordan	No. Customarily, maximum 5.
	Malaysia	No. Customarily, maximum 3–4.
	Peru	No. Customarily, maximum 3.
	Portugal	No. Customarily, <3 except in women >35 y.
	Romania	No. Customarily, maximum 3.
	Uruguay	No. Customarily, ≤2 in women <34 y, maximum 3 in women >34 y.
	Venezuela	No. Customarily, 2–5 maximum.

Note: RTAC = Reproductive Technology Accreditation Committee; RTCOG = Royal Thai College of Obstetricians and Gynaecologists.

Cohen. Number of embryos for transfer in ART. Fertil Steril 2007.

public centers are usually inferior to those of private centers. Disagreement about identifying the so-called best-quality embryo greatly restricts selection of the embryos to be transferred in some countries, such as Italy, Switzerland, and Germany, where the law permits cryopreservation only with pronuclear stages.

All this explains why it appears impossible to contemplate one single law that would apply all over the world. However, an overly permissive attitude may allow some excesses. On a national basis, self-regulation has not worked so far. The alternatives are the use of guidelines with sanctions imposed by the medical profession, or the development of specific laws. At least a responsible attitude to embryo transfer should be adopted, which would include the following:

- The priority of eSET for women <35 years of age during their first IVF cycle, with at least one good-quality embryo;
- The transfer of no more than two embryos, and only under exceptional conditions; and
- The improvement of results with cryopreservation in all centers.

SUMMARY

As of 2007, more countries have adopted guidelines or legislation to decrease the number of embryos to transfer. The worldwide trend appears to be the elective transfer of one embryo for at least the first cycle. Although some countries have adopted measures through legislation or clinical guidelines to address the major problem of multiple gestations after IVF, further progress is needed. There is also a need to educate both healthcare professionals and the lay population that multiple gestation is not a desirable outcome of IVF.

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CHAPTER 6: Cryopreservation

Sperm cryopreservation is an established procedure; however, its use has recently diminished. The availability of intracytoplasmic sperm injection has reduced the need for sperm donation, but removal of anonymity (Chapter 9) has markedly reduced the number of donors, to the point that current demand is no longer being met.

Cryopreservation of fertilized eggs (prezygotes to blastocysts) makes them available for future use by the couple. There are large numbers of these fertilized eggs in storage, which creates disposal problems for clinics. Family breakdown has been followed by court disputes over ownership, so specific instructions for time-limited disposal should always be in place. The legal issues involved have been reviewed (1). At the time of cryopreservation, decisions can be made for donation to other couples or to research or for destruction of the embryos. There appears to be an increasing proportion that are being donated for research rather than destroyed (2). Cryopreservation of oocytes may reduce these problems but then leads to longer term issues of disposal, particularly in the event of death after cancer treatment.

The progress toward eSET may influence the rate of cryopreservation (3). Cryopreservation of blastocysts, to optimize selection of embryos, has been used in an attempt to reduce the number of multiples. It also has been used after embryo biopsy to await results.

Tissue from the testis may be cryopreserved so that sperm can be removed for ICSI and at the time of biopsy for maldescended testes (4). Ovary and testis specimens are increasingly being cryopreserved before treatment for malignancy. Use in future partnerships has been limited.

ANALYSIS OF SURVEY

Twenty-five countries have statutes that allow cryopreservation of fertilized eggs (Table 6.1). Switzerland only allows pronucleate freezing, and Ireland permits cryopreservation of zygotes but does not allow deliberate destruction of embryos. Patient consent is required in France, Korea, and the United Kingdom. The duration of storage is limited to 5 years in Norway, Singapore, Sweden, and Switzerland, and an additional 5 years may be possible on request in Greece, Slovenia, Tunisia, and the United Kingdom. The limit is 2 years in Denmark but is 10 years in Austria, Hong Kong, Hungary, and New Zealand. In New Zealand, the time may be extended further on application to an ethics committee. In the Netherlands, storage cannot last beyond a patient's age of 44 years, but in Spain, it may last until the end of the reproductive years. In Latvia, export of embryos is prohibited. Italy is the only country to prohibit cryopreservation of embryos.

Rather than under statute law, activities are conducted within guidelines in a further 17 countries (Table 6.1). Cryopreservation of fertilized eggs is also performed in Belgium, Bulgaria, Canada, Hungary, Italy, Korea, Taiwan, and Vietnam and is used experimentally in the Netherlands. In Hong Kong, application is restricted to married couples, and consent is required in Brazil, Chile, Egypt, India, and Japan. More detailed instructions from the couple are required in Singapore. In India, consent may extend to donation to other couples or to research, which must be noncommercial. In Morocco, the couple must be present at thawing. In Chile, a decision must be made about the fate of the remaining embryos 2 years after the birth of offspring from a fresh transfer. Storage can last for 5 years in Argentina, Australia, Croatia, Philippines, and Singapore, as well as in India, unless there is default from maintenance payments. Hong Kong allows storage for 10 years; Japan and the United States, until the end of reproductive life; and Morocco, until separation of the couple or death. In Brazil, Chile, Egypt, Mexico, South Africa, and Thailand, there is no limit. In the United States cryopreservation remains an experimental procedure.

In addition to the above, cryopreservation of fertilized eggs is also practiced in another eight countries (Table 6.1). In Colombia, there is usually a medical indication; the duration of storage varies. In Ecuador, it is 1 year; it is 3 years in Morocco, 5 in Uruguay, 10 in Malaysia, and ≤ 15 in Venezuela.

There are 21 countries that have statutes permitting oocyte cryopreservation (Table 6.1), and only 1, Turkey, that prohibits it. Eleven countries practice oocyte cryopreservation under guidelines (Table 6.1), and it is also performed in a further 5 countries (Table 6.1).

Ovarian and testicular tissue may be preserved under statute in 16 countries (Table 6.1). There are guidelines covering this subject in 13 countries (Table 6.1), and it also is practiced in Brazil, Thailand, Uruguay, and Venezuela.

Donor sperm are used for non-IVF infertility in Argentina, Chile, India, Japan, Mexico, Singapore, and the United States. In Japan, the sperm must be obtained from a clinic registered with the national society. In Chile, sperm are mostly used from commercial banks. In the Philippines, donation is used only within marriage. In Croatia, Egypt, and Morocco, donation is not used, although this may lead to patients being referred abroad.

TABLE 6.1

Which cryopreservation procedures are allowed or practiced?

How ART is governed	Country	Cryopreservation of oocytes	Cryopreservation of embryos	Cryopreservation of ovarian or testicular tissue
Covered by statutes	Austria	Allowed	Allowed	Allowed
	Belgium	Allowed	Allowed	Not mentioned
	Bulgaria	Not mentioned, practiced	Not mentioned	Not mentioned
	Canada	Not mentioned, practiced	Not mentioned	Not mentioned
	Czech Republic	Allowed	Allowed	Allowed
	Denmark	Allowed	Allowed	Allowed
	France	Allowed	Allowed	Allowed
	Germany	Allowed	Allowed	Allowed
	Greece	Allowed	Allowed	Allowed
	Hong Kong	Allowed	Allowed/guideline	Allowed/guideline
	Hungary	Not mentioned, practiced	Allowed	Not mentioned
	Israel	Allowed	Allowed	Allowed
	Italy	Allowed	Not allowed	Not mentioned
	Korea	Allowed	Allowed	Not mentioned
	Latvia	Not mentioned	Allowed	Not mentioned
	Netherlands	Not mentioned, practiced	Allowed	Not mentioned
	New Zealand	Allowed	Allowed	Allowed
	Norway	Allowed	Allowed	Allowed
	Russia	Allowed	Allowed	Not mentioned
	Saudi Arabia	No data	No data	No data
	Singapore	Allowed	Allowed	Allowed
	Slovenia	Allowed	Allowed	Allowed
	Spain	Allowed	Allowed	Allowed
	Sweden	Allowed	Allowed	Allowed
	Switzerland	Allowed	Allowed	Allowed
	Taiwan	Not mentioned, practiced	Not mentioned	Not mentioned
	Tunisia	Allowed	Allowed	Not mentioned
	Turkey	Not allowed	Allowed	Not mentioned
	United Kingdom	Allowed	Allowed	Allowed
	Vietnam	Not mentioned, practiced	Allowed	Not mentioned
Covered by guidelines	Argentina	Allowed	Allowed	Allowed
	Australia	Allowed	Allowed	Allowed
	Brazil	Not mentioned, practiced	Allowed	Practiced
	Chile	Allowed	Allowed	Allowed
	China	No data	No data	No data
	Croatia	Not mentioned	Allowed	Allowed
	Egypt	Allowed	Allowed	Allowed
	India	Allowed	Allowed	Allowed
	Ireland	Not mentioned, practiced	Allowed	Not mentioned
	Japan	Allowed	Allowed	Allowed
	Lithuania	No data	No data	No data
	Mexico	Allowed	Allowed	Allowed
	Morocco	Not used	Allowed	Allowed
	Philippines	Not mentioned	Allowed	Allowed
	Singapore	Allowed	Allowed	Allowed
	South Africa	Allowed	Allowed	Not mentioned
	Thailand	Allowed	Allowed	Practiced
	United States	Allowed	Allowed	Allowed

Cooke. Cryopreservation. Fertil Steril 2007.

TABLE 6.1

Continued.

How ART is governed	Country	Cryopreservation of oocytes	Cryopreservation of embryos	Cryopreservation of ovarian or testicular tissue
None	Colombia	Used	Used	Not used
	Ecuador	Not used	Used	Not used
	Finland	Don't know	Used	Don't know
	Jordan	Not used	Not mentioned	Not mentioned
	Malaysia	Not used	Used	Not used
	Peru	Practiced	Not used	Not used
	Portugal	Practiced	Used	Not used
	Romania	Practiced	Used	Not used
	Uruguay	Not used	Used	Used
	Venezuela	Practiced	Used	Used

Cooke. Cryopreservation. Fertil Steril 2007.

SUMMARY

The emphasis on sperm cryopreservation has moved from the freezing process to service provision. Use has declined, most recently by reducing the availability of donors.

The time for which cryopreservation of fertilized eggs is permitted is generally restricted. It is specified by statute in most countries, but also by Guidelines. Even in those countries without regulation, most still impose time limits. Oocyte as well as ovarian and testicular tissue cryopreservation have also been regulated by statute in many countries.

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CHAPTER 7: Posthumous insemination

The retrieval of sperm from the body of a recently dead man for later insemination has raised profound ethical issues about which there is no consensus, there being permissive (1, 2) and restrictive views (3). The supportive opinions nonetheless offer suggestions for regulation of this activity that respect ethical constraints and have influenced the creation of legal frameworks.

ANALYSIS OF SURVEY

Posthumous insemination is allowed in the following 11 countries (Table 7.1): Australia, Austria, Belgium, Greece, India, Israel, the Netherlands, New Zealand, South Africa, Spain, and the United Kingdom, although it does not appear to have been used in all of these. It is not permitted in 19 countries: Argentina, Bulgaria, Denmark, Egypt, France, Germany, Hong Kong, Italy, Japan, Korea, Morocco, Norway, Philippines, Singapore, Slovenia, Sweden, Switzerland, Taiwan, and Tunisia. There are variable requirements in those countries in which it is used. In Australia, South Africa, and the United Kingdom, a written agreement before death is needed. In New Zealand, the specimens can only be used by a named person, and prior informed consent is essential. In Israel, the procedure can only be used by a spouse or common-law wife and after court application. In Spain, its use is only allowed for 6 months after death, and in Belgium, for 1 year. In the United Kingdom, the welfare of the child must be considered, and extensive counseling is required; dead fathers may be named on the birth certificate.

There appear to be no countries in which posthumous insemination is used without its being permissible to do so.

In countries without statutes or guidelines, posthumous insemination is not used in Ecuador, Finland, Jordan, Malaysia, Peru, Portugal, or Venezuela. It is unclear whether it is used in Colombia or Romania, but it is used in Uruguay.

SUMMARY

Posthumous insemination is not widely used but is performed within a framework that may stipulate conditions of use.

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TABLE 7.1

Posthumous insemination practices.

How ART is governed	Country	Allowed/used	Not allowed/not used	Not mentioned
Covered by statutes	Austria	+		
	Belgium	+		
	Bulgaria		+	
	Canada			+
	Czech Republic			+
	Denmark		+	
	France		+	
	Germany		+	
	Greece	+		
	Hong Kong		+	
	Hungary			+
	Israel	+		
	Italy		+	
	Korea		+	
	Latvia			+
	Netherlands	+		
	New Zealand	+		
	Norway		+	
	Russia			+
	Saudi Arabia	No response	No response	No response
	Slovenia		+	
	Spain	+		
	Sweden		+	
	Switzerland		+	
	Taiwan		+	
	Tunisia		+	
	Turkey			+
	United Kingdom	+		
	Vietnam			+
Covered by guidelines	Argentina		+	
	Australia	+		
	Brazil			+
	Chile			+
	China		+	
	Croatia			+
	Egypt		+	
	India	+		
	Ireland			+
	Japan		+	
	Lithuania			+
	Mexico			+
	Philippines		+	
	Singapore		+	
	South Africa	+		
	Thailand			+
	United States			+
None	Colombia			Don't know
	Ecuador		/+	
	Finland		/+	
	Jordan		/+	
	Malaysia		/+	
	Morocco		/+	
	Peru		/+	
	Portugal		/+	
	Romania			Don't know
	Uruguay	/+		
	Venezuela		/+	

Cooke. Posthumous insemination. Fertil Steril 2007.

CHAPTER 8: Donation

Although there has been a reduction in the use of donor sperm because of ICSI and the impact of the removal of anonymity in some countries (1), sperm donation is still used and has a role even when ICSI is available. Some countries continue to provide anonymous donation, and there may be a change in the type of donor in those countries that have removed anonymity.

With the further development of oocyte cryopreservation by vitrification, egg donation is becoming more realistic. The demand for oocytes will increase because it avoids the ethical issues of embryo donation (2).

There is increasing pressure for embryo donation for stem cell research, and there is some evidence that patients are beginning to recognize that, resulting in a positive change in their attitudes (3).

Tissue donation remains at the case report stage.

ANALYSIS OF SURVEY

Donor Sperm

Donor sperm are not allowed by law to be used for IVF in Austria, Germany, Italy, Tunisia, or Turkey. The law does permit it in 23 countries (Table 8.1); however, there are many restrictions. The sperm must be obtained from specific registered banks in France, Norway, and Sweden. Only known donors may be used in the Netherlands, Norway, Sweden, and the United Kingdom, but only anonymous in Singapore, Slovenia, and Vietnam. Altruistic donors are required in Korea. In Switzerland, the recipients must be married, but single women and lesbians may be treated in the United Kingdom. In Taiwan, there must be no previous history of donation to achieve a live birth. Case-by-case approval by an ethics committee is required in New Zealand if donor sperm and donor egg are used or for cross-generational donation and also in Slovenia for donor sperm. Informed consent is needed in Israel and the United Kingdom. Screening of donors is emphasized in Taiwan and Vietnam. Donors must be aged 18–50 years in Spain and may be aged $\leq$55 in Vietnam. Storage of samples cannot be for $>$10 years or past the death of the donor in Latvia. In the United Kingdom, the welfare of the child needs to be considered. There are various limits on the number of offspring: families may include 2 in Slovenia, 3 (other than multiples) in Latvia, 6 in Spain, and 10 in the United Kingdom. Other restrictions apply in Hong Kong, Hungary, and Russia.

Most of the details in the previous paragraph hold true for use other than in IVF. The use of donor sperm for other than IVF is prohibited by law in Hong Kong, Italy, Slovenia, Tunisia, and Turkey. Anonymity persists in France and Greece, but donors are identifiable in the Netherlands, Norway, and Sweden. Donors are not paid in France and Greece, but expenses are allowed in Greece. In Switzerland, the identity of all parties is kept in a central registry for 80 years, and the child can have access on reaching adulthood. Donors are screened in Austria, and donation to only one clinic is permitted. There is a limit of three couples per donor. Services are available on request in New Zealand under the Human Rights Act, although there must be counseling, but donation requires a fee in Germany. There is an age restriction for the woman in Sweden.

Guidelines do not allow donor sperm to be used in IVF in Egypt, Japan, Morocco, or the Philippines, although they do allow it in 12 countries. These are Argentina, Australia, Brazil, Chile, China, India, Lithuania, Mexico, Singapore, South Africa, Thailand, and the United States. Screening of samples is required in Argentina, Australia, Hong Kong, Mexico, Thailand, and the United States. Six months' quarantine is specified in the United States. An age range of 18–55 years is given in Hong Kong. A genetic link of the donor with the couple is required in Singapore, although the woman's brother is not acceptable. Three live birth events are allowed. However, semen donation from siblings is prohibited in Thailand. Prospective consent is obtained in India, in case mature sperm have not been obtained at egg recovery, in which case donor sperm are permitted. In South Africa, appropriate legal documents must be completed.

Argentina, Australia, Brazil, India, Ireland, Japan, Singapore, South Africa, Thailand, and the United States have other laws or guidelines referring to the use of donor sperm in treatment for infertility apart from its use in IVF. Units must be accredited in Australia, Brazil, and Japan. In India, donors must be between the ages of 21 and 45 years. Screening procedures are specified in India and the United States. In Japan, donation is voluntary and must continue for 2 years, and the treatment is only for married couples. Donor sperm are not used for these indications in Croatia, Egypt, Morocco, or the Philippines, although they are in Chile and Mexico.

In Ecuador and Uruguay, donor samples are used for azoospermia. In Finland and in Malaysia, donor sperm are used in nongovernment centers. Donation is also used in Peru; in Portugal, with anonymous donors after informed consent; in Romania; and in Venezuela, if there are no sperm at egg retrieval. There is also use of donor sperm for indications other than IVF in Columbia, Finland, and Peru and

TABLE 8.1

Donation of gametes.

		Sperm donation						Oocyte donation	
		IVF			Non-IVF				
	Country	Allowed	Not allowed	Used	Allowed	Not allowed	Used	Allowed/ used	Not allowed/ not used
Covered by statutes	Austria		+		+				+
	Belgium	+					Not mentioned	+	
	Bulgaria			Not mentioned			Not mentioned		Not mentioned
	Canada	+						+	
	Columbia	+			+			/+	
	Czech Republic	+			+		+	+	
	Denmark	+			+		+	+	
	France	+			+		+	+	
	Germany		+		+		+		+
	Greece	+			+		+	+	
	Hong Kong	+		Guideline		+		+	
	Hungary	+			+		+	+	
	Israel	+			+		+	+	
	Italy		+			+			+
	Korea	+					Not mentioned	+	
	Latvia	+					Not mentioned	+	
	Netherlands	+			+		+	+	
	New Zealand	+			+		+	+	
	Norway	+			+		+		+
	Russia	+			+		+	+	
	Saudi Arabia			No response			No response		No response
	Slovenia	+				+		+	
	Spain	+			+		+	+	
	Sweden	+			+		+	+	
	Switzerland	+			+		+		+
	Taiwan	+						+	
	Tunisia		+			+			+
	Turkey		+			+			+
	United Kingdom	+			+		+	+	
	Vietnam	+						+	

Cooke. Donation. Fertil Steril 2007.

TABLE 8.1

Continued.

		Sperm donation						Oocyte donation	
		IVF			Non-IVF				
	Country	Allowed	Not allowed	Used	Allowed	Not allowed	Used	Allowed/ used	Not allowed/ not used
Covered by guidelines	Argentina	+			+			+	
	Australia	+			+			+	
	Brazil	+			+			+	
	Chile	+			+			+	
	China	+			+				+
	Croatia					+			+
	Egypt		+			+			+
	India	+			+			+	
	Ireland				+				
	Japan		+		+				+
	Lithuania	+				+			Not mentioned
	Mexico	+			+			+	
	Morocco		+			+			+
	Philippines		+			+			+
	Singapore	+			+		+	+	
	South Africa	+			+			+	
	Thailand	+			+			+	
	United States	+				+		+	
None	Ecuador			+			Used	/+	
	Finland			+			Used	/+	
	Jordan						Not mentioned		/+
	Malaysia			+			Not mentioned		/+
	Peru			+			Used	/+	
	Portugal			+			Used	/+	
	Romania			+			Not used	/+	
	Uruguay			+			Not used	/+	
	Venezuela			+			Used	/+	

Cooke. Donation. Fertil Steril 2007.

specifically in intrauterine insemination in Ecuador, Portugal, and Venezuela.

Donor Eggs

Donor eggs for IVF are not allowed by law in Germany, Italy, Norway, Switzerland, Tunisia, or Turkey but are in 21 other countries. There is an age limit for the donor, who must be <35 years of age, in the Czech Republic, Singapore, and United Kingdom, and there is an age range of 18–35 years in Latvia, Spain, and Vietnam. Other screening takes place in the Czech Republic, Taiwan, and Vietnam. Anonymous donation takes place in France, Greece, India, Israel, and Slovenia, but identifiable donors are required in Sweden and the United Kingdom. Donors may be paid in France and in India but not in Greece, Korea, Slovenia, Thailand, or Vietnam. In Hungary, the donor should be a relative of the infertile couple, but in Singapore, this cannot be the sister of the husband. The donor should be married in Israel and in Singapore, where she should preferably have children of her own, although the recipient may be single in Israel. In Sweden, Taiwan, and the United Kingdom, the requirements are those for sperm donation. In Slovenia, a donor can have children in two families, although the indications must be confirmed by committee, as in the Netherlands, and in Spain, up to six children are allowed. In Slovenia, 6 months' quarantine after freezing is required. In France, the waiting time is 4–6 years, so couples seek help abroad. In Denmark, only egg sharing is permitted.

Under guidelines, donor eggs are not allowed in China, Croatia, Egypt, Japan, Morocco, or the Philippines; they are permitted in Argentina, Australia, Brazil, Chile, Hong Kong (Hong Kong is a statute country), India, Mexico, Singapore, South Africa, Thailand, and the United States. In India, no donation from the friends or relatives of either partner is allowed. In Thailand the donation cannot be from any relative of the husband. The United States has donor-screening guidelines.

Although there is no legislation, donor eggs are used in Columbia; in Ecuador for women >40 years of age and after poor response; and in Finland, Peru, Portugal, Romania, Uruguay, and Venezuela for older women and those with premature ovarian failure. They are not used in Malaysia and Morocco.

Identifying information about the donor is not customarily provided in Columbia, Ecuador, Jordan, Peru, Portugal, Romania, or Uruguay. Donors can authorize it in Uruguay, and in Venezuela, the treated couple can decide, although it is not customary for the couple to agree. Nonidentifying information about the donor is customarily provided to the offspring of donor gametes in Columbia and India, and in Venezuela it depends on the couple. In Portugal, only phenotypic information is given, and it is not customary to provide information in Ecuador, Peru, or Uruguay.

Donor Embryos

Embryo donation is not permitted under law in 13 countries (Austria, Denmark, Germany, Israel, Italy, Latvia, Norway, Slovenia, Sweden, Switzerland, Taiwan, Tunisia, or Turkey), although it is in 12 countries (Belgium, the Czech Republic, France, Greece, Hong Kong, the Netherlands, New Zealand, Russia, Singapore, Spain, the United Kingdom, and Vietnam). Nevertheless, in the Netherlands it is not used. The practice is controlled in Hungary, Hong Kong, and Russia. There is genetic screening of both partners in the Czech Republic. Anonymity is required in Greece, Singapore, Spain, and Vietnam. There is no payment for donation in Greece and Vietnam. In Greece, specific consent is required from the donor, and case-by-case approval by the ethics committee is required in New Zealand. In Spain, no more than six children may be born from each donor. In the United Kingdom, the conditions are the same as those for donor sperm. In France, adoption is necessary.

Donor embryos are prohibited under guidelines in the same countries, and the list of those that do permit the use of donor embryos is almost the same as well, with the addition of Ireland, where the couple must make a valid decision not to use their own fertilized ova. Additional features are the need to consent to donation to research in India, unless default in payment of maintenance charges continues after two reminders, at which point such consent is waived.

In India, the offspring of donor embryos and the social parents have the right to nonidentifying genetic information about the donor. Further, this information cannot be withheld from the child if it is sought. Nonidentifying information about the donor also can be provided to the offspring in Australia and South Africa and is provided at the discretion of the clinic in the United States; none can be given in Argentina or Singapore, and the issue is under discussion in Japan. However, identifying information can be provided in Argentina, Australia, Japan, and South Africa.

Donor embryos are also used without a legislative framework in Columbia; in Finland, where each center uses its own criteria; and in Portugal, Romania, Uruguay, and Venezuela.

Ovarian and Testicular Tissue Donation

Ovarian or testicular donation is possible in Belgium, Russia, and Taiwan and is not specifically mentioned by statute in Canada, Hong Kong, Hungary, Italy, or Korea. It is not possible in Bulgaria, the Netherlands, Tunisia, Turkey, or Vietnam.

SUMMARY

Gamete donation has been proscribed by statute in a few countries for religious or cultural reasons; more countries deny egg donation, and even more, embryo donation. These lists have been extended by guidelines that prevent donation. There is some movement of patients to other countries in

response, but most populations support their government's regulations.

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CHAPTER 9: Anonymity

Traditionally, throughout much of the world, gamete donation has been treated with anonymity to protect the donor, physician, and parents. The importance attached to genetics has now led some countries to review the ethics of their statutes on anonymity. The laws have been changed in Sweden, the Netherlands, Austria, Australia, the United Kingdom (1), and Canada. As early as 1985, Sweden enacted legislation that requires semen donors to provide information on themselves when the offspring reach maturity. New Zealand, too, has had a so-called open system of information sharing for some time. The Netherlands introduced a law in 2004 giving offspring conceived by donated semen or oocyte the right to know the identity of the donor when they reach the age of 16 years. The United Kingdom enacted an anonymity law protecting donors in 1990. This was reversed in 2006, and gamete donors now are required to provide information to offspring when they reach the age of 18 years. The changes in that law include limiting donor compensation. In the United States, where there is a lack of such legislation and anonymity has always been assumed, a few cases now have been settled through the court legal system in favor of the offspring requiring donor identification. This is now causing a reluctance to participate among some potential donors. Anonymity is protected by law in France. There, through their Bioethics Law of 1994, donation is voluntary, nonremunerated, anonymous, and confidential (2).

The lack of anonymity has become a major stumbling block to oocyte and sperm recruitment in some countries. In the United Kingdom, where a wait for an oocyte donor of 1–2 years is not unusual, there is concern that these delays may be further lengthened as donors become more reticent (3). Along with anonymity or the lack of it, there are the moral, ethical, and legal issues that present themselves in every country regarding appropriate compensation of the donors. In Canada, where the government passed legislation in 2004 prohibiting all purchase or sale of gametes, there is serious concern over future donor gamete availability. Furthermore, that federal government will record all donor and donor offspring information.

ANALYSIS OF SURVEY

As shown in Tables 9.1 and 9.2, guidelines dealing with anonymity are changing in many countries. The data from this survey indicate that there are now 18 countries, one third of the 54 surveyed, where information on the donor must be or customarily is provided to the offspring when requested, usually after the age of 18 years. In only 3 of these countries, Canada, Greece, and Slovenia, can this be limited to nonidentifying information. In the case of 16 other countries, the respondents indicated that their statutes or guidelines did not address this issue, and those from 6 other countries did not know whether providing offspring with nonidentifying information about the donor was customary. In Latvia, where donors remain anonymous, they must be willing specifically to provide genetic and anthropologic information. In New Zealand, by statute, donors may request information on their offspring's identity, but the children can decline. With respect to oocyte donation, Hungary has adopted legislation requiring the donor to be a relative of the couple.

DISCUSSION

When anonymity of donors has been traditional, any changes in anonymity rules can create new issues. Systems whereby offspring can obtain information on the donor are generally well received by the public and by those on the psychological and theoretical side of patient care. However, as a result, some gamete donors themselves may become reticent to participate, and there is associated difficulty recruiting sufficient numbers of donors. This potential for decreased availability of gametes is a source of concern to infertility physicians. For example, the number of egg donation cycles in the United Kingdom and Europe has lagged behind that of the United States in the past 2 decades, which largely is attributed to governmental restrictions in these countries, as compared with the lack of regulation in the United States (4). Furthermore, there are important ethical and legal issues regarding appropriate compensation for donors. In most countries where federal legislation prohibits anonymity, there are significant legal restraints on compensation of donors. This may further restrict availability of donor gametes. In countries without these legal restraints, donor compensation is variable, and self-regulation remains a challenge.

SUMMARY

Traditionally, anonymity has protected gamete donors through guidelines, statutes, or generally accepted practice. A greater understanding and awareness of the importance of genetics and hereditary issues has caused an increasing number of countries to enact laws that provide offspring access to identifying information on the donor. Many of these statutes also significantly limit compensation to donors. In these countries, potential donors often become reticent and chose not to become involved. The lack of anonymity and restricted compensation is making the recruiting of sufficient numbers of donors more difficult in many countries.

TABLE 9.1

Anonymity overview.

How ART is governed	Country	Has legislation or guidelines on anonymity of donors been modified?			Nonidentifying information about donor provided on request			Identifying information about donor provided on request		
		Yes[a]	No	Not mentioned or don't know	Allowed/ customary	Not allowed/ not customary	Not mentioned/ don't know	Allowed/ customary	Not allowed/ not customary	Not mentioned/ don't know
Covered by statutes	Austria		+				+	+		
	Belgium		+				+			+
	Bulgaria		+				+			+
	Canada		+		+				+	
	Czech Republic		+				+		+	
	Denmark		+			+			+	
	France		+			+			+	
	Germany		+		+			+		
	Greece		+		+				+	
	Hong Kong		+		+					+
	Hungary	+			+					+
	Israel		+			+			+	
	Italy		+			+				
	Korea		+				+			+
	Latvia	+				+			+	
	Netherlands	+			+			+		
	New Zealand	+			+			+		
	Norway	+			+			+		
	Russia	+					+			+
	Saudi Arabia			+			No response			No response
	Slovenia		+		+ (Medical reasons)				+	
	Spain		+		+			+ (If life threatening)		
	Sweden		+		+			+		
	Switzerland		+			+		+ (Once >18 y)		
	Taiwan		+			+			+	
	Tunisia			+			+			+

Kempers. Anonymity. Fertil Steril 2007.

TABLE 9.1

Continued.

How ART is governed	Country	Has legislation or guidelines on anonymity of donors been modified?			Nonidentifying information about donor provided on request			Identifying information about donor provided on request		
		Yes[a]	No	Not mentioned or don't know	Allowed/ customary	Not allowed/ not customary	Not mentioned/ don't know	Allowed/ customary	Not allowed/ not customary	Not mentioned/ don't know
	Turkey			+		+			+	
	United Kingdom	+			+			+ (Once >18 y)		
	Vietnam		+			+			+	
Covered by guidelines	Argentina		+			+				+
	Australia	+			+			+		
	Brazil		+				+			+
	Chile			+			+			+
	China	+					No response			No response
	Croatia			+			+			+
	Egypt			+			+			+
	India	+					+		+	
	Ireland		+				+			+
	Japan		+				+			+
	Lithuania	+				+				
	Mexico		+				+			+
	Morocco			+			/+			/+
	Philippines			+		+				+
	Singapore		+			+			+	
	South Africa	+			+			+		
	Thailand		+				+			+
	United States		+				+			+
None	Colombia			+	/+		+		/+	
	Ecuador			+		/+			/+	
	Finland			+			/+			/+
	Jordan			+			/+			/+
	Malaysia			+			/+			/+
	Peru			+		/+			/+	
	Portugal			+			/+		/+	
	Romania			+			/+		/+	
	Uruguay			+		/+			/+	
	Venezuela			+		/+			/+	

[a] Details, Table 9.2.

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TABLE 9.2

Specific modifications to anonymity.

Country	Main modifications
Australia	Gamete donors must consent to release of identifying information. ART units must not facilitate treatment unless offspring has the right to know genetic parents.
China	Double blind.
Hungary	Anonymity of oocyte donation has been solved since December 2005: the oocyte donor should be a relative of the couple.
India	Children born through donor gametes shall not have any right to know the identity (such as name, age, address, etc.) of their genetic parents. A child thus born will, however, be provided all other information about the donor or and when desired by the child when the child becomes an adult.
Latvia	Law of sexual and reproductive health of Latvia Republic, article 14, point 1.2. Donor has to be anonymous, and potential parents are able to get information only about genetic and anthropometric data.
The Netherlands	Anonymity now forbidden by law.
New Zealand	Donors become identifiable. When children are born from donor gametes, the clinic must give their name and the donor's name to the Department of Birth, Deaths, and Marriages. Children can access the donor's identity when they reach 18; parents may access the donor's identity once a child is born. The donor may request access to donor children's identity when they reach 18, but children can decline. Donors and offspring involved in donor sperm or donor egg treatment before commencement of the Act can elect to join a voluntary register.
Norway	The sperm donor cannot be anonymous. The child has a right to know the identity.
Russia	Just a statement.
South Africa	Several years ago, legislation was modified to allow children conceived with donor gametes to access information about the donors.
United Kingdom	Only gametes willing to give their name to offspring at maturity to be recruited Destroy other samples by 31 March 2006, only keep samples for siblings. As previously specified, allowing the identification of a biological parent to a child resulting from donor egg or sperm treatment when they reach the age of 18 y.

Kempers. Anonymity. Fertil Steril 2007.

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CHAPTER 10: Micromanipulation

Intracytoplasmic sperm injection (ICSI) was first reported in human assisted reproduction in Belgium in 1992. Today, this technology has become the treatment of choice worldwide for a variety of male-factor infertility issues, including obstructive and nonobstructive azoospermia and for those who require preimplantation genetic diagnosis (PGD). Men with severely impaired spermatogenesis require genetic evaluation before ICSI because increasingly they have been found to have a high degree of Y-chromosomal microdeletions, as well as other karyotypic anomalies. The ICSI procedure is considered to be quite safe. However, statistically, there appears to be an associated slight increase in congenital anomalies that are chiefly hypospadias. In severe azoospermia particularly, a direct genetic transmission of Y chromosome microdeletions to the offspring has been shown consistently (1). Much needed long-term follow-up studies of children born through ICSI were begun several years ago in Belgium and continue there, as well as in a number of other centers around the world.

Assisted hatching, a therapeutic option for improving the capacity of embryos to implant, has been investigated and widely utilized in ART centers for many years. As quoted in "IFFS Surveillance 2004," it has been shown to increase the pregnancy, implantation, and ongoing-pregnancy rates in patients >35 years of age who have thick zona pellucida and two or more IVF failures (2). However, some centers have experienced less consistent benefits. The technology involves either thinning of the zona pellucida (ZP), drilling a hole in the ZP, or total removal of the ZP. However, variable experiences with its use in IVF and ICSI continue to make the procedure somewhat controversial (3).

Cytoplasmic transfer, using heterologous cytoplasm, has been used in a few countries where it is permitted, and several live births have been reported. As described in "IFFS Surveillance 2004," "Mitochondria are self-replicating, maternally inherited organelles that use the oxidative phosphorylation pathway to supply adenosine triphosphate for all energy requiring cellular activities. It has been suggested that a reduction in embryo development competence may be related to an inadequate capacity to generate levels of adenosine triphosphate sufficient to support normal chromosomal segregation. Normal development potential has been restored to eggs with ooplasmic deficiencies by transfer of ooplasm from a normal donor egg." This technology is prohibited in many countries because of concerns raised over the introduction of third-party mitochondria DNA that appears to be maintained in the offspring. To date, there has been no evidence of abnormalities in these children as a result of this foreign DNA.

ANALYSIS OF SURVEY

Intracytoplasmic sperm injection is generally accepted in every country surveyed (Table 10.1). In no country is it disallowed by statute or guidelines. It is specifically allowed in the statues of 22 countries and in the guidelines of 14 others. In all others, it is not mentioned. It is practiced without restrictions in all countries, including the 10 surveyed countries that have neither statutes nor guidelines.

Assisted hatching, with the exception of Norway, also is a generally accepted procedure in the 57 countries surveyed. It is specifically allowed in approximately half of the countries with statutes, 14 of 29, as well as in the guidelines of 13 of the 18 with guidelines. In the remaining countries, it is not mentioned in either their statutes or guidelines. It is being used in 15 countries with statutes, although infrequently in some countries. In the United Kingdom, it is used only in the content of a research study. It is being used in 13 of the 18 countries with guidelines but is not recommended in Australia because of lack of good evidence to support a benefit, and it is used with decreasing frequency in the United States. These survey data indicate that the procedure is being used in 60% of the countries that have statutes or guidelines. It is also being used in most of the countries with neither of these directives, but exact information on this could not be accurately determined through this survey.

Cytoplasmic transfer is used infrequently throughout the world (Table 10.1). It is being used only in the following 5 countries: Egypt, Greece, Hong Kong, Peru, and Thailand. Its use is not allowed in 13 countries, including 8 of 29 with statutes and 5 of 18 with guidelines. In addition, it is not being used in 8 countries that have neither statutes nor guidelines.

DISCUSSION

As was found in the 2004 survey, ICSI continues to be widely used and is consistently successful for the treatment of a number of male infertility disorders. Genetic evaluation of the male is strongly advised because of the high incidence of Y-chromosome microdeletions, reported to be 3%–8%, in men with spermatogenic failure and with sperm concentrations of <5 million per milliliter (1). Similarly, genetic evaluation of the offspring should be encouraged because of the potential for direct transmission of this and possibly other chromosomal aberrations.

Assisted hatching appears to be used less frequently, perhaps because of inconsistent reports about its benefits. The

TABLE 10.1

Micromanipulation.

How ART is governed	Country	Is ICSI allowed or used?			Is assisted hatching used or allowed?			Are other types of micromanipulation (for cloning see cloning section) e.g., is cytoplasmic transfer allowed?		
		Allowed/ used	Not allowed/ not used	Not mentioned	Allowed/ used	Not allowed/ not used	Not mentioned	Allowed/ used	Not allowed	Not mentioned
Covered by statutes	Austria	+					+			+
	Belgium	+			+				+	
	Bulgaria			+			+			+
	Canada			+			+			+
	Czech Republic	+			+					+
	Denmark	+					+			+
	France	+			+				+	
	Germany	+			+					+
	Greece	+			+			+		
	Hong Kong	+					+/Used	+		
	Hungary	+			+					+
	Israel	+			+					+
	Italy			+			+			+
	Korea			+			+			+
	Latvia	+			+				+	
	Netherlands	+					+		+	
	New Zealand	+			+				+	
	Norway	+				+			+	
	Russia	+			+					+
	Saudi Arabia			No data			No data			No data
	Slovenia	+					+			+
	Spain			+			+			+
	Sweden	+			+					+
	Switzerland	+			+					+
	Taiwan			+			+			+
	Tunisia	+					+			+
	Turkey	+			+				+	
	United Kingdom	+			+					+
	Vietnam	+			+				+	

Kempers. Micromanipulation. Fertil Steril 2007.

TABLE 10.1

Continued.

How ART is governed	Country	Is ICSI allowed or used?			Is assisted hatching used or allowed?			Are other types of micromanipulation (for cloning see cloning section) e.g., is cytoplasmic transfer allowed?		
		Allowed/ used	Not allowed/ not used	Not mentioned	Allowed/ used	Not allowed/ not used	Not mentioned	Allowed/ used	Not allowed	Not mentioned
Covered by guidelines	Argentina	+			+					+
	Australia	+			+				+	
	Brazil			+			+		+	
	Chile	+			+					+
	China			No data			No data			No data
	Croatia	+			+					+
	Egypt	+			+			+		
	India	+			+					+
	Ireland			+			+		+	
	Japan	+					+			+
	Lithuania			No data			No data			No data
	Mexico	+			+					+
	Morocco	+			+					+
	Philippines	+			+				+	
	Singapore	+			+					+
	South Africa	+			+					+
	Thailand	+			+			+		
	United States	+			+				+	
None	Colombia	/+					No data		/Not used	
	Ecuador	/+					No data		/Not used	
	Finland	/+					No data			/Don't know
	Jordan	/+					No data		/Not used	
	Malaysia	/+					No data		/Not used	
	Peru	/+					No data	/Used		
	Portugal	/+					No data		/Not used	
	Romania	/+					No data		/Not used	
	Uruguay	/+					No data		/Not used	
	Venezuela	/+					No data		/Not used	

Kempers. Micromanipulation. Fertil Steril 2007.

number of countries using it, however, has remained about the same as was found in the 2004 survey. As was the case in 2004, it is not now used in Norway. Although not prohibited by statute, it is specifically mentioned as a technique that is regarded as new and accordingly cannot be practiced until it has been evaluated in each given clinic and a license has been granted. In the United Kingdom, its use is prohibited, except in the context of a research study conducted according to established guidelines.

Physicians in a few countries working without statutes but with guidelines specifically cannot use cytoplasmic transfer under established federal mandates or restrictions imposed by particular administrative bodies. This includes Australia, Japan, and the United States and is expected soon to be the case in South Africa. In several countries where the statutes do not specifically mention this technology and where it is not being used, there are established committees or boards that would need to approve its use. In Israel, its use would require approval by the local ethics committee. In New Zealand, there would have to be approval by the Public Health Advisory Committee, and in Taiwan there would have to be a review by the governmental institutional board. In Singapore, it can only be used in conjunction with PGD and then only on a case-by-case basis.

SUMMARY

Intracytoplasmic sperm injection is the treatment of choice for a large number of male infertility issues, such as severely impaired spermatogenesis. The results are consistently satisfactory. Genetic evaluation is recommended because of the high incidence of Y-chromosome deletions in some of these men and the risk of direct transmission of this as well as other chromosomal abnormalities to their offspring. Assisted hatching with the potential of improving embryo implantation is being used infrequently, perhaps because of inconsistent benefits. Cytoplasmic transfer using heterologus cytoplasm raises concern over the introduction of third-party DNA and is being used in only five of the countries surveyed.

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CHAPTER 11: Oocyte maturation

Although oocyte maturation in an IVF program is usually achieved by hCG administration before follicle aspiration, the term is more frequently applied to the maturation of an immature oocyte in vitro (in vitro maturation; IVM). The indications are usually polycystic ovary syndrome and a high risk of ovarian hyperstimulation syndrome. It is also being used in severe male infertility, for those with repeated poor-quality embryos or who are poor responders (1), as well as in natural cycles (2). More recently it has been used in oocyte donation and for fertility preservation (3). In Italy, cryopreservation of embryos has been proscribed, driving effort towards expanding IVM (4).

Clinical outcomes need to improve, perhaps by changing culture conditions. Confocal microscopy has identified a higher frequency of abnormal meiotic spindles and chromosomal alignment using current culture methods (5).

ANALYSIS OF SURVEY

Oocyte maturation is allowed under statute in the Czech Republic, Denmark, France, Germany, Israel, Italy, Norway, Sweden, Switzerland, and the United Kingdom (Table 11.1). It is not permitted in New Zealand. Under guidelines, it is allowed in Argentina, Australia, Chile, Egypt, India, Mexico, Philippines, Singapore, Thailand, and the United States. There appear to be no sets of guidelines that prohibit it. In Bulgaria, Finland, Japan, Jordan, Peru, South Africa, and Venezuela it is also practiced; in Slovenia, it is a research procedure. It is not practiced in Ecuador, Malaysia, Morocco, or Romania.

SUMMARY

The use of oocyte maturation has become more widespread since the 2004 report. Restrictive regulation (such as has occurred in Italy) will likely spur greater development of the technique.

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TABLE 11.1

Is oocyte maturation allowed or used?

How ART is governed	Country	Allowed/used	Not allowed/not used	Not mentioned
Covered by statutes	Austria			+
	Belgium			+
	Bulgaria			+
	Canada			+
	Czech Republic	+		
	Denmark	+		
	France	+		
	Germany	+		
	Greece			+
	Hong Kong			+
	Hungary			+
	Israel	+		
	Italy	+		
	Korea			+
	Latvia			+
	Netherlands			+
	New Zealand		+	
	Norway	+		
	Russia			+
	Saudi Arabia			No data
	Spain			+
	Sweden	+		
	Switzerland	+		
	Taiwan			+
	Tunisia			+
	Turkey			+
	United Kingdom	+		
	Vietnam			+
Covered by guidelines	Argentina	+		
	Australia	+		
	Brazil			+
	Chile	+		
	China			No data
	Croatia			+
	Egypt	+		
	India	+		
	Ireland			+
	Japan	/+		
	Lithuania			No data
	Mexico	+		
	Morocco			Don't know or not used
	Philippines	+		
	Singapore	+		
	South Africa			+
	Thailand	+		
	United States	+		
None	Colombia			/+
	Ecuador		/+	
	Finland	+		
	Jordan		/+	
	Malaysia		/+	
	Morocco		/+	
	Peru	+		
	Portugal			Don't know
	Romania		/+	
	Slovenia	Research		
	South Africa	/+		
	Uruguay	/+		
	Venezuela	/+		

Cooke. Oocyte maturation. Fertil Steril 2007.

CHAPTER 12: Welfare of the child

In 2004, the United Kingdom was the only country to take into account the welfare of the child by imposing law. In the United Kingdom, the statutory Human Fertilisation and Embryology Authority's Code of Practice speaks of "the importance of a stable and supportive environment for any child produced as a result of treatment." It also enjoins the program to take "all reasonable steps to ascertain who would be legally responsible for any child as a result of the procedure and who it is intended to bring up the child." Finally, the list of factors to "bear in mind" when taking into account the welfare of the child includes "commitment, age, medical histories, ability to meet the needs of child or children, any risk to the child, including that of inherited disorders, and the effect on any existing child of the family."

ANALYSIS OF SURVEY

In 2007, two new countries imposed laws to take into account the welfare of the child: Greece and New Zealand. In the United Kingdom, the law has been clarified; thus, it is no longer necessary to check with the general practitioner whether concerns are present.

In some countries, there have been modifications regarding the welfare of the child. In Sweden, India, and Slovenia there is now traceability of donors and a possibility that they may be asked for medical history in case of child health problems related to genetics.

In many other countries, information about the parents, official demands of the parents, or registers about the baby's health exist in view of the welfare of the child (e.g., Australia, Chile, France, Japan, and Slovenia). However, current information indicates that in the United Kingdom, where there is a statutory mention, no official action has been taken under this statute. The status of the child has evolved, and the notion of "welfare of the child" is varied in quality and difficult to assess because of its large psychosocial components. This notion is important in ART, because doctors or biologists are implicated in responsibility for an unhealthy child.

CONCLUSION

In general, consent to treatment legally provides for assurance of responsibility for the future children from both parents, whatever their marital status. Although there are at least three statutes in place, and some comments have been made about the welfare of the child, action does not appear to have been taken under these.

As in ART, the best interests of the child must be our priority, so counselors are morally obliged to obtain a realistic picture of the expected conditions for the offspring and to survey the condition of the children who are born.

CHAPTER 13: Fetal reduction

Multifetal pregnancy reduction (MFPR) is the technique used to reduce the adverse outcome of multiple gestation. *Selective termination* (ST) refers to this technology when fetal reduction is used for a significant developmental abnormality or heterotopic implantation site. The procedure is usually conducted between 12 and 14 weeks of gestation, when structural evaluation of the fetus can be conducted. The success rate is higher with the abdominal than the vaginal approach. In large series with experienced hands, the overall unexpected pregnancy loss rate is very low. For ST, it is reported to be 4% (1), and for MFPR, it is 5.4% (2). Although the risks of the procedure are very small, it does raise difficult ethical, moral, and psychological dilemmas for many couples.

This survey primarily addresses the use of MFPR to diminish the risk of adverse complications of multiple gestation.

ANALYSIS OF SURVEY

Fetal reduction is specifically not allowed in 8 (14%) of 56 countries surveyed on this question (Table 13.1). This includes 1 with statutes, Norway, and 7 with guidelines. It is being practiced in 20 (36%) of 56 countries surveyed. As would be expected, fetal reduction is not practiced in countries where abortion is illegal or considered socially unacceptable. These include those countries surveyed in South America and Central America, as well as in Spain, Italy, and Ireland.

One intent of this survey was to determine whether there has been any progress in the past few years in documenting the consequences of fetal reduction. Only in one, Egypt, has there been some progress. In that country there have been some published reports on outcome. The respondent from Denmark noted that although there has been no progress in documenting, today there is more awareness of the issue.

DISCUSSION

The usefulness of MFPR has been well summarized. "Over the past 25 years fetal reduction has been utilized to reduce the risks of higher-order multiple pregnancies that resulted from overly successful infertility therapies. The demographics of multiple pregnancy patients have evolved over the past decade, with increasing proportions coming from IVF as opposed to ovulation induction, being older and a higher proportion with donor eggs. Genetic diagnosis before reduction is becoming more common and is very safe in experienced hands. For all starting numbers, including twins, reduction to a lower number of fetuses reduces fetal losses, prematurity, and infant mortality and morbidity" (3).

There are troublesome consequences from the lack of long-term data on fetal reduction. Without these data, it is not possible to evaluate the full health outcome of babies born after this procedure. It is noteworthy and very disappointing to find that in only one country, where fetal reduction is allowed, has there been any progress in documenting these long-term consequences. Naturally, the question was not applicable to the countries where it is not allowed. Although long-term follow-up remains to be performed at this time, the rate of congenital anomalies does not appear to be increased. One study looking at cerebral palsy in multiple pregnancies (4) concluded there is a lower rate of cerebral palsy after selective fetal reduction, perhaps because lower-order multiples were delivered at a later gestational age.

The ultimate decision by patients to undertake fetal reduction has been shown to be determined by the extent of their religious and antiabortion sentiments, whether they have medical-scientific careers, and how proactive the advice from their physicians has been (5). Because some patients identify emotional issues including moral and ethical dilemmas, for them, this procedure may carry immediate and long-term consequences. Awareness of these issues is critical to counseling of these patients and long-term follow-up.

Fetal reduction is a widely accepted and practiced technology. However, there are currently no data on how frequently it is being used. Although it would be very helpful to have national registries collect this information, as quoted in "Surveillance 04," none do so except for the French National Register on in vitro fertilization. Their data in 2002, measured against live births, indicated a reduction of 1.78% in IVF and of 1.42% in ICSI.

SUMMARY

Fetal reduction is a widely accepted procedure. It is useful in reducing the morbidity and mortality of multiple gestation. Many patients who undergo fetal reduction experience a wide variation of emotional experiences as they deal with the distinction between medical and moral issues. In experienced hands, it is a very low-risk procedure. Long-term follow-up of infants born after fetal reduction must be conducted, but at present there is no great reason to be concerned.

TABLE 13.1

Is selective reduction allowed or used?

How ART is governed	Country	Allowed/ used	Not allowed/ not used	Not mentioned/ don't know
Covered by statutes	Austria			+
	Belgium			+
	Bulgaria			+
	Canada			+
	Czech Republic	+/Used		
	Denmark	+/Used		
	France	+/Used		
	Germany	+/Used		
	Greece			+
	Hong Kong	+/Used		
	Hungary	+/Used		
	Israel	+/Used		
	Italy			+
	Korea			+
	Latvia			+
	Netherlands			+
	New Zealand			+
	Norway		+	
	Russia	+/Used		
	Saudi Arabia			No data
	Slovenia			+
	Spain			+
	Sweden	+/Used		
	Switzerland			+
	Taiwan			+
	Tunisia			+
	Turkey	+/Used		
	United Kingdom	+/Used		
	Vietnam			+
Covered by guidelines	Argentina		+	
	Australia			+/Don't know if used
	Brazil		+	
	Chile		+	
	China	+/Used		
	Croatia		+	
	Egypt	+/Used		
	India	+/Used		
	Ireland		+	
	Japan			+/Used
	Lithuania			+/Not used
	Mexico			+/Not used
	Morocco	/Used		
	Philippines		+	
	Singapore		+	
	South Africa			+/Used
	Thailand			+/Used
	United States			+/Used
None	Colombia		/+	
	Ecuador		/+	
	Finland		/+	
	Jordan	/Used		
	Malaysia		/+	
	Peru		/+	
	Portugal		/+	
	Romania		/+	
	Uruguay		/+	
	Venezuela		/+	

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CHAPTER 14: Preimplantation genetic diagnosis

Preimplantation genetic diagnosis was first reported in the medical literature in 1990 for genetic testing of embryos developed through IVF. Since then, its use and popularity has grown steadily, and it has become one of the fastest growing techniques in reproductive medicine. It is offered as a method of allowing couples at risk for having children with genetic aberrations an opportunity to transfer only unaffected embryos and to discard embryos with genetic abnormalities. Preimplantation genetic diagnosis typically involves the removal of one or two blastomeres at around the eight-cell stage at day 3 after fertilization. The laboratory work usually takes about a day, and unaffected embryos are transferred back on day 4 or 5. It is an alternative to postconception diagnosis and termination of pregnancy. Although it obviates possible termination of pregnancy, it does require that a moral distinction be made by the couple between abortion and the discarding of affected nontransferred embryos.

The reliability of PGD is well established, and the error rate is extremely low. The principal drawbacks to PGD are the relatively high cost and the fact that the procedure leaves fewer available embryos to transfer.

Preimplantation genetic diagnosis theoretically could be used in any of >1,000 genetic tests now available. A number of these are very controversial. The following are the six general types of PGD testing:

- Autosomal single gene disorders such as thalassemia, cystic fibrosis, Tay-Sachs disease, and sickle cell disease;
- Chromosomal rearrangements (inherited chromosomal abnormalities);
- Aneuploidy;
- X-linked diseases;
- Nonmedical sex selection; and
- Human leukocyte antigen (HLA) typing.

Because of increased aneuploidy rates reported in people with impaired fertility, such as those with recurrent pregnancy loss, who have undergone transfer of good-quality embryos without achieving a viable pregnancy, or who are of advanced age, PGD screening for preembryo aneuploidy has been suggested in this population. Cytoplasmic and nuclear aberrations in the oocyte may lead to chromosomal nonjunction during meiosis and mitosis. This may result in chromosomal aneuploidy with monosomy, trisomy, complex abnormal, or haploidy patterns. In some countries, such as the United States, the use of PGD for aneuploidy screening has now become one of the most frequent indications.

Although PGD is used to select the sex of the embryo to avoid the birth of children with X-linked genetic diseases, its use for nonmedical purposes, such as satisfying the preference of the couple, is very controversial because of the complex ethical and moral issues involved. In a number of countries, such as the United Kingdom and Canada, PGD is specifically prohibited from use for this purpose by statute.

ANALYSIS OF SURVEY

The first category in the survey was countries practicing with statutes. Preimplantation genetic diagnosis is allowed under statute in 20 of 29 countries surveyed (Table 14.1). It is not allowed in 3 countries: Germany, Italy, and Switzerland. The statute does not mention it in 6 countries. It is actually being used in 18 countries. Although allowed, it is not used in Norway or Tunisia. The law allows its use in Norway, but it cannot be used until the ban or research on human embryos is lifted. In France, it is allowed by law in only three centers. In the Netherlands, it is allowed in one center. In two other centers in that country, preimplantation genetic screening for embryo selection and transfer is allowed for research purposes only. In Singapore, PGD cases are approved by the Ministry of Health on an individual basis. In New Zealand, PGD is publicly funded when the chance of the child being affected is ≥25%.

The second category in the survey was countries where physicians practice under national guidelines. There are 12 countries in this group that permit PGD. In 5 others with guidelines, it is not mentioned. None prohibit it. Although it is being used in 9 counties, in the majority of these it is performed on a very limited basis. In Croatia, Japan, and Morocco, the respondents specifically noted that it is not being used.

Including the third category in the survey, countries where physicians are practicing with neither statues nor guidelines, PGD is being used in 34 (63%) of 54 of the countries responding to this survey.

The study also specifically surveyed the use of PGD screening for aneuploidy. It is being used for this screening in 23 (43%) of 54 of the countries surveyed. Among the 29 countries with statutes, this type of PGD is allowed in 13, not mentioned in 10, and not allowed in 6. These are France, Germany, Greece, Italy, Norway, and Switzerland. It is allowed for research purposes only in the Netherlands and Sweden. Of the 23 countries where it is allowed or not mentioned, it is actually being used for this purpose in only 12.

Among the 16 countries surveyed with guidelines, PGD for aneuploidy screening is not allowed for this purpose in 3 countries, Chile, Japan and Singapore, and is not mentioned in 7 others. It is actually being used in only the following 5 of these 16 countries: Argentina, Australia, Egypt, Thailand, and the United States.

TABLE 14.1

Use of PGD.

How ART is governed	Country	Is PGD allowed/used?			Is PGD for embryo screening (aneuploidy) allowed/used?		
		Allowed/ used	Not allowed/ not used	Not mentioned	Allowed/ used	Not allowed/ not used	Not mentioned
Covered by statutes	Austria			+			+
	Belgium	+/+			+/+		
	Bulgaria			+			+
	Canada			+			+
	Czech Republic	+/+			+/+		
	Denmark	+/+			+/−		
	France	+/+				+	
	Germany		+			+	
	Greece	+/+			+/+		
	Hong Kong			+/+	+/+		
	Hungary	+/+					+
	Israel	+/+			+/+		
	Italy		+			+	
	Korea	+/+			+/+		
	Latvia			+			+
	Netherlands	+/+			+/+		
	New Zealand	+/+			+/+		
	Norway	+/Not used				+	
	Russia	+/+			+/+		
	Saudi Arabia			No data			No data
	Slovenia	+/+					+
	Spain	+/+					+
	Sweden	+/+			+/+		
	Switzerland		+			+	
	Taiwan			+			+
	Tunisia	+/Not used					+
	Turkey	+/+			+/+		
	United Kingdom	+/+			+/+		
	Vietnam			+			+
Covered by guidelines	Argentina	+/+			+/+		
	Australia	+/+			+/+		
	Brazil			+			+
	Chile	+/+				+	
	China			No data			No data
	Croatia	+/Not used					+
	Egypt	+/+			+/+		
	India	+/+			+/?		
	Ireland			+			+
	Japan	+/Not used				+	
	Lithuania			No data			No data
	Mexico			+			+
	Morocco	+/Not used				/+	
	Philippines			+			+
	Singapore	+/+				+	
	South Africa	+/+			+/Not common		
	Thailand	+/+			+/+		
	United States	+/+			+/+		
None	Colombia	/+			/+		
	Ecuador		/Not used			/+	
	Finland	/+			/+		

Kempers. Preimplantation genetic diagnosis. Fertil Steril 2007.

TABLE 14.1

Continued.

How ART is governed	Country	Is PGD allowed/used?			Is PGD for embryo screening (aneuploidy) allowed/used?		
		Allowed/ used	Not allowed/ not used	Not mentioned	Allowed/ used	Not allowed/ not used	Not mentioned
	Jordan	/Used			/+		
	Malaysia	/Used			/+		
	Peru	/Used			/+		
	Portugal	/Used			/+		
	Romania		/Not used			/+	
	Uruguay	/Used			/+		
	Venezuela	/Used			/+		

Kempers. Preimplantation genetic diagnosis. Fertil Steril 2007.

Among the 11 countries with neither statutes nor guidelines for this screening, PGD is being used in 6 of them.

DISCUSSION

This survey indicates that PGD is widely available throughout the world. Among 54 countries in this survey, PGD is not allowed in only 3 countries. Although allowed, it is actually being used in only 34 (63%) of 54 of these counties. In the majority, it is used only on a very limited basis and, often, in a controlled and restricted way. The percentage of countries where PGD is being used is essentially unchanged over that reported 3 years ago in "Surveillance 04". Those data indicated that it was being used in 34 (69%) of 49 countries surveyed.

In this survey asking specifically about the use of PGD in screening for aneuploidy, respondents noted that it is not allowed in 7 of the 54 countries. Among these 47 countries where it is permitted, including 2 restricting it to research only, it is being used in only 23 (51%) of them.

Although these data offer valuable information about how available PGD is worldwide and in what countries it is actually being used, it does not attempt to provide information about how often it is performed, its overall efficacy, by whom it is being performed, and with what clinical outcomes. A number of organizations with concerns about these issues have surveyed and are conducting surveys in specific countries and regions to try to answer some of these questions. One such is the European Society of Human Reproduction and Embryology (ESHRE) consortium, formed in 1997. Their published report for the year 2000 (1) analyzed data from 25 centers and was summarized in "Surveillance 04." Their reporting is ongoing (2). Looking at data only from the United States, the Genetics and Public Policy Center at Johns Hopkins University conducted an extensive poll of all IVF centers in the United States in 2006 (3). Responses were obtained from 186 of the 415 centers polled. In the United States, the most common indication for PGD is aneuploidy, 66%; followed by autosomal disorders, 12%; chromosomal rearrangements, 9%; X-linked diseases, 3%; nonmedial sex selection, 9%; and HLA typing, 1%. Another important related publication is the recent report from the collaboration of the European Commission, European Society of Human Genetics, and ESHRE, interfacing genetics and medically assisted reproduction with respect to technical, social, ethical, and legal issues (4).

Although the benefits of the technology are undeniable, a number of concerns have been raised in some circles. These include moral and ethical issues, such as the potential of parents to exercise excessive control over their children's characteristics, costs and availability dependent on the financial status of the parents, safety, accuracy, regulation, and monitoring. Self-regulation in countries with and without guidelines remains a challenge.

SUMMARY

The availability of PGD provides significant benefits to couples worldwide. Not only does it prevent women from delivering offspring with serious genetic disease, but it avoids abortion. Considerable variations in applications exist. For example, its use for aneuploidy screening is becoming more common in some parts of the world. There is a very low incidence of errors in PGD, and it can be generally considered to be safe.

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CHAPTER 15: IVF Surrogacy

This survey is limited to that type of surrogacy requiring IVF. Often referred to as *full surrogacy* or *IVF surrogacy,* this procedure is used by women who have functioning ovaries but no uterus, either by virtue of congenital absence or by previous hysterectomy. The sperm are supplied by the husband of the rearing mother.

A distinction is drawn from so-called partial surrogacy, where the surrogate supplies not only the uterus but also the egg, with the sperm being supplied by the husband of the intended rearing mother. As this latter type of surrogacy does not require the services of a physician and is often practiced without a physician or with only the token participation of a physician, it is not included in this survey.

In IVF surrogacy, it is obviously necessary that the legal situation in the particular jurisdiction be thoroughly understood; that adoption procedures, if necessary, are properly attended to; and that the legal as well as the medical aspects of the procedure are completely covered.

ANALYSIS OF SURVEY

Less than one half of all surveyed jurisdiction appear to use IVF surrogacy (Table 15.1). The frequency with which surrogacy is used is very difficult to ascertain. It may be pertinent that in the data for the United States for the year 2003, there were 112,872 cycles, and there are listed 72 surrogate cycles. Presumably, all of these are IVF surrogacy or they would not be included in the report, but the use of donor eggs in some of these cases cannot be excluded.

Some countries have particular regulations, such as the following:

- Argentina requires evaluation by a Special Committee for case-by-case evaluation;
- West Australia allows such surrogacy for compassionate use only;
- South Australia under the Family Relations Act bans commercial surrogacy, but altruistic surrogacy is allowed by default;
- The state of Victoria, Australia, allows only altruistic surrogacy, and no payment or reward must be exchanged;
- Brazil does not allow the ART center to be involved in any financial arrangement with regard to the surrogacy;
- Greece has a court decision requiring the consent of all parties and no payment exchange. The commissioning woman must be medically incapable of bearing the fetus, and the surrogate must be medically fit to bear the fetus;
- Israel stipulates that the couple must be married, the surrogate mother must be single, and permission must be given by a special committee of the Ministry of Health; and
- The United States has state by state variation, depending on the legislative action of each particular state.

DISCUSSION

When the female partner is without a uterus, IVF surrogacy offers several advantages, but the role and outcome for all concerned remains subject to considerable uncertainty, particularly in some legislative jurisdictions. The difficulty revolves around the fact that for many years, the birth mother has been considered the real mother. This has been revised by legislation in some jurisdictions to accommodate the surrogacy situation, but the practical point is that the legal aspect of the matter must be precisely clarified before IVF surrogacy is considered. Some legislation in the United States has indicated that the surrogate has the right to make a decision as to whether she will abide by the contract until after the birth of the baby. All in all, the legal uncertainties associated with IVF surrogacy make it one of the more problematic procedures available to the hysterectomized infertile woman.

Furthermore, there have been no follow-up studies of the effect of surrogacy on family development after the fact. The lack of study is likely associated with the limited number of cases available and with the fact that children born under this circumstance are even now rather young.

Although it is generally stated that treatment assessment and counseling during and after the procedure are desirable, the fact remains that the counselor can call on very little practical experience.

The payment to the surrogate raises special concerns. Several jurisdictions have provided that no payment to the surrogate can be made. From a practical point of view, this greatly limits the availability of suitable surrogates and raises the question of the real motivation for being a surrogate.

There have been a few instances in which IVF surrogacy has been considered for social reasons; that is, the parents have wished to have a child borne by a surrogate for other than medical reasons. This has generally been considered inappropriate.

SUMMARY

When parenting partners cannot reproduce because the woman lacks a functioning uterus, IVF surrogacy is useful. This type of surrogacy must be clearly distinguished from surrogacy in which the surrogate supplies the female genetic component as well as the uterus. Although less problematic than partial surrogacy, IVF surrogacy still presents difficulties, particularly in its legal and practical aspects, and thus has not gained wide use or recognition.

TABLE 15.1

Is IVF surrogacy allowed and/or used?

How ART is governed	Country	Allowed/used	Not allowed/not used	Not mentioned
Covered by statutes	Austria		+	
	Belgium			+
	Bulgaria			+
	Canada	+/+		
	Czech Republic			+
	Denmark		+	
	France		+	
	Germany		+	
	Greece	+/+		
	Hong Kong	+/?		
	Hungary	+/−		
	Israel	+/+		
	Italy		+	
	Korea			+
	Latvia		+	
	Netherlands	+/+		
	New Zealand	+/+		
	Norway		+	
	Russia	+/+		
	Saudi Arabia			No data
	Slovenia		+	
	Spain		+	
	Sweden		+	
	Switzerland		+	
	Taiwan		+	
	Tunisia		+	
	Turkey		+	
	United Kingdom	+/+		
	Vietnam		+	
Covered by guidelines	Argentina		+	
	Australia	+		
	Brazil	+		
	Chile			+
	China			No data
	Croatia		+	
	Egypt		+	
	India	+		
	Ireland			+
	Japan		+	
	Lithuania			No data
	Mexico			+
	Morocco		/+	
	Philippines		+	
	Singapore		+	
	South Africa	+		
	Thailand	+		
	United States	+		
None	Colombia	/+		
	Ecuador	/+		
	Finland	/+		
	Jordan		/+	
	Malaysia		/+	
	Peru	/+		
	Portugal		/+	
	Romania	/+		
	Uruguay		/+	
	Venezuela		/+	

Jones. IVF surrogacy. Fertil Steril 2007.

CHAPTER 16: Experimentation on the preembryo

Research on the preembryo is not easy to define. For example, variations in the culture media in an effort to improve development of a preembryo certainly appear to be research on the preembryo, but generally speaking, many laboratories in the United States use alternate culture media in an attempt to improve results without considering this to be experimentation in the sense of requiring third-party approval. However, it appears quite clear that if the experimental design necessarily results in the destruction of a preembryo by the experimental procedure, as for example in obtaining cells from the inner cell mass for stem cell development, such experimentation needs third-party approval. For example, in the United Kingdom, such approval would be by the Human Fertilisation and Embryology Authority; in the United States, by an institutional review board; and in other countries, by corresponding mechanisms.

The availability of preembryos for research is very controversial and often is a bottleneck in research plans. For the most part, availability of preembryos is related to the moral status of the preembryo, which is discussed in a separate chapter. Many entities confine research to so-called spare preembryos. Indeed, in a presidential decree in the United States authorizing the use of federal funds to develop stem cell lines, it was specified that the available preembryos must be discard embryos from embryos created for reproductive purposes. Furthermore, some states in the United States and other nations have specifically passed legislation prohibiting the creation of preembryos for research. However, such was certainly performed at one time in the United Kingdom and has been performed in the United States.

All of this raises the question about the genetic background of the material available for research. Discard material is just that—designated for discard. It can be strongly argued that for research, it would be very desirable to have the best possible genetic material that could be obtained by genetic screening of designated donors. It is to be noted that many contracts signed before cryopreservation specify that the genetic contributors to the cryopreserved material have the right to designate the use of any cryopreserved material not used for reproduction. Among these options is research, and it is this material that has for the most part been used in such cases that have involved experimentation on the preembryo. This, of course, raises the moral issue of the appropriateness of using material that was intended for reproduction for purposes other than the original intention.

ANALYSIS OF SURVEY

About half of the entities indicated in the reply to the questionnaire that the use of human preembryos for experimental purposes was not acceptable (Table 16.1). About half of the replies were based on law, and half, on societal grounds. The effect is probably essentially the same as far as research in those entities is concerned.

However, about half of the entities indicated that research was acceptable. But it is extremely likely that the experimentation would have to be performed in such countries at a time before which human personhood was assumed to be acquired; this varies greatly from nation to nation, as indicated in the chapter devoted to this subject.

Great public attention has been devoted to the stem cell controversy, which is indeed experimentation on the preembryo. However, its importance has risen to such a level that stem cell research is treated in a separate chapter.

It is very clear that there is no international consensus on the appropriateness of research on the preembryo.

SUMMARY

About half of the surveyed nations indicate that experimentation on the preembryo is unacceptable. About half of those answers were based on law, and about half, on societal grounds. Furthermore, where research is authorized, it is often subject to various time limits with respect to embryonic development, as indicated in the chapter devoted to that subject.

Over and above all, the definition of what constitutes research is a cloudy issue, although if the experimental design implies the destruction of the preembryo, that clearly falls under the heading of experimental. Where experimentation is authorized, this generally requires the approval of a third-party governing body.

There is no international consensus.

TABLE 16.1

Use of human pre-embryos for experimental purposes.

How ART is governed	Country	Is the use of human pre-embryos for experimental purposes an acceptable procedure? Yes	No	Is the yes or no by virtue of law? Of guidelines? Of cultural practice? Of recognized and prevailing religious decree?	If yes, is specific approval of the research proposal required, and if so, by what body?
Covered by statutes	Austria		+	Forbidden by law	
	Belgium	+		Law on the protection of the embryo in vitro (May 2003)	Institutional ethical committee and federal commission on the protection of the embryo in vitro
	Bulgaria		+	No, by virtue of general feeling of society	
	Canada	+		Current practice guidelines and by pending law	No, only by individual IRBs
	Czech Republic	+		There has been prepared law	
	Denmark	+		Law	Research approval required
	France	+		Law	Biomedicine agency
	Germany		+	Law	
	Greece	+		Laws 3089/2002 and 3305/2005	From the authority
	Hong Kong	+		Code of practice	Refer to code of practice
	Hungary	+		Law	By the Committee of Human Reproduction of the Ministry of Health
	Israel		+		
	Italy	+		Law	
	Korea	+		Law	Minister of Health and Welfare
	Latvia		+	Law	
	Netherlands				
	New Zealand		+	Donation of embryos to research is currently being considered by the advisory committee	If the advisory committee approves embryo donation to research, applications would be considered on a case-by-case basis

Jones. Experimentation on the preembryo. Fertil Steril 2007.

TABLE 16.1

Continued.

How ART is governed	Country	Is the use of human pre-embryos for experimental purposes an acceptable procedure? Yes	No	Is the yes or no by virtue of law? Of guidelines? Of cultural practice? Of recognized and prevailing religious decree?	If yes, is specific approval of the research proposal required, and if so, by what body?
	Norway		+	Law	
	Russia		+	Don't know	
	Saudi Arabia				No data
	Slovenia	+		Embryos cannot be created for research purposes; viable embryos can only be used if both potential parents agree by informed consent and embryos can only be used in research if benefit for embryos can be demonstrated; research on embryos not suitable for transfer (or those frozen embryos that will be left to die after 5 y of storage) is allowed	Ethical committee of Republic of Slovenia; approval from the parents
	Spain	+		Law 45/2003 only for embryos frozen before 2003	Yes, by the centro nacional de transplantes y medicina regenerativa
	Sweden	+		Law and guidelines	Research proposal required. By patient and the local ethics committees
	Switzerland	+		The law on embryo research stipulates stringent criteria for the production of embryonic stem cells exclusively; this can only be performed on so-called spare embryos	Yes, the local ethics committee and an approval has to be acquired from the federal ministry of health in Bern
	Taiwan		+	Cultural practice	IRB of hospital
	Tunisia		+	Law	
	Turkey		+	Law	

Jones. Experimentation on the preembryo. Fertil Steril 2007.

TABLE 16.1

Continued.

How ART is governed	Country	Is the use of human pre-embryos for experimental purposes an acceptable procedure? Yes	No	Is the yes or no by virtue of law? Of guidelines? Of cultural practice? Of recognized and prevailing religious decree?	If yes, is specific approval of the research proposal required, and if so, by what body?
Covered by guidelines	United Kingdom	+		Law: Human Fertilisation and Embryology Act 1990 + Human Reproductive Cloning Act 2001	Yes, approval of the national regulator HFEA under license
	Vietnam		+	Law, guideline	
	Argentina	+		Guidelines	The current guidelines propose an IRB; in addition, some institutions have an IRB
	Australia	+		Law	Yes; license from NHMRC licensing committee—Research Involving Human Embryos Act 2002
	Brazil	+		We are allowed to do research on stem cells in frozen embryos in the lab, but we have a lot of cultural discussion on what is life	Project and lab conditions must be submitted to sanitary department
	Chile		+	Ethical committees of the institutions have set the guidelines, not approving even PGD	
	China				No data
	Croatia		+		
	Egypt	+		Guidelines, prevailing religious decree	Yes, by ethics committee
	India	+		It is an acceptable procedure within the first 14 d of embryonic life	Yes, approval by institutional ethics committee is required

Jones. Experimentation on the preembryo. Fertil Steril 2007.

TABLE 16.1

Continued.

How ART is governed	Country	Is the use of human pre-embryos for experimental purposes an acceptable procedure? Yes	No	Is the yes or no by virtue of law? Of guidelines? Of cultural practice? Of recognized and prevailing religious decree?	If yes, is specific approval of the research proposal required, and if so, by what body?
	Ireland		+	The creation of new forms of life for experimentation purposes is professional misconduct	
	Japan	+		Guideline by JSOG. Governmental levels: [1] Human Cloning Regulation Act (2000), [2] guideline on human ES cells (2001), [3] guideline on human embryo (2005)	Dual application and examination is required by IRB and government
	Lithuania				No data
	Mexico		+	There is no specification related to this topic	
	Morocco		+	Recognized and prevailing religious decree, but debates are made to study these questions	Still working on it
	Philippines		+	Cultural and religious practice	
	Singapore	+		Directives from Ministry of Health: law under the Human Cloning And Other Prohibited Practices Bill 2004	Yes, final approval must come from the Ministry of Health, after the appropriate IRB approvals
	South Africa	+		Not specified in regulations and not specifically disallowed	All research involving human subjects or material must be approved by local scientific and ethics committees

Jones. Experimentation on the preembryo. Fertil Steril 2007.

TABLE 16.1

Continued.

How ART is governed	Country	Is the use of human pre-embryos for experimental purposes an acceptable procedure? Yes	No	Is the yes or no by virtue of law? Of guidelines? Of cultural practice? Of recognized and prevailing religious decree?	If yes, is specific approval of the research proposal required, and if so, by what body?
	Thailand	+		There is actually no guideline or law governing this. However, in the consent form for freezing that is issued by the RTCOG, there is a statement asking the couples what they would like the clinic to do if they decide they no longer want to use their frozen embryos. They can either ask the center to destroy the embryos or give the embryos for donation, or they can give the embryos to the center for research. This indirectly implies that the RTCOG allows the use of pre-embryos for research if the couples give their informed consent.	The research proposal must be approved by the local ethical committee.
	United States	+		Guidelines. With IRB approval and only with private funds with a few exceptions	Yes, an IRB
None	Colombia		+	Cultural practice and religious	
	Ecuador		+	Cultural practice and religious	

Jones. Experimentation on the preembryo. Fertil Steril 2007.

TABLE 16.1

Continued.

How ART is governed	Country	Is the use of human pre-embryos for experimental purposes an acceptable procedure? Yes	No	Is the yes or no by virtue of law? Of guidelines? Of cultural practice? Of recognized and prevailing religious decree?	If yes, is specific approval of the research proposal required, and if so, by what body?
	Finland	+		Law on medical research (including gametes and embryos)	Research proposal, by ethical committee of hospital. Approval to do embryo research (for the institute), by Ministry
	Jordan		+	Cultural practice; needs a special permit	Yes, by the family and IRB
	Malaysia		+	Cultural practice	
	Peru		+		
	Portugal		+	Cultural practice	
	Romania	+		No	
	Uruguay		+	Cultural practice	
	Venezuela		+	Recognized and prevailing religious decree	

Note: IRB = institutional review board; HFEA = Human Fertilisation and Embryology Authority; NHMRC = National Health and Medical Research Council; JSOG = Japan Society of Obstetrics and Gynecology; ES = embryonic stem; RTCOG = Royal Thai College of Obstetrics and Gynecology.

Jones. Experimentation on the preembryo. Fertil Steril 2007.

CHAPTER 17: Cloning

Cloning is often considered as a subheading under the general concept of experimentation on the preembryo. However, cloning does not involve the union of a sperm and an egg. Rather, it is the creation of a developing entity by the transfer of a whole exogenous genome, that is, of 46 chromosomes into an enucleated oocyte. This is often referred to as *somatic cell nuclear transfer.* Nuclear cloning was first successful with the use of an embryonic cell of an amphibian, but the embryonic cell transfer concept has been applied to many other species, including the mammal. In 1997, the use of a somatic cell nucleus in the sheep resulted in the birth of the famous Dolly. This has been followed by success in rodents, cats, pigs, cows, sheep, mules, dogs, and horses.

The cloning process, quite aside from its potential to create an identical twin, has great research potential. For example, a cloned entity could be the source of an inner cell mass cell for the creation of a stem cell line.

It is clear that a sharp distinction needs to be made between nuclear cloning for reproductive purposes and nuclear cloning for therapeutic or investigational purposes. This distinction is sometimes not made, and in an analysis of the survey, it's entirely possible that some of the opinions about therapeutic cloning have their origin in and considerations about the potential and usefulness of reproductive cloning.

ANALYSIS OF SURVEY

The use of somatic cell nuclear transfer for reproduction, that is, the creation of an identical twin, is not approved, nor is it being worked on in any of the responding political entities. In those entities in which this matter has been a subject of legislation, the legislation has been uniformly opposed to it. Thus, there appears to be no investigative effort directed toward the use of cloning for reproductive purposes.

It is interesting, as noted in Table 17.1, that therapeutic cloning is not allowed or not used in well over one half of the respondent political entities. One may suspect that in some countries, the attitude against reproductive cloning is so strong that this has spilled over into the thought about therapeutic cloning, despite the fact that that therapeutic cloning, if successful, offers great therapeutic possibilities. However, there are a number of entities opposed to therapeutic cloning that are based in the strong tradition of the Roman Catholic persuasion, where anything dealing with reproduction outside of the normal is considered illicit. Among the nations where therapeutic cloning is not allowed or not used, in about one half of the remaining nations there is no mention of therapeutic cloning, either in the law or in public opinion that is vocal enough to be recorded. However, there are somewhat fewer than 20 nations where therapeutic cloning is allowed and is actually being used.

DISCUSSION

The experience in mammals with somatic nuclear cloning indicates that there is great inefficiency and a high degree of abnormalities. This is, of course, one of the reasons that it has not been thought that reproductive cloning is a reasonable clinical objective. It is true that there have been a number of newspaper reports about its successful application, but the fact is that in no instance has there been a scientific confirmation that this has been successfully applied in human beings. As indicated in the analysis of the survey, there is no nation that has specifically authorized the use of reproductive cloning. There are some nations that are silent about it, and there is a majority of nations where there is a law against it.

Experimental cloning does offer great research potential. As judged from the survey, there is no unanimity of opinion about the appropriateness of using cloning for experimental purposes. Therefore, activity in this area will be limited to a handful of nations.

SUMMARY

Somatic nuclear cloning is beset by many biological problems, and its clinical application for reproduction is therefore not likely to be pursued in the immediate future. In addition, there are many countries that have legislation against it. It appears that there has been some legislation against therapeutic cloning that may indeed be a carryover from concerns about reproductive cloning.

TABLE 17.1

Is therapeutic cloning allowed and/or used?

How ART is governed	Country	Allowed/used	Not allowed/not used	Not mentioned
Covered by statutes	Austria		+	
	Belgium	+		
	Bulgaria			+
	Canada		+	
	Czech Republic	+		
	Denmark	+		
	France		+	
	Germany		+	
	Greece			+
	Hong Kong			+
	Hungary			+
	Israel		+	
	Italy		+	
	Korea	+		
	Latvia		+	
	Netherlands	+		
	New Zealand		+	
	Norway		+	
	Russia	+		
	Saudi Arabia			No data
	Slovenia			+
	Spain		+	
	Sweden	+		
	Switzerland	+		
	Taiwan			+
	Tunisia			+
	Turkey		+	
	United Kingdom	+		
	Vietnam		+	
Covered by guidelines	Argentina	+		
	Australia			+
	Brazil			+
	Chile			+
	China			No data
	Croatia			+
	Egypt	+		
	India	+		
	Ireland			+
	Japan	+		
	Lithuania			No data
	Mexico			+
	Morocco		+	
	Philippines		+	
	Singapore		+	
	South Africa			+
	Thailand			+
	United States	+		
None	Colombia		/+	
	Ecuador		/+	
	Finland		/+	
	Jordan		/+	
	Malaysia		/+	
	Peru		/+	
	Portugal		/+	
	Romania		/+	
	Uruguay		/+	
	Venezuela		/+	

Jones. Cloning. Fertil Steril 2007.

CHAPTER 18: Gamete intrafallopian transfer

Gamete intrafallopian transfer (GIFT) emerged in 1983 as an alternative to IVF. It requires laparoscopy, although in some centers eggs are harvested by vaginal ultrasonography and placed in the fallopian tubes along with the sperm by laparoscopic procedure. Because GIFT is a more complicated technique, its use is generally confined to special circumstances, which may be either medical or regulatory.

ANALYSIS OF SURVEY

Gamete intrafallopian transfer does not appear to be used under any circumstances in the Czech Republic, Denmark, Finland, Morocco, New Zealand, Slovenia, Sweden, or Switzerland. In most countries, the statutes, guidelines, or practice customs do not recognize any difference between IVF and GIFT. In some countries, such as Ecuador, Ireland, Italy, Japan, Malaysia, Taiwan, and the United Kingdom, GIFT is not covered by the umbrella of IVF.

Some countries do not have stated limits on the number of oocytes or preembryos to be used when GIFT is applied: others do, including the following:

- In Peru, four maximum;
- In Argentina, Denmark, India, Japan, Singapore, and Slovenia, three maximum;
- In Singapore, a maximum of four oocytes can be replaced if [1] all children conceived can be delivered in a hospital that has level 2 neonatal intensive care facilities, [2] the patient has undergone two unsuccessful ART cycles, and [3] the patient is >35 years of age;
- In Italy, two maximum; and
- In the United States, the number is the same as that of the IVFs, plus one.

DISCUSSION

Gamete intrafallopian transfer is indicated in women who have at least one functioning fallopian tube. It was never demonstrated in comparable cases that GIFT had any advantage over standard IVF. For this reason, and because it requires laparoscopy, whereas IVF does not, GIFT is now used only in niche situations.

A curious situation now exists in Italy. In theory, after oocyte retrieval, Italian teams can transfer a couple of oocytes with sperm in the tubes by GIFT and the others by IVF-ET, because the law concerns only the three oocytes for fertilization in vitro (without mentioning those in vivo), and the teams are not allowed to use frozen embryos.

SUMMARY

Gamete intrafallopian transfer is currently used only in niche situations. As we noted in Analysis of Survey, several countries have special legislative limits on the number that can be used with GIFT.

CHAPTER 19: Status of the conceptus

The moral and legal status of the preembryo—that is, the moral and legal status of the early developing human conceptus—is often key to the acceptability of many procedures that are made available by IVF technology. The large umbrella is experimentation on the conceptus. However, under this umbrella, there would be included such things as PGD, selection for transfer, and discard of the nontransferred embryos, either with or without PGD; cryopreservation, with its loss of material by virtue of the procedure; surrogacy, with its violation of the genetic lineage; and other experimental procedures discussed in the chapters devoted to these subject.

Not the least of the problem is that the moral and legal status may differ from each other in the minds of some individuals. For example, in the United States, according to the Supreme Court decision of Roe v. Wade, personhood, as defined as an entity deserving protection by society, begins only with viability, but many individuals hold that preembryos should not be used for experimentation because they are persons, or at least require the respect of an individual who is in being, that is, a human being.

Further, it needs to be mentioned that the law has difficulty in dealing with an entity that is neither a thing nor a person. A case can be made for maintaining that the human conceptus is neither one nor the other.

ANALYSIS OF SURVEY

The survey brought out the fact that there is a great diversity among nations regarding the time during development when a human person is considered to exist. In this context, a human person can be defined as the entity that deserves protection by society. The diversity could not be greater. Respondents from several nations indicated that personhood began with fertilization, whereas one respondent (from Canada) indicated that personhood began at delivery. It needs to be noted that the time limit for experimentation may or may not correspond to the time of the acquisition of personhood. This point requires that the answers to the survey (Table 19.1) may require interpretation. About one half of the respondents indicated in their reply to the questionnaire that personhood was considered to begin with fertilization. Indeed, some Latin American countries have such a provision in their constitution.

In addition, one unsurveyed Latin American country, Costa Rica, also has a constitutional provision with the same statement, that personhood begins with fertilization. Indeed, the constitutional court in Costa Rica has held that this provision outlaws the use of IVF. Because of this ruling, IVF is not available in Costa Rica.

Germany has a law that states that personhood exists after the pronuclear stage.

It is extremely interesting and indeed significant that various nations reply with varying numbers of days after which personhood is considered to exist. It has been mentioned that about one half of the countries indicate that personhood exists with fertilization. However, as mentioned, Germany indicates that personhood begins after 1 day, that is, after the commingling of the genetic material. Many respondents indicated that 14 days is the time after which personhood exists.

It is clear that religious tradition has greatly influenced this issue. It is sometimes difficult to know whether the respondent to the questionnaire was stating a legislative position or a religious tradition. According to the Roman and Greek traditions, ensoulment occurs with fertilization, and ensoulment is equated with protection by society. It is clear that there is no international consensus on the time during development after which protection should be guaranteed by society.

SUMMARY

The moral status of the conceptus is often a controlling issue with respect to research. The questionnaire did not intend that the moral status be related to research, but in many instances the answer is so related that the replies must be evaluated in that connection. It is interesting that the 14-day rule is widely applied with respect to research. This corresponds to the time of the appearance of the primitive streak and indeed is the time at which biologic individuation is guaranteed. It appears clear that a religious tradition has had a great influence on this particular question. It is also clear that there is a complete lack of consensus on when society should protect the developing conceptus.

TABLE 19.1

Is there a recognized time during human development after which a human person is considered to exist?

How ART is governed	Country	Yes, by: Law	Yes, by: Guidelines	Yes, by: Cultural or religious beliefs	No	What is the recognized time?
Covered by statutes	Austria				+	
	Belgium				+	
	Bulgaria				+	
	Canada	+				At delivery
	Czech Republic	+				12 wk of pregnancy
	Denmark	+				2 wk
	France				+	
	Germany	+				Fusion of the oocyte and the sperm nucleus defines the beginning of a new individual
	Greece	+				After birth
	Hong Kong		+			14 d? Zygote stage?
	Hungary		+			2 wk after fertilization
	Israel			+		Religious definition: 40 d after fertilization
	Italy	+				The contact of sperm with oocytes!!!
	Korea				+	
	Latvia				+	
	Netherlands				No data	
	New Zealand				+	
	Norway	+				Currently, a fertilized oocyte is defined as the beginning of life in biological, moral, and legal terms. There is no special definition of a fertilized oocyte. Since 1978, when our first law regulating the field was in place, life was defined in a legal sense as starting at fertilization (the reason for the ban on research on human embryos). The arguments were successfully put forward by conservative Protestant Christians. There is of course not a consensus in Norway about this, but until now, the religious argument has had the upper hand.

Jones. Status of the conceptus. Fertil Steril 2007.

(*Continued on next page*)

TABLE 19.1

Continued.

How ART is governed	Country	Yes, by Law	Guidelines	Cultural or religious beliefs	No	What is the recognized time?
	Russia				+	
	Saudi Arabia				No data	
	Slovenia				+?	14 d, can be cultured in vitro
	Spain				+	
	Sweden				+?	14 d
	Switzerland	+				For pregnancies in utero, life is protected from the 12th week of pregnancy onward. For embryos in vitro, life is protected from syngamy. I always state to my medical students that for embryos, life become dangerous as soon as they reach the uterine cavity.
	Taiwan	+				Not mentioned
	Tunisia	+				Usually 15 d
	Turkey			+		By the fetal cardiac activity, its accepted as a human being.
	United Kingdom	+				14 d? At birth of a live child?
	Vietnam				+	
Covered by guidelines	Argentina				+	The Argentinean civil code (1871) states that a person is considered to be one from the conception inside the mother's womb. Since this statement, there have been millions of interpretations that up to date haven't agreed. Interpretations will vary on the basis of religions and personal beliefs, according to the conceptualization of conception. A never-ending discussion.
	Australia	+				Varies
	Brazil			+		For public opinion, from the fertilization. We have a very big Catholic influence.

Jones. Status of the conceptus. Fertil Steril 2007.

TABLE 19.1

Continued.

How ART is governed	Country	Yes, by Law	Yes, by Guidelines	Yes, by Cultural or religious beliefs	No	What is the recognized time?
	Chile			+?		In discussion is a law that would consider the time to begin with conception; it was vetoed by the president, who asked to exclude infertility therapy from such a definition, and it is being reconsidered in congress.
	China				No data	
	Croatia				+	
	Egypt		+			Six wk after fertilization
	India				+?	Approximately 45 d after last menstrual period or 30 d after fertilization. Though by religious decree, it is generally accepted that before this short period of human development a human person is considered not to exist, the law in India includes the Medical Termination of Pregnancy Act in 1971, which liberalized termination of pregnancy on medical, social, or voluntary grounds at up to 20 wk of gestation. Of course, this act was introduced with the objective of population control.
	Ireland				+	
	Japan				+?	14 d after fertilization
	Lithuania				No data	
	Mexico				+	
	Morocco			+		From the beginning. implantation
	Philippines			+		On fertilization
	Singapore		+			It is different for the different races in the country (first 14 d after fertilization)
	South Africa				+	
	Thailand			+?		Not sure, believe it is the point of penetration of sperm into egg

Jones. Status of the conceptus. Fertil Steril 2007.

(*Continued on next page*)

TABLE 19.1

Continued.

How ART is governed	Country	Yes, by Law	Guidelines	Cultural or religious beliefs	No	What is the recognized time?
	United States				+?	Viability
None	Colombia			+		In terms of religion, when the embryo has fetal heart frequency
	Ecuador			+		As a religious country, before implantation
	Finland				+	
	Jordan			+		40 d
	Malaysia				+	
	Peru	+				At implantation
	Portugal				+	
	Romania				+	
	Uruguay			+		
	Venezuela				+?	Cardiac frequency

Jones. Status of the conceptus. Fertil Steril 2007.

CHAPTER 20: Conclusion

In more than half of the countries surveyed, there is clearly a desire to regulate and control assisted reproduction. At least it can be claimed that laws and guidelines are highly divergent. There are not two countries with similar laws or guidelines. At the end of the questionnaire we ask the following two questions:

1. Please point out any regulations that appear to be medically naïve, or even contradictory, or not in the best interest of the infertile couple.
2. How can current regulations be improved?

Of course, we did not get an answer from each country. The comments that were received were extremely divergent. Only three countries consider the situation to be satisfactory, in other words, Belgium, Latvia, and the United Kingdom. Three countries consider the situation to be disastrous for patients, doctors, and biologists; those being Germany, Italy, and Switzerland. Some countries believe that they need a law, for example, Bulgaria, or new guidelines, for example, Brazil and Chile.

In other countries, there was a desire to modify the regulations for specific items.

Preimplantation genetic diagnosis must be adopted in Chile, Japan, Latvia, Philippines, and Norway. In Greece, PGD is discussed for the detection of cancer predisposition.

Gamete donation is not permitted in Austria, Tunisia, and Norway. These countries would wish to abolish this restriction. Oocyte donation is permitted in France, with strict regulations. Thus, infertile couples requiring donation have to go abroad.

Most countries where offspring can obtain information about the donor consider that the loss of anonymity has restricted the possibility of donation. For example, Canada, the Czech Republic, and so on.

A ban on embryo research is deployed by most countries.

These important differences between countries have led to traffic of infertile couples across legislative borders to seek solutions to their problems. There are numerous examples of so-called fertility tourism in different countries. For example, Italian couples travel to the United Kingdom or Switzerland; French couples, to Spain or Belgium. Couples from the Nordic countries travel from one to another according to the type of technique needed. Couples from Latin America often go to the United States.

When Jean Cohen and Howard Jones started the first "Surveillance 98" in 1997, the intention was to reach an authoritative international document setting forth what the medical and scientific community would regard as feasible and desirable. It turned out that such a consensus could not be reached because of a diversity of traditions, political situations, and medical practices. An international "consensus" appears to be a utopia, and we can imagine that if it existed, it would reflect the lowest common denominator. The actual situation is illogical, unfair to couples, and difficult for doctors and scientists. However, the situation still allows some couples to find solutions that they would never have found with an international consensus. We can hope that in the future, little by little, harmonization of national legislation will benefit from each country's experience and thus avoid outsourcing of this helpful medical procedure.

It may also be hoped that at some time in the future and perhaps the not-too-distant future, an international convention may be called. This has been done on a smaller scale in some individual countries, for example, Sweden, to bring together gynecologists, obstetricians, economists, insurance executives, legislators, and others who have an interest in the subject to discuss legislation and guidelines that are based on reason and the best interest of the patient, to obtain some international consensus to take advantage of the great strides that have been made in the treatment of infertility.