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Statement of general purpose

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Internationally, there is a wide divergence in views on the methods and the content of surveillance of assisted reproductive technologies. This was clearly brought out by "IFFS Surveillance 98," published in *Fertility and Sterility* 1999;71(Suppl 2), and "IFFS Surveillance 01," published in *Fertility and Sterility* 2001;76(Suppl 2).

The 1998 data were presented to the national delegates who had participated in the 1998 survey at the International Federation of Fertility Societies 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, as 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 with the 98 survey, this effort was not repeated with the data collected and published in "IFFS Surveillance 01." An effort was made simply to record the situation as existed. Indeed, that will probably be the fate of "IFFS Surveillance 04," although it will be presented to the delegates at the IFFS meeting in 2004.

The divergence of views on various issues makes it seem 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 feels 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 is evident of this scientific aspiration.

In the final analysis, the purpose of this survey, "IFFS Surveillance 04," 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

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The development of in vitro fertilization (IVF) and its subsequent variations and extensions, all now included under the umbrella of assisted reproductive technology (ART), seems 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/regulations have taken various forms. They often express not only a particular medical perspective, but sometimes reflect the social and religious mores of the particular sovereign state. Some of the guidelines/regulations have been formulated to accommodate special interest groups. Furthermore, surveillance of compliance with guidelines/regulations ranges from none at all, to the issuance of a license by a governing body after designated requirements are fulfilled, and often including periodic follow-up inspections.

The specific purposes of this project are:

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

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Materials and methods

A survey form was developed (see the appendix), and one or more individuals from the principal sovereign nations known to be practicing ART were invited to fill out the questionnaire. These individuals were recruited in various ways but with emphasis on recommendations from the members of IFFS. The response rate has been very satisfactory. Completed questionnaires were codified by the coordinator, Dr. Henk J. Out, with the capable assistance of his staff, especially Heidi van Berkom; the situation as of April 30, 2003, was tabulated under various subheadings of the questionnaire.[1] Blank rows in the tables mean "not filled out." If participating countries are not mentioned in some tables, this indicates that information was not available. It was attempted to represent the comments of as many of the participants as possible in footnotes.

Results from 49 countries were tabulated. However, Australia is tabulated four times because three states, South Australia, Victoria, and West Australia, operate under regulations, and the remaining states (indicated as "Remainder") operate under guidelines; hence, a total of 52 political entities are provided. The number of individual centers is only an estimate and not accurate; however, according to the reports of the survey (Table A), well over 2,000 individual centers are represented.

The analysis of the survey, the discussion, and the summary were prepared by the editors.

[1] At the end of 2003, a new law was passed in Italy. Key points were: stable relationship, no donor insemination, no surrogacy, no preimplantation genetic diagnosis, no freezing, and no more than three embryos to be created and all to be transferred. The tables in this current surveillance supplement do no reflect these changes.

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TABLE A

Number of centers.

Country	Number of centers
Argentina	19
Australia (West)	5
Australia (South)	2
Australia (Victoria)	5
Australia (Remainder)	30
Austria	23–24
Bangladesh	1
Belgium	18
Brazil	90
Bulgaria	9
Canada	26
Chile	7
Czech Republic	17
Denmark	19
Ecuador	Approx. 10
Egypt	>30
El Salvador	1
Finland	18–19
France	140
Germany	108
Greece	46
Hong Kong	6
Hungary	11
Iran	35
Ireland	6
Israel	24
Japan	513
Jordan	12
Korea	93
Mexico	11
Morocco	14
Netherlands	13
Norway	10
Poland	21
Portugal	17–18
Romania	5
Saudi Arabia	>15
Singapore	7
Slovenia	3
South Africa	11–12
Spain	203 (38 public, 165 private centers)
Sweden	15
Switzerland	17–18
Taiwan	67
Tunisia	6
Turkey	56
United Kingdom	75
Uruguay	1
United States	>400
Venezuela	8

CHAPTER 1: Legislation and guidelines

ANALYSIS OF SURVEY

Since "Surveillance 01," we have obtained information of 11 new countries: Bangladesh, Bulgaria, Chile, Ecuador, El Salvador, Iran, Morocco, Poland, Romania, Tunisia, and Uruguay. Among these new participants, Tunisia has laws, Morocco and Poland have guidelines, and the others have neither legislation nor guidelines (Table 1A).

The technique of surveillance fell into three categories:

1. Those sovereign nations or political entities with legislative (i.e., governmental) regulations that are mandatory and statutory;
2. Those sovereign nations or political entities with guidelines intended to be followed voluntarily by those practicing ART; and
3. Those sovereign nations or political entities with neither guidelines nor regulations, although many of these (e.g., Canada) are considering implementing legislation.

Nations or states with laws or statutes

There are 25 surveyed entities with laws or statutes pertaining to ART (Tables 1A and 1B). Australia is counted four times as three states have regulations and the remaining five are under guidelines.

Of the 26 entities with legislation, only 4 of them (Brazil, Denmark, Greece, and Tunisia) have no specific licensing body. The composition of these licensing bodies varies considerably, as do the criteria for a license. The criteria, in general, have to do with the competence of the practitioner and the health care needs of patients. The clinical surveillance is carried out by periodic report in 17 entities or on-site inspection in 14 (see Table 1A).

Penalties for violations are imposed in the large majority of the countries. The penalties are severe, varying from withdrawal of license to criminal prosecution and imprisonment (Table 1C).

Surveillance of the embryologic laboratory sometimes differs from that of the general program. Most nations require a periodic report of the embryologic activities and have on-site inspection of the embryologic facilities. Specific penalties are provided for violations in the embryologic laboratory, such as withdrawal of license, fines, or imprisonment.

Sovereign nations or political entities with voluntary guidelines

There are 16 surveyed nations that follow voluntary guidelines for ART (Tables 1A and 1D).

These guidelines are usually promulgated by a scientific society, such as the Society of OB/GYN in Japan, the Soci-

TABLE 1A

Legislation and guidelines.

Country	Legislation	Guidelines	Neither
Argentina		+	
Australia (West)	+		
Australia (South)	+		
Australia (Victoria)	+		
Australia (Remainder)		+	
Austria	+		
Bangladesh			+
Belgium	+		
Brazil	+		
Bulgaria			+
Canada			+[a]
Chile			+
China		+	
Czech Republic	+		
Denmark	+		
Ecuador			+
Egypt		+	
El Salvador			+
Finland			+
France	+		
Germany	+		
Greece	+		
Hong Kong	+		
Hungary	+		
Iran			+
Ireland		+	
Israel	+		
Italy		+	
Japan		+	
Jordan			+
Korea		+	
Mexico			+
Morocco		+	
Netherlands	+		
Norway	+		
Poland		+	
Portugal		+	
Romania			+
Saudi Arabia		+	
Singapore	+		
Slovenia	+		
South Africa		+	
Spain	+		
Sweden	+		
Switzerland	+		
Taiwan	+		
Tunisia	+		
Turkey	+		
United Kingdom	+		
Uruguay			+
United States		+	
Venezuela			+

[a] Bill is before Parliament.

TABLE 1B

Countries with statute/law.

Country	Where can a copy of the statute be obtained?	Is there a licensing body?	What is the composition?	What are the criteria for a license?
Australia (West)		Yes	Health authorities	
Australia (South)	http://www.dhs.sa.gov.au/reproductive_technology Reproductive Technology Act 1988	Yes	Department of Human Services	Adherence to Reproductive Technology Act + accreditation. License must fulfill a genuine and substantial social need.
Australia (Victoria)	http://www.ita.org.au	Yes		Infertility Treatment Act 1995 What is not covered by legislation reverts to guidelines of the RTA.
Austria		Yes	Federal Republic Governors Office	Recommendation of the Austrian Society for Reproductive Medicine and Endocrinology on quality and equipment standards.
Belgium		Yes		
Brazil	CFM no. 1.358/92	No		
Czech Republic		Yes	ART society, ministry of health, insurance companies	All IVF centers have to work according to "Minimal standard for an IVF center."
Denmark		No		
France	Published in Journal Officiel 30.07.94/ Law of 27.07.94	Yes	Clinicians, embryologists, urologists, researchers, geneticians, patient association, etc.	Diplomas, formation, experience
Germany	http://www.bundesrecht.juris.de/budesrecht/eschg	Yes	Government	Approbation, equipment, license for ART, laboratory, specialty for obstetrics and gynecology
Greece		No		
Hong Kong		Yes		
Hungary		Yes	"Committee of Reproduction," gynecologists, other medical doctors, lawyers, priests, representatives of MoH and Health Insurance; National Public Health and Medical Officer Service	
Mexico	Ley General de Salud, Titulo XIV Capitulos 1,2,3 http://www.salud.gob.mx http://www.asambleadf.gob.mx	Yes	Ley General de Salud and Rules	
Netherlands	Planningsbesluit IVF, ART 2 Wet Bijzondere Medische Verrichtingen	Yes	Governmental	See "Planningsbesluit"
Norway		Yes	Governmental	Need of service, qualifications of staff
Singapore		Yes	Ministry of Health physicians, embryologists, and laboratory	
Slovenia		Yes	Committee for Biomedically Assisted Procreation (BMAP) at Ministry of Health	Criteria are defined by code of practice at Ministry of Health of Slovenia. License is based on the report of a commission named by Ministry of Health.
Spain		Yes	Physicians, bioethics	No: According to the Royal Decree 413/1996 Yes: Only for advice to government
Sweden		Yes	Governmental Central Authority, doctors, politicians	Full requirements
Switzerland	LPMA	Yes	Left to cantonal administration	LPMA
Tunisia		No		
Turkey		Yes	Clinicians and scientists who are representatives of university government and private IVF clinics, and also includes the representatives of Ministry of Health (15 people)	The IVF centers that are organized according to the guidelines released by Ministry of Health can get the license.
United Kingdom	Human Fertilization + Embryology Authority, Pexton House, 30, Artillery Lane, London	Yes	Laid down in legislation; authority with executing and inspectorate	Compliance with code of practice and satisfactory inspection by inspections team of HFEA.

TABLE 1C

Countries with statute/law.

Country	How is clinical and/or embryological surveillance carried out?	Are penalties designated for violation of statutes with regard to clinical and/or embryological practice?	If yes, what are they?
Australia (West)	Periodic report. On-site inspection.	Yes	Refer to Act. Loss of license, jail sentence, AU$10,000
Australia (South)	Periodic report. On-site inspection.	Yes	Removal of license, criminal prosecution (imprisonment)
Australia (Victoria)	Periodic report. On-site inspection.	Yes	Fine and/or jail term
Austria	Periodic report.	Yes	Fines, closure of clinic after severe or repeated violations
Brazil	On-site inspection.	Yes	According to CFM 1358/92 and civil laws
Czech Republic	Periodic report. On-site inspection.	Yes	Withdrawal of license
Denmark	No systematic surveillance.	Yes	Fine imprisonment
France	Periodic report. On-site inspection.	Yes	Fines, prison, activity suspension
Germany	Inspection only in case of suspicion. Periodic report.	Yes	Prison or money penalty, withdrawal of license
Greece	This law does not mandate clinical surveillance.	No	
Hong Kong	Periodic report. On-site inspection.	Yes	Section 39 of HRTO, pg. A1751
Hungary	On-site inspection.	Yes	Withdrawal of license
Mexico	On-site inspection.	Yes	Administrative fines or even jail, depending on the nature of the violation
Netherlands	Periodic report. On-site inspection.	Yes	License is withdrawn
Norway	Periodic report.	Yes	Fines or prison, withdrawal of license
Singapore		Yes	Removal from registry
Slovenia	Periodic report. On-site inspection by the commission of experts. Report presented to committee for BMAP.	Yes	Article 33: prison between 6 mo and 5 y. Articles 31, 37, 38: prison up to 3 y. Financial penalty: Euro 2500–25,000. Articles 43, 44, 45 of Infertility and BMAP Law, Republic Slovenia 2000.
Spain	Periodic report.[a]	No	
Sweden	Periodic report. On-site inspection (occasionally).	Yes	Loss of license to perform ART
Switzerland	Periodic report. On-site inspection.	Yes	Fines or prison
Tunisia	Periodic report.	Yes	Fine and/or prison
Turkey	Periodic report. On-site inspection.	Yes	Ministry of Health (by the suggestion of licensing committee) can stop the activity of IVF center for a period of time or close the IVF center permanently.
United Kingdom	Periodic report. On-site inspection. Submission of treatment outcome.	Yes	Criminal liability, removal of license

[a] Only in Catalonia, not in all the states.

ety for Assisted Reproductive Technology (SART) in the United States, National Administration of Health in China, or the Fertility and Sterility Association in Poland.

Even with guidelines, surveillance may be conducted via periodic reports or on-site inspection.

Penalties for violation of the guidelines are few. In the United States, expulsion from the SART is stated as a possible penalty, but to date no one has been expelled for a violation.

As with statutes, embryologic surveillance sometimes differs from general program surveillance; it is often carried out by a somewhat different body, and embryologic surveillance may require a periodic report or on-site inspection.

Entities Operating Without Guidelines or Regulations

There are 13 surveyed nations without any guidelines or regulations of ART (see Table 1A). It is notable that practices in these national entities do not differ greatly from those in nations with legislation or voluntary guidelines.

DISCUSSION

Since "Surveillance 01," some countries have adopted laws, such as Greece, Slovenia, and Tunisia. Nations or states with legislative regulation seem to be generally satisfied with the format of surveillance. Nevertheless, concerns have been expressed about the content of some regulations and about delay in updating regulations. France has been waiting since

TABLE 1D

Countries with guidelines.

Country	Where can a copy of the guidelines be obtained?	Is any clinical and/or embryological surveillance carried out?	How is this done?	If yes, what body carries out the surveillance?
Argentina	http://www.saef.org	Yes	Periodic report. On-site inspection.	SAEF and RED LARA
Australia (Remainder)	http://www.fsa.com.au	Yes	On-site inspection.	Inspection Committee (multidisciplinary) of RTAC
China	Chinese Administration of Health	Yes	On-site inspection.	The National Administration of Health
Egypt	AZHAR University Egyptian Medical Syndicate	Yes	Periodic report. On-site inspection (before the start). Voluntary reporting.	The Egyptian IVF + ET Center, Maadi, Cairo
Ireland	Medical Council New guidelines expected in 2004	No		
Italy		No		
Japan		Yes	Periodic report.	Japan Society of Obstetrics and Gynecology, Japan Society of Fertility and Sterility
Morocco		Yes	On-site inspection.	Not filled out
Poland		Yes	Periodic report.	Fertility and Sterility Association of Polish Gynecological Society
Portugal		No		
South Africa		Not yet	On-site inspection (planned).	Peer review committee
United States	http://www.asrm.org	Yes	Periodic report. On-site inspection.	Society for Reproductive Technology (SART) + CDC

1999 for a legal modification of the 1994 law. Belgium has adopted new legislation that agrees to fund six cycles of ART for women under 42 years of age on the condition of respecting criteria for the number of embryos to transfer. Mexico has a preproject being considered before passing it to congress. Italy is under the threat of the vote by the Parliament of a very restrictive law.

Because of the sensitivity of the materials, penalties under the statutory systems are difficult to identify and document. Nevertheless, there is anecdotal information that, in some countries with legislation, penalties have indeed been imposed, including withdrawal of licenses either temporarily or on a permanent basis. These incidents have been rare.

It is difficult to document the degree to which guidelines are followed. Abundant anecdotal evidence suggests that violations of some aspects may be widespread. For example, in the United States, evidence indicates that guidelines on the number of embryos to be transferred have been violated, in view of the very high rate of reported multiple pregnancies. As in countries where legislative regulations are in force, violations of the voluntary guidelines have not been widely published, so their documentation is difficult.

This state of affairs is understandable, but perhaps is not in the best interest of all concerned if guidelines are seriously considered to be for the public good. Publication of violations and penalties from infringements would be an important method of ensuring compliance.

SUMMARY

There continues to be no consensus on the ideal method of surveillance of ART worldwide.

Legislation is becoming more frequent worldwide. Countries with legislative surveillance seem to agree that it works quite well, although there are understandable complaints about the slowness of the legislative process and the difficulty of having regulations changed once they are in place.

Countries with voluntary guidelines seem to enjoy public confidence, and public pressure for a change appears to be very minimal. In some countries, however (such as Canada, Mexico, and Italy), legislative proposals have been discussed for several years without adoption.

CHAPTER 2: Insurance coverage

Third-party payment for clinical assisted reproductive technology is subject to great variation from nation to nation (Table 2).

ANALYSIS OF SURVEY

Of the respondent entities (51), essentially half (26) have no third-party reimbursement by any national health plan or private insurance company.

There are 16 entities (30%) with coverage from a national health plan and no available private insurance.

The countries with complete financial coverage are France, Germany, Belgium (under the recent criteria), Czech Republic (IVF only), Slovenia (four cycles), and Israel (until the birth of two children).

Seven entities (14%) provide coverage from a national health plan, but coverage also is available from private insurance.

In two entities (4%), Turkey and the United States, the only available coverage is by private insurance.

In essentially all jurisdictions where there is coverage by a national health plan or a private carrier, there are restrictions—some quite liberal, others quite severe. They are quite varied. In Belgium, new legislation in 2003 provided for six cycles of ART for women under 42 years of age provided certain criteria are met:

- Aged <35 years: first cycle, single embryo transfer; second cycle, one or two embryo transfers; third to the sixth cycle, two maximum embryo transfers
- Aged >35 to <39 years: first and second cycle, two maximum embryo transfers; third cycle, three maximum embryo transfers
- Aged >39 years: No maximum embryo transfers
- For frozen thawed embryos, two embryos maximum

In contrast, 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 costs must be partially paid by the patient. In the United States, insurance coverage is mandated in 15 of the 50 states, with variable restrictions from state to state.

The footnotes to Table 2 catalogue many other restrictions.

DISCUSSION

It is clear that third-party payment for ART is subject to wide variation. At one extreme are countries like France with unlimited coverage, at the other extreme are one-half of all reporting countries which have neither public nor private coverage.

Although this survey did not query the causes of noncoverage, it seems evident that it is mostly economic, both in the public and private sectors. However, it is also associated with opposition to IVF by the Roman Catholic tradition, as no surveyed Latin American country has either public or private insurance coverage.

Insurance coverage might well be a suitable subject for a symposium at an international meeting.

SUMMARY

There is no international consensus on the insurance coverage for ART. One-half of surveyed entities had neither public nor private coverage. On the other hand, a few countries—for example, France and Belgium—offer very sophisticated coverage through the public sector.

TABLE 2

Are the techniques of ART covered or reimbursed?

Country	National health plan (complete/partial)	Private insurance (complete/partial)	No coverage
Argentina			+
Australia (West)	+, partial	+, partial	
Australia (South)	+, partial[a]	+, partial[a]	
Australia (Victoria)	+, partial[b]	+, partial[b]	
Australia (Remainder)	+	+	
Austria	+, partial[c]		
Bangladesh			+
Belgium	+, complete		
Brazil			+
Bulgaria			+
Canada			+[d]
Chile			+
China			+
Czech Republic	+, complete[e]		
Denmark	+, complete		
Ecuador			+
Egypt			+
El Salvador			+
Finland	+, partial[f]		
France	+, complete		
Germany	+, complete (mainly)[g]	+, complete (mainly)[g]	
Greece	+, partial		
Hong Kong	+, partial		
Hungary	+, partial[h]		
Iran			+
Ireland			+[i]
Israel	+, complete[j]		
Italy	+		
Japan			+
Jordan			+
Mexico			+
Morocco			+
Netherlands	+, partial[k]		
Norway	+, partial		
Poland			+
Portugal	+, partial[l]	+, partial[l]	
Romania			+
Saudi Arabia			+
Singapore			+
Slovenia	+, complete[m]		
South Africa			+
Spain	+, partial		
Sweden	+		
Switzerland	+, partial[n]		
Taiwan			+
Tunisia	+, partial		
Turkey		+, complete[o]	
United Kingdom	+, partial[p]		
Uruguay			+
United States		+, partial[q]	
Venezuela			+

[a] Patient supplement varies—usually up to AU$2500.
[b] Currently excludes costs associated with newer technologies (ICSI, testicular biopsy, etc.): under review.
[c] Reimbursement of 70% of total costs of assisted reproduction. Only tubal and severe male factor infertility, women until age 40 years, men until age 50 years.
[d] Only one province (Ontario) pays for IVF in case of bilaterally obstructed fallopian tubes.
[e] Standard IVF is fully reimbursed; ICSI, embryo freezing, and assisted hatching are not reimbursed.
[f] Not reimbursed according to law, but as part of "routine" health care system.
[g] Possibly no further reimbursement after January 2004. Current coverage only under preconditions: e.g.; age <40 years, marriage of couple, free of hepatitis B and C and human immunodeficiency viral infections.
[h] Medication should be paid partially by the patient.
[i] But is tax deductible. Medication supplied under National Health Plan.
[j] Complete until birth of two children to a couple.
[k] Three cycles of IVF, none for ICSI (is seen as plain IVF).
[l] ART in public hospitals is free of charge. Medication is partially covered (± 40%). In private practice, medication is covered (± 40%)
[m] Four cycles.
[n] IUI: covered for 3 cycles. Ovarian stimulation: covered for 12 cycles. IVF and ICSI: not covered.
[o] Some private insurance companies have just started to cover IVF treatment.
[p] National Health Service funds 25% of IVF cycles in the United Kingdom. The NICE guidelines to be published February 2004.
[q] A minimal number of states offer varying degrees of coverage, as well as a limited number of third-party payers.

CHAPTER 3: Marital status in ART

ANALYSIS OF SURVEY

In the nations with statutes, views about marriage and ART show considerable divergence (Table 3).

Marriage is a requirement in Egypt, Hong Kong, Iran, Jordan, Korea, Morocco, Saudi Arabia, Singapore, Taiwan, Tunisia, and Turkey.

A stable relationship is required in Austria, France, Germany, Hungary, Japan, Argentina, the Czech Republic, Denmark, Italy, Norway, Poland, Portugal, Slovenia, Switzerland, and Uruguay.

Some nations seem to have *no requirement*, such as Chile, Salvador, and Mexico.

In some nations, it is also possible for single women or lesbian couples to be treated: Australia (West, South, and Remainder), Belgium, Bulgaria, Canada, Finland, Greece, Israel, the Netherlands, Romania, South Africa, the United Kingdom, and Venezuela.

DISCUSSION

Our survey results show that society, either as expressed through legislation or as influenced by religious or cultural issues, seems to prefer a traditional heterosexual family (marriage or stable relationship) and hesitates to provide full access to alternative groups. However, some 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 to alternative groups, there is a procreative tourism toward countries where it is permitted (e.g., Belgium, Finland, Greece, and Spain).

Very few studies have been performed of the children of relationships other than heterosexual. Such studies concern essentially donor insemination children. Brewaeys et al. (Hum Reprod 1997;12:1349–59) 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. (Hum Reprod 2001;16:2019–25) studied 41 children (7 to 17 years of age) of lesbian parents: 46% of children wanted to meet their donor. No solid data are available about offering ART either to single women or to others not in a heterosexual relationship.

SUMMARY

In most countries, ART is supposed to be performed only for heterosexual couples, 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 lacking.

TABLE 3

Marital status in ART.

Country	Legislation	Guidelines	Couple restrictions
Argentina		+	Stable relationship, heterosexual couples
Australia (West)	+		Stable relationship; permitted for single women and lesbian couples
Australia (South)	+		Demonstrable infertility by normal diagnostic criteria (not allowed to discriminate on basis of marriage or sexual preference)
Australia (Victoria)	+		Stable relationship
Australia (Remainder)		+	No requirements; permitted for single women and lesbian couples (depends and varies with local institutional ethics committee)
Austria	+		Marriage, stable relationship
Bangladesh			Stable relationship (permission from guardian and relation is needed because of socioeconomic status)
Belgium	+		No requirement; permitted for single women and lesbian couples
Brazil	+		Stable relationship
Bulgaria		+	Not an issue; permitted for single women
Canada			Not an issue; permitted for single women and lesbian couples
Chile			Stable relationship
China		+	Marriage
Czech Republic	+		Stable relationship
Denmark	+		Stable relationship (man + woman)
Ecuador			Stable relationship
Egypt		+	Marriage
El Salvador			Not an issue
Finland			Not an issue (permitted for single women and lesbian couples)
France	+		Marriage, stable relationship
Germany	+		Marriage; exceptions are possible for stable relationships after application
Greece	+		Marriage, stable relationship (single women permitted if they are infertile; lesbian couples not specifically prohibited, but a recent clarification of the law indicates prohibition)
Hong Kong	+		Marriage
Hungary	+		Marriage or stable relationship
Iran		+	Marriage
Ireland		+	No requirement (for child protection some units ask for a stable heterosexual relationship)
Israel	+		Stable relationship; permitted for single women and lesbian couples (using only donor sperm with or without egg donation)
Italy		+	Stable relationship
Japan		+	Marriage, stable relationship (exceptions: after passing examination of a local ethics committee)
Jordan			Marriage
Korea		+	Marriage
Mexico	+		No requirements
Morocco		+	Marriage
Netherlands	+		No requirement (permitted for single women and lesbian couples)
Norway	+		Stable relationship
Poland		+	Stable relationship
Portugal		+	Stable relationship
Romania			Not an issue (permitted for single women)
Saudi Arabia	+	+	Marriage
Singapore	+		Marriage
Slovenia	+		Stable relationship
South Africa		+	No requirement (permitted for single women and lesbian couples)
Spain	+		Marriage, stable relationship; permitted for single women
Sweden	+		Marriage, stable relationship
Switzerland	+		Stable relationship
Taiwan	+	+	Marriage
Tunisia	+		Marriage
Turkey	+		Marriage
United Kingdom	+		No requirement; permitted for single women and lesbian couples
Uruguay			Stable relationship
United States		+	No requirement; stable relationship
Venezuela			Not an issue; permitted for single women

CHAPTER 4: The number to transfer in ART

ANALYSIS OF SURVEY

Multiple gestation is now recognized as a major problem associated with ART. This survey only deals with IVF, and was not able to register intrauterine insemination (IUI) in association with ovulation induction/ovulation enhancement.

According to Reynolds et al. (Pediatrics 2003;111:1159–62), ART accounted for 13.6% of all multiple-birth infants in the United States in 2000: 11.8% of all twin births and 42.5% of all triplet and higher order multiple births. In Europe in 1997, the total multiple delivery rate after IVF was 28.2% (Hum Reprod 2001;16:790–800). For IVF, the clinical delivery rates for singleton, twin, triplet, and quadruplet births were 70.4%, 25.6%, 3.5%, and 0.2%, respectively. Those following intracytoplasmic sperm injection (ICSI) were 71.7%, 25.2%, 2.9%, and 0.1%, respectively.

Since the publication of "IFFS surveillance 01" (2001), we have observed a general worldwide decrease of the limit number of embryos to transfer from 3–4 to 2–3, regardless of the legislative situation. Many years ago, the United Kingdom first issued penalties for violation of the number of embryos to transfer. Recently, Belgium has decided to transfer only 1 embryo during the first cycle and 2 for the following ones. Nordic countries without imperative legislation are accustomed to not transferring more than 2 embryos.

Many countries such as Poland, Singapore, or Hong Kong have customary limits of two or three, with exceptions made for older women.

The status of legislation and the number to transfer is shown in Table 4.

DISCUSSION

By limiting the number of embryos transferred per IVF cycle, the multiple gestation rate is reduced. In countries where this policy has been formally adopted, the number of multiple gestations has notably decreased. Elective single embryo transfer (eSET) with a top-quality embryo or elective dual-embryo transfer (eDET) result in a very good on-going pregnancy rate. The suggestion to apply eSET to all patients is being vigorously debated by many centers, and eDET is largely accepted for patients younger than 35 years.

Whether it is appropriate to develop specific laws concerning the number of embryos to transfer is widely discussed. On a national basis, self-regulation has not worked so far. The alternatives are the use of guidelines with sanctions imposed by medical profession, or the development of specific laws.

TABLE 4

ART—the number to transfer.[a]

Country	Transfer limit	Unlimited
Argentina		+[b]
Australia (West)		+
Australia (South)	3	
Australia (Victoria)		+ (2, rarely 3)
Australia (Remainder)	2, rarely 3	
Austria		+
Bangladesh		+ (2)
Belgium	1st cycle: 1 2nd cycle: 2	
Brazil	4	
Bulgaria	3–4	
Canada		+
Chile		+
China	3	
Czech Republic		+
Denmark	2, rarely 3	
Ecuador	2	
Egypt		+
El Salvador		+
Finland		+ (2)
France		+
Germany	3	
Greece		+
Hong Kong	3[c]	
Hungary	3–4	
Iran		+
Ireland		+
Israel		+
Italy		+
Japan	3	
Jordan		+
Korea		+
Mexico		+[d]
Morocco	2–3	
Netherlands		+
Norway		+
Poland	2–3[e]	
Portugal	3–4	
Romania		+ (6)
Saudi Arabia	3–5	
Singapore	3–4[f]	
Slovenia	2–3	
South Africa		+
Spain		+
Sweden	1–2	
Switzerland	3	
Taiwan		+ (4–5)
Tunisia		+
Turkey		+

Although some countries have adopted measures through legislation or clinical guidelines to address the major problem of multiple gestation after IVF, further progress is

TABLE 4 Continued.

Country	Transfer limit	Unlimited
United Kingdom	2–3[g]	
Uruguay		+(4)
United States		+ (2–5)
Venezuela	3–4	

Note: Number in parentheses indicates customary number of embryos transferred.

[a] Please refer to chapter 1 to check for existence guidelines or legislation.

[b] However, it is stated that high-order multiple pregnancies (n = >2) should be avoided.

[c] For women >34 years, maximum of n = 4 at first cycle, n = 5 in subsequent cycle.

[d] Waiting for the final number in October (probably n = 3).

[e] That is, n = 2 for women <35 years, n = 3 for women >35 years.

[f] That is, n = 4 if >35 years and two failed previous attempts.

[g] That is, n = 3 in exceptional cases.

needed. We agree with the conclusions of the Bertarelli Foundation Expert meeting (Reprod Biomed Online 2003;7, suppl 2): "With increasingly better protocols being applied for ovarian stimulation, cell culture, cryopreservation, and prediction of implantation, there comes a recognized need to update current embryo transfer guidelines in order to reduce the incidence of high-order and twin gestation."

There is also a need to educate both healthcare professionals and the lay population that multiple gestation is not a desirable outcome of IVF.

SUMMARY

As of 2004, more countries have adopted guidelines or legislation to decrease the number of embryos to transfer. The worldwide trend seems to be to replace two embryos in women younger than 35 years. The elective transfer of one embryo has been adopted in some countries for the first cycle at least.

The worldwide trend seems to be to replace fewer preembryos. However, the problem has yet to be solved, particularly in the United States where factors on the part of the patient and the ART program seem to require acceptance of an undesirably high multiple pregnancy rate.

CHAPTER 5: Cryopreservation

The major aim of embryo cryopreservation is to provide further possibilities for conception in addition to those obtained through the initial cycle and fresh transfer. This goal is achieved through an increase in birth rate for women who have had embryos cryopreserved. Embryo freezing has decreased the risk of multiple pregnancies by allowing the transfer of fewer embryos, and reduced the risk of ovarian hyperstimulation by cancelling fresh transfer. It also simplifies the process of oocyte donation.

ANALYSIS OF SURVEY

Of the 52 countries, 27 have statutory regulations and 16 have guidelines (43 in total).

Embryo cryopreservation is permitted or used in all countries with the exception of Bangladesh and El Salvador. In Germany and Switzerland, it is only permitted at the pronuclear stage (PN). The duration of storage varies from one country to another (Table 5A).

The duration of 5 years can be expanded to 10 years in South Australia and Israel. In the United Kingdom, the maximum storage of 5 years can be reviewed and extended for a further 5 years, with an absolute limit of 15 years. The cryopreservation period should not exceed the donor's age of reproducibility in Korea, Japan, and the United States. In some countries the duration is 1 or 2 years (Chile).

Oocyte cryopreservation is not allowed or not used in Bangladesh, Bulgaria, Chile, Ecuador, El Salvador, Morocco, Norway, Portugal, Romania, Slovenia, Uruguay, and Venezuela.

Cryopreservation of ovarian or testicular tissue is not allowed or not used in Bangladesh, Bulgaria, Chile, El Salvador, Morocco, Portugal, Romania, and Taiwan.

DISCUSSION

There seems to be general agreement on the importance and necessity of having cryopreservation available in any competent ART program. It is clear that the overall pregnancy rate can be enhanced by supplementing pregnancies achieved by fresh transfer with those from cryopreservation. Although cryopreservation presents logistical difficulties, the total reproductive potential (i.e., the summation of pregnancies by fresh transfer and possible pregnancies by cryopreserved material from the same harvest) is a more precise and accurate estimate of the potential of any one stimulated cycle. There has been great reluctance to use the total reproductive potential, because of the troubling aspects of summating the cryopreserved to fresh pregnancy rates.

No consensus on duration of storage has been reached. A commonly used interval is 5 years, but there seems to be no scientific basis for this duration as opposed to another interval. In general, the options for the frozen embryos are to hold the cryopreserved material for future reproduction, to donate "surplus" preembryos to other couples, to donate excess frozen preembryos to research, or to dispose of the preembryos.

Oocyte Preservation

Despite human oocytes having been frozen and thawed successfully, survival rates remain low. Exposure to cryoprotective compounds or variations of temperature are claimed to have deleterious effects on oocytes structures such as zona pellucida, cortical granules, spindle microtubules, cytoplasmic microfilaments, and organelles. For the moment, oocytes freezing techniques are considered to have a low efficacy rate. The matter is still controversial.

Freezing oocytes instead of embryos offers the possibility of establishing an oocyte banking system. Other possible applications are:

- Alternative to embryo freezing
- Use in patients with ovarian hyperstimulation syndrome
- Treatment of congenital infertility disorders
- Treatment of premature ovarian failure
- Prevention of fertility loss through surgery

But it cannot be ruled out that freezing oocytes does not alter the imprinted genes from the mother.

The procedure of cryopreserved *ovarian or testicular transplantation* is already a future possibility. It can offer hope to cancer patients who want to safeguard their fertility against sterilizing chemotherapy or radiotherapy. It may also be of use in preventing premature ovarian failure. The first pregnancies with these techniques recently have been achieved.

Posthumous Insemination

Because of the existence of cryopreservation procedures for gametes, gonadal tissue, and embryos, one partner has the option to create offspring after the other partner's death. Posthumous reproduction can present an array of dilemmas arising from the nature of consent and the process of decision making. Many international programs for ART have consent forms that stipulate the disposition of gametes and embryos after the death of one or both partners (Table 5B).

Posthumous insemination is allowed in:

- Australia (Victoria and Remainder), if the donor has agreed.
- Israel, after permission of court only, 1 year after storage.
- Spain, if there is a previous consent only, 6 months after death.
- The United Kingdom, under the governance of the Human Fertilization and Embryology Authorities (HFEA).

TABLE 5A

Cryopreservation.

Country	Embryo cryopreservation			Oocyte cryopreservation		
	Allowed/ permitted/used	Not allowed/ not permitted/ not used	Not mentioned	Allowed/used	Not allowed/ not used	Not mentioned
Argentina	+			+		
Australia (West)	+			+		
Australia (South)	+			+[a]		
Australia (Victoria)	+			+		
Australia (Remainder)	+					+
Austria	+			+		
Bangladesh		+			+	
Belgium	+			+		
Brazil	+[b]			+		
Bulgaria	+[c]				+	
Canada	+			+		+
Chile	+				+[d]	
China	+			+		
Czech Republic	+			+		
Denmark	+			+		
Ecuador	+				+	
Egypt	+[e]			+		
El Salvador		+			+	
Finland	+			+		
France	+					+
Germany	+[f]			+[g]		+[g]
Greece	+[h]			+		
Hong Kong	+			+		
Hungary	+			+		
Iran	+					+
Ireland	+[i]			+		
Israel	+			+		+[j]
Italy			+			+
Japan	+[k]			+		
Jordan	+					+
Korea	+			+		
Mexico	+			+		
Morocco	+				+	
Netherlands	+					+[l]
Norway	+				+	
Poland	+			+		
Portugal	+				+	
Romania	+[m]				+	
Saudi Arabia	+			+		
Singapore	+				+	

Some cases of posthumous insemination have been reported in the Czech Republic, the United States, and Venezuela. In the Netherlands, a lawsuit has opened possibility for posthumous insemination, but it does not appear to have been used.

SUMMARY

There is general agreement that cryopreservation facilities are a necessity for every ART program.

Some agreement has been reached on the duration of the storage, but there seems to be no scientific basis for selecting a particular length of time with respect to the viability of the preembryos. The duration of storage seems to be more of a social than a scientific decision.

All ART programs and all donors of cryopreserved material must agree in writing on the disposition of any unused cryopreserved material.

TABLE 5A Continued.

Country	Embryo cryopreservation			Oocyte cryopreservation		
	Allowed/ permitted/used	Not allowed/ not permitted/ not used	Not mentioned	Allowed/used	Not allowed/ not used	Not mentioned
Slovenia	+			+		
South Africa	+			+		
Spain	+			+[n]		
Sweden	+			+		
Switzerland	+[o]			+		
Taiwan	+[p]			+		
Tunisia	+					+
Turkey	+					+
United Kingdom	+[q]			+		
Uruguay	+				+	
United States	+			+		
Venezuela	+				+	

[a] Maximally 10 years.
[b] Discharges are prohibited.
[c] Good quality embryos.
[d] Only experimentally.
[e] To be used during valid marriage contract only.
[f] Only prezygotes.
[g] One correspondent says "allowed/used," another "not mentioned."
[h] Before the procedure, the couples should consent in writing that the unused material would be donated, used for research or therapeutic purposes, or destroyed.
[i] All units freeze as it is not banned, but deliberately destroying embryos is not allowed.
[j] Performed when there is failure to produce sperm on the day of IVF or to retain fertility before chemotherapy or radiation for malignancy. Cannot be done on patient's request for other reasons.
[k] Restricted to married couples.
[l] Only experimental (University Groningen).
[m] For 5 years.
[n] Only under controlled circumstances after a general authorization by Royal Decree.
[o] Limited to 2 PN (pronuclear) zygotes.
[p] Maximally 10 years of storage.
[q] Compliance with the HFEA code of practice. Storage of all embryos is notified to the HFEA.

TABLE 5B

Is posthumous insemination allowed?

Country	Allowed/ used	Not allowed/ not used	Not mentioned/ don't know
Argentina			+, don't know if used[a]
Australia (West)		+	
Australia (South)	+, used[b]		
Australia (Victoria)		+	
Australia (Remainder)	+, used[c]		
Austria		+[d]	+, don't know if used[d]
Bangladesh		+	
Belgium	+		
Brazil		+	
Bulgaria		+	
Canada			+
Chile		+	
China		+	
Czech Republic			+, used[e]
Denmark		+	
Ecuador		+	
Egypt		+	
El Salvador		+	
Finland		+	
France		+	
Germany		+[d]	+, not used[d]
Greece	+, used		
Hong Kong		+	
Hungary		+	
Iran			+, don't know if used
Ireland			+, not used[f]
Israel	+, used[g]		
Italy		+	
Japan			+, used
Jordan		+	
Mexico		+	
Morocco		+	
Netherlands			+, not used[h]
Norway		+	
Poland		+	
Portugal		+	
Romania		+	
Saudi Arabia		+	
Singapore			+
Slovenia		+	
South Africa	+[d]		+, don't know if used[d]
Spain	+, used[i]		
Sweden		+	
Switzerland		+	
Taiwan		+	
Tunisia		+	
Turkey		+	
United Kingdom	+, used[j]		
Uruguay		+	
United States	+[d]		+, used[d]
Venezuela	+[k]		

[a] Not a case in Argentina, yet but one center has offered such service.
[b] Male must have signed consent before his death.
[c] Where donor has agreed to this.
[d] Conflicting reports from correspondents.
[e] There was one case (after court decision).
[f] Consent form requires both partners alive in most units.
[g] Used with limitation after permission of court.
[h] Lawsuit has opened possibility for posthumous insemination, but probably not used (or rarely).
[i] It is allowed only in the 6 mo after death and if there is a previous consent.
[j] Falls under the governance of the HFEA. Welfare of child should be taken into account.
[k] Extremely rare.

CHAPTER 6: Donation of gametes

Gamete and oocytes donation may be the only solution to remedy the lack of female and/or male gametes, enabling the accomplishment of a parental offspring without a genetic link. It may also be applied to avoid the transmission of genetic conditions to the offspring. The result is intended to satisfy a desire for a child, which is more important than treating the infertility. Donor sperm have been widely used for almost a half a century. In the past few years, the tendency has been to require the isolation of donor sperm for 6 months; the donor is tested for human immunodeficiency virus (HIV) before and after this interval to reduce the chance that HIV will be transmitted by donor sperm.

The donation of oocytes began with the onset of IVF. Donation of preembryos has been practiced within the last few decades, although it is not widespread.

The use of donor eggs, sperm, or embryos is more of a social or cultural problem than a medical one (Table 6).

Use of donor sperm in IVF is not allowed by law in Austria, Norway, Saudi Arabia, Tunisia, and Turkey. It is not allowed according to guidelines in Egypt, Iran, Japan, and Morocco.

Oocyte donation is not allowed in 14 countries: Austria, Bangladesh, Egypt, El Salvador, Germany, Japan, Jordan, Morocco, Norway, Portugal, Saudi Arabia, Switzerland, Tunisia, and Turkey.

But in many countries the answer is more subtle than yes or no.

In general, in Muslim countries, oocytes donation, sperm donation, or embryo donation is not practiced.

Worldwide, positions are conflicting on the rights and interests of gamete donors who wish to stay anonymous vs. the rights or interest of the offspring to know their origin. For example, a 1985 law in Sweden mandates availability of information about the donor's identity to the offspring; in contrast, for more than 20 years the Centre d'Etude et de Conservation du Sperme in France has had a tradition of anonymous donation, which was confirmed by legislation in 1994.

Since the 2001 surveillance report, more countries now permit the offspring to request nonidentifying information about the donor. A minority of countries allow identifying information about the donor.

DISCUSSION

Gamete donation is a sensitive subject because it challenges the genetic affiliation of the family, which is the central unit in most societies. The practice is based on the premise that the genetic link has no intrinsic characteristics. The rights and obligations connected to a genetic connection are a matter to be decided by society, usually by means of legislation.

The availability of donor gametes largely reflects the cultural climate, not medical capability.

Very few studies have considered the psychological and developmental well-being of the children of gamete donation in IVF. The secrecy about their conception has meant that researchers are not able to approach all these children. The problem of anonymity as no single, ideal solution. Several different rights are at stake: the right of autonomy and privacy of the parents, the right of privacy of the donor, and the right of the child to know his or her origins.

There are options to improve the level of information available to donor offspring that do not require full disclosure. International policy is moving away from anonymity and toward donor identification and registration. The medical community must be prepared for the consequences of identification in the coming years.

SUMMARY

In most countries where it is practiced, donation of gametes seems to have worked well, although scientific studies are lacking.

The use of donor sperm generally requires quarantine for 6 months, with a negative HIV test result being obtained for the donor before and after the interval. In addition, genetic screening by history in sperm or egg donors is widely practiced, and some centers require negative testing results for hepatitis B and C and other antigens. The risks associated with donor gametes seem to be minimal, although cases of mixed identity have occurred. Opinions differ on whether donors should be anonymous, but there is general agreement that any payment other than to meet the expenses associated with donation is inappropriate. The number of donations has been limited; some countries allow only one, but others allow up to 10 on the basis that the possibility of consanguinity in offspring is minimized.

For the large majority of the donations, the collaboration of the medical profession is needed. This contribution implies the responsibility of the health provider, both as a professional and as private citizen. In addition, it is at all times essential to take into consideration the welfare of the future child.

TABLE 6

Donation of gametes.

Country	Sperm donation						Oocyte donation	
	IVF			Non-IVF				
	Allowed	Not allowed	Used	Allowed	Not allowed	Used	Allowed/ used	Not allowed/ not used
Argentina	+					+	+	
Australia (West)	+			+			+	
Australia (South)	+			+			+	
Australia (Victoria)	+			+			+	
Australia (Remainder)	+			+			+	
Austria		+		+				+
Bangladesh			+			+		+
Belgium	+			+			+	
Brazil	+				+		+	
Bulgaria			+			+		
Canada			+			+	+	
Chile			+			+	+	
China	+			+			+	
Czech Republic	+			+			+	
Denmark	+			+			+	
Ecuador			+			+	+	
Egypt		+			+			+
El Salvador			+			+		+
Finland			+			+	+	
France	+					+	+	
Germany						+		+
Greece	+			+			+	
Hong Kong	+					+	+	
Hungary	+			+			+	
Iran		+			+		+	
Ireland	+			+			+	
Israel	+			+			+	
Italy				+				
Japan		+				+		+
Jordan								+
Korea	+			+			+	
Mexico						+	+	
Morocco		+			+			+
Netherlands	+			+			+	
Norway		+		+				+
Poland	+			+			+	
Portugal	+			+				+
Romania			+			+	+	
Saudi Arabia		+			+			+
Singapore	+			+			+	
Slovenia	+			+			+	
South Africa	+			+			+	
Spain	+			+			+	
Sweden	+			+			+	
Switzerland	+			+				+
Taiwan	+			+			+	
Tunisia		+			+			+
Turkey		+			+			+
United Kingdom	+			+			+	
Uruguay			+			+	+	
United States	+			+			+	
Venezuela			+			+	+	

Note: In Germany, Italy, and Mexico, legislation or guidelines do not mention sperm or oocyte donation.

CHAPTER 7: Micromanipulation

ANALYSIS OF SURVEY

Among all surveyed countries, intracytoplasmic sperm injection (ICSI) seems to be an accepted clinical practice. Some countries have no regulation at all. Microinsemination is allowed or used in all countries except El Salvador. No answer was provided for this question from Argentina and Ireland.

Assisted hatching is mostly allowed (Table 7A). It is not allowed or used in Bangladesh, Bulgaria, El Salvador, and Norway.

Cytoplasmic transfer is prohibited in many countries (Table 7B). Mitochondria are self-replicating, maternally inherited organelles that use the oxidative phosphorylation pathway to supply adenosine triphosphatase for all energy-requiring cellular activities. It has been suggested that a reduction in embryo developmental competence may be related to an inadequate capacity to generate levels of adenosine triphosphatase sufficient to support normal chromosomal segregation. Normal developmental potential has been restored to eggs with ooplasmic deficiencies by transfer of ooplasm from a normal donor egg. Cytoplasmic transfer is not allowed in Australia, Austria, Bangladesh, Brazil, Bulgaria, Chile, Ecuador, El Salvador, Finland, Germany, Greece, Ireland, Japan, Jordan, Morocco, Norway, Portugal, Romania, Switzerland, Taiwan, the United States, the United Kingdom, and Venezuela.

In a few countries it is allowed or used: Korea and Uruguay.

DISCUSSION

The ICSI procedure has proven to be consistently successful in achieving fertilization across a large spectrum of male factor infertility issues, including severe oligo/astheno/zoospermia. With surgically retrieved sperm, ICSI is the mechanism of choice for patients with obstructive azoospermia or functional azoospermia.

Despite the reassuring clinical evaluations to date, different aspects of ICSI outcome need to be surveyed. Genetic counseling for patients with male factor infertility is strongly suggested. Defects due to inherent genetic difficulties with the sperm, such as microdeletions, may be transmitted to children born from ICSI. Children born by ICSI from normal sperm seem to have no greater rate of congenital abnormalities that usual, although the rate of defects due to sex chromosome abnormalities may be slightly increased. These may be procedure-related difficulties. Patients should clearly understand these risks.

Assisted hatching has been proposed as a method for improving the capacity of the embryos to implant. It can be achieved by thinning the zona pellucida (ZP), drilling a hole in the ZP, or total removal of ZP. It can be performed chemically, mechanically, or by using a laser beam.

The efficacy of assisted hatching in all cases of IVF and ICSI is controversial, and may be related to the heterogeneity of the studies. A meta-analysis of patients of "poor prognosis" (over 35 years old with thick zona pellucida and two or more previous IVF failures) concluded that assisted hatching increased the pregnancy, implantation, and ongoing pregnancy rates in this category of patients (Sallam et al., J Assist Reprod Genet 2003;20:332–42).

Other types of micromanipulation, such as cytoplasmic transfer, are sporadically used around the world, and several live births using this technology have been reported. Concern has been expressed that use of heterologous cytoplasm introduces foreign mitochondrial DNA that seems to be maintained in the infant, although abnormalities attributable to this foreign DNA have yet to be identified. Because of the introduction of third-party DNA, cytoplasmic transfer is prohibited by statute, guidelines, or custom in several countries.

SUMMARY

Intracytoplasmic sperm injection has been widely used and can be considered to be a standard technology. Follow-up studies of children born by ICSI mostly seem to show no increase in congenital abnormalities over background, although clear evidence indicates that certain Y chromosome defects (such as microdeletions) can be transmitted. The risk for sex chromosome abnormalities in otherwise normal children may be slightly increased.

Although assisted hatching is widely used, definitive sophisticated data attesting to its usefulness are lacking.

TABLE 7A

Is assisted hatching used or allowed under the guidelines/statutes?

Country	Allowed/ used	Not allowed/ not used	Not mentioned
Argentina			+, used
Australia (West)	+, used		
Australia (South)	+, used		
Australia (Victoria)			+, used
Australia (Remainder)	+, used		
Austria	+, used		
Bangladesh		+	
Belgium	+, not used		
Brazil			+, used
Bulgaria		+	
Canada	+		
Chile	+		
China	+, used		
Czech Republic			+, used
Denmark			+, used
Ecuador	+		
Egypt	+, used		
El Salvador		+	
Finland	+		
France	+, used		
Germany	+, used[a]		+, used[a]
Greece			+, used
Hong Kong			+, used
Hungary	+, used		
Iran	+		
Ireland			+, used
Israel	+, used[b]		
Italy			+, used
Japan	+, used[a]		+, used[a,c]
Jordan	+		
Korea	+, used		
Mexico	+, used		
Morocco	+, used		
Netherlands			+, used
Norway		+	
Poland			+, don't know if used
Portugal	+		
Romania	+		
Saudi Arabia			+, used[d]
Singapore			+
Slovenia	+, used		
South Africa	+, used		
Spain			+, used
Sweden	+, used		
Switzerland	+, used		
Taiwan	+, used		
Tunisia			+, not used
Turkey			+, used
United Kingdom	+[e]		
Uruguay	+		
United States	+, used		
Venezuela	+		

[a] Conflicting reports from correspondents.
[b] Used routinely for many years as standard.
[c] Used by many programs of different centers.
[d] On a limited scale in patients with repeated IVF failure, older age, and oocytes with thick zona pellucids.
[e] Subject to same provision on IVF.

TABLE 7B

Are other types of micromanipulation (cytoplasmic transfer or nuclear transfer) allowed?

Country	Allowed/ used	Not allowed/ not used	Not mentioned/ don't know
Argentina			+
Australia (West)	+		
Australia (South)		+	
Australia (Victoria)		+	
Australia (Remainder)		+	
Austria		+	
Bangladesh		+	
Brazil		+	
Bulgaria		+	
Canada			+
Chile		+	
China			+
Czech Republic			+
Denmark			+
Ecuador		+	
Egypt	+		
El Salvador		+	
Finland		+[a]	+[a]
France			+
Germany		+[a]	+[a]
Greece		+[b]	
Hong Kong			+
Hungary			+
Iran			+
Ireland		+[c]	
Israel			+[d]
Italy			+
Japan		+	
Jordan		+	
Korea	+		
Mexico			+
Morocco		+	
Netherlands			+
Norway		+	
Poland			+
Portugal			+
Romania		+	
Saudi Arabia			+[e]
Singapore			+
Slovenia			+
South Africa			+
Spain			+
Sweden		+	
Switzerland		+	
Taiwan		+	
Tunisia			+
Turkey			+
United Kingdom		+	
Uruguay			+
United States		+[e]	
Venezuela		+	

[a] Conflicting reports from correspondents.
[b] Reproductive cloning is specifically prohibited.
[c] This would be experimental. Not allowed with embryos.
[d] Any new technique, not mentioned by the guidelines, should be presented to the ethics committee. After approval by the committee, it should be approved also by the ministry of health.
[e] Cytoplasmic and nuclear transfer are considered investigational and require institutional review board approval. The federal Food and Drug Administration also has oversight in this area. Investigational drug (IND) approval is required.

CHAPTER 8: Oocyte maturation

In the early days of IVF, in the natural cycle or in cycles stimulated with the techniques that were then in vogue, regularly harvesting at least some few eggs in the germinal vesicle stage along with the more mature eggs was not unusual. Some of these immature eggs could be matured in vitro with fertilization and developed to a few cell stage by 48 to 72 hours. Many of these eggs were transferred along with the eggs that were M2 at harvest, so the behavior of those eggs could not be evaluated.

However, in some instances, the only transferable eggs from a particular case were those harvested at the germinal vesicle stage. When these eggs were fertilized and transferred at 48 to 72 hours at the four-cell to eight-cell stage, very few pregnancies developed. An estimated pregnancy rate would have been in the 2% to 3% range. The cause of these poor rates has never been sorted out. It may have been related to intrinsic germinal vesicle egg problems. Or perhaps a difficulty arose with asynchrony of the endometrium, in that the germinal vesicle eggs were delayed in their development by at least 24 hours and so might have been placed into endometrium with the implantation window already closed.

With improvements in stimulation technology and the harvesting of large numbers of M2 eggs, efforts to mature germinal vesicle eggs in vitro became of less interest.

However, in the last few years, there has been a renewal of interest in harvesting immature eggs without prior stimulation with gonadotropins. In some instances, hCG is given before harvest, but in other instances the harvest is done and hCG is placed in the culture medium. Such efforts are confined almost entirely to patients with polycystic ovary syndrome, as multiple follicles are spontaneously available. The present survey is an attempt at surveillance, to measure the extent of this new approach to in vitro maturation.

ANALYSIS OF SURVEY

This procedure seems to be prohibited by 10 (20%) of the 50 reporting jurisdictions (Table 8).

Sixteen entities (32%) seem to provide for such a procedure, but comments have indicated that it has had very limited application and in many instances is regarded for experimental use only.

The majority of reporting entities (40%) do not specifically mention this procedure in their rules and regulations. However, in Argentina, Victoria (Australia), Ireland, Israel, Japan, Taiwan, the United Kingdom (by license), the United States (by institutional review board approval), some activity in a few programs seems to be in progress.

TABLE 8

Is oocyte maturation allowed under the statute/guidelines? (Is it used?)

Country	Yes	No	Not mentioned
Argentina			+, practiced
Australia (West)	+		
Australia (South)		+	
Australia (Victoria)			+[a]
Australia (Remainder)			+[a]
Austria	+		
Bangladesh		+	
Belgium	+		
Brazil			+, don't know if practiced
Bulgaria		+	
Canada	+		
Chile	+[a]		
China	+		
Czech Republic			+
Denmark			+, practiced
Ecuador	+		
Egypt	+[b]		+, not used[b]
El Salvador		+	
Finland	+		
France			+
Germany	+[b]		+, not practiced[a,b]
Greece			+
Hong Kong			+
Hungary			+
Iran	+		
Ireland			+, practiced
Israel			+, practiced
Italy			+, don't know if practiced
Japan			+, practiced
Jordan	+		
Mexico			+
Morocco		+	
Netherlands			+
Norway			+
Poland			+, not practiced
Portugal			+
Romania		+	
Saudi Arabia		+	
Singapore			+
Slovenia	+		
South Africa	+[b]		+[b], don't know if used
Spain			+
Sweden	+		
Switzerland			+
Taiwan			+, practiced
Tunisia			+
Turkey			+, practiced
United Kingdom			+[c]
Uruguay		+	
United States			+, practiced[a]
Venezuela		+	

[a] Mainly for research or experimental purposes.

[b] Conflicting reports from correspondents.

[c] Subject to special individual license.

DISCUSSION

Although only a limited number of programs attempt in vitro maturation without stimulation, the number of pregnancies to date has been quite limited, and studies are essentially available only on a case report basis. It is clear that with present techniques the pregnancy rate is quite modest. A definitive study of the relative role of intrinsic oocyte problems vs. endometrial asynchrony needs to be resolved with this new approach to in vitro fertilization. At the present time, such techniques must be considered experimental. There seem to be no regulatory uncertainties or problems.

SUMMARY

In vitro maturation of unstimulated germinal vesicle eggs is, at the present time, under serious study in a few centers around the world. The results are not encouraging, and the problem must be considered experimental at this time. There seem to be no regulatory uncertainties or problems.

CHAPTER 9: Welfare of the child

ANALYSIS OF SURVEY

The aim of ART is to allow an infertile couple to get a child, a healthy and normal child. The welfare of the child is defined here as "well-being" applied to the total health of babies until they enter life, and not only as regards their relationship with parents.

Most societies have undergone radical changes in the last 30 years; as seen in chapter 1, most legislation or guidelines will treat equally couples whether married or cohabiting. The status of the child also has evolved, and the notion of "welfare of the child" is varied in quality and difficult to assess because of its large psychosocial components. The notion of welfare of the child is very important in ART, because doctors or biologists are implicated in responsibility for an unhealthy child.

The United Kingdom is the only country to take in account the welfare of the child by imposing law (Table 9). In the United Kingdom, the statutory Human Fertilization and Embryology Authorities 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: "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."

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.

SUMMARY

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

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.

TABLE 9

Does the statute/guideline/custom impose on the IVF program any admonition about consideration of the welfare of any resulting offspring?

Country	Yes	No	Not mentioned
Argentina			+
Australia (West)	+		
Australia (South)	+		
Australia (Victoria)	+[a]		
Australia (Remainder)			+
Austria			+
Bangladesh		+	
Brazil			+
Bulgaria	+[b]		
Chile		+[c]	
China			+
Czech Republic			+
Denmark	+		
Ecuador		+	
Egypt			+
El Salvador		+	
Finland	+[d]	+[d]	
France	+		
Germany			+
Greece			+
Hong Kong	+		
Hungary			+
Iran			+
Ireland			+[e]
Israel			+
Italy			+
Japan			+
Jordan		+	
Korea		+	
Mexico			+
Morocco	+		
Netherlands			+
Norway	+[f]		
Poland			+
Portugal			+
Romania	+[g]		
Saudi Arabia			+
Singapore			+
Slovenia	+[h]		
South Africa			+
Spain			+
Sweden			+
Switzerland	+		
Taiwan			+
Tunisia			+
United Kingdom	+[i]		
Uruguay	+		
United States			+
Venezuela		+	

[a] Compulsory reporting of abnormalities identified at or about the time of birth.
[b] Implement amniocentesis in all ICSI pregnancies.
[c] All couples receive a document that includes an education tool and consent form. Both address the item of welfare of offspring.
[d] Conflicting reports between correspondents.
[e] Must be considered.
[f] Only in general terms.
[g] Regarding the quality of the embryos.
[h] Committee for Biomedically Assisted Procreation (BMAP) procedures should be performed in the best interest of child.
[i] Welfare of the child must (should be) considered before agreeing to provide treatment as per the HFE Act (1990).

CHAPTER 10: Fetal reduction

Multifetal pregnancy reduction is the accepted term for reduction to prevent the complications of multiple pregnancies. Selective fetal reduction is the accepted term for reduction of a fetus determined to have a serious developmental abnormality.

This survey primarily concerns the use of multifetal pregnancy reduction to avoid the complications of multifetal pregnancies.

ANALYSIS OF SURVEY

Fetal reduction seems to be an accepted procedure in most of the surveyed political entities. Indeed, it is prohibited in only 29% of the 52 respondent countries (Table 10). As might be anticipated, the procedure is not approved nor practiced among nations where abortion is specifically illegal or socially unacceptable, including Ireland and many of the Latin American countries such as Argentina, Brazil, Chile, Ecuador, El Salvador, and Venezuela.

DISCUSSION

Several studies have confirmed the utility of fetal reduction. However, the procedure does carry a small risk for the total loss of the pregnancy. The magnitude of this risk seems to decrease with provider experience, but it cannot be considered to be zero. Long-term follow-up of children born from continuing sacs remains to be done; thus far, the rate of congenital abnormalities in this group does not seem to be greater than background, and there is no reason to think that there may be difficulty in the remaining children. Many investigators have commented that the use of this procedure should have a low priority in view of the psychological and emotional trauma experienced by mothers, even in social situations where therapeutic termination of pregnancy is a usual and accepted procedure. Clearly, some couples may wish not to use the procedure for personal reasons, despite the risk of multiple pregnancies. It certainly follows that prevention of multiple pregnancies is ideal.

Although reduction is a widely accepted procedure, there are certainly no data in this survey or elsewhere as to the frequency with which reduction is actually used. Regrettably, none of the national registries with the exception of FIVNAT (France) collect data on this procedure. The information would be extremely helpful in measuring the frequency of multiple pregnancies, which at present are measured largely with live-birth data. In 2002, FIVNAT reported 1.78% reductions for IVF and 1.42% for ICSI.

SUMMARY

Fetal reduction has been established as a means of enhancing the welfare of the mother and the remaining vital fetuses, although the psychological and emotional trauma experienced by those undergoing the procedure remains a concern, even in a social situation where abortion is accepted. The procedure is widely accepted around the world, but there are actually no data on the frequency with which it is used in any political entity. Furthermore, no long-term follow-up evaluations of children born after the procedure have been performed, although anecdotal data suggest no great reason to be concerned.

TABLE 10

Is selective reduction allowed by statute, or approved by the guidelines or practice if there is no statutory act or guideline for IVF?

Country	Approved/ allowed/ practiced	Not approved/ not allowed/ not practiced	Not mentioned
Argentina		+	
Australia (West)	+, practiced		
Australia (South)			+, practiced
Australia (Victoria)			+, practiced
Australia (Remainder)			+, practiced
Austria			+, practiced
Bangladesh		+	
Belgium	+		
Brazil		+	
Bulgaria	+		
Canada			+
Chile		+	
China	+, practiced		
Czech Republic	+, practiced		
Denmark	+, practiced		
Ecuador		+	
Egypt	+, practiced		
El Salvador		+	
Finland		+	
France			+, practiced
Germany	+, practiced[a]		+, not practiced[a]
Greece			+, practiced
Hong Kong	+, practiced		
Hungary	+, practiced		
Iran			+, don't know if practiced
Ireland		+	
Israel	+, practiced		
Italy			+, practiced
Japan		+[b]	
Jordan	+		
Korea	+		
Mexico			+, practiced
Morocco			+, practiced
Netherlands			+
Norway		+	
Poland		+	
Portugal		+	
Romania	+		
Saudi Arabia			+, practiced
Singapore		+, not practiced	
Slovenia	+, practiced[c]		
South Africa			+, practiced
Spain			+, practiced
Sweden	+, practiced		
Switzerland	+, practiced		
Taiwan	+		
Tunisia			+, practiced
Turkey			+, practiced
United Kingdom	+, practiced		
Uruguay		+	
United States	+		
Venezuela		+	

[a] Conflicting reports from correspondents.
[b] Some exceptions.
[c] No need in IVF anymore.

CHAPTER 11: Preimplantation genetic diagnosis

Since its introduction in 1990, preimplantation genetic diagnosis (PGD) has provided a choice for couples at risk of having children with a known genetic aberration, permitting the transfer of unaffected preembryos and the discard of preembryos affected by genetic abnormality. The great advantage of PGD over other prenatal diagnostic techniques is that termination of pregnancy is avoided, allowing high risk couples to obviate possible abortion and providing an option in societies where abortion is prohibited and other prenatal diagnostic methods cannot be used. However, it requires a moral distinction be made between termination of an affected fetus and the discarding of a similarly affected nontransferred preembryo. Many patients are prepared to make such a distinction.

The reliability of the method has been established. Its main disadvantages are the relatively high cost and low pregnancy rate, because fewer normal preembryos are available to transfer and because IVF is required in couples who otherwise might not require assistance with their reproduction.

The conditions currently diagnosed by PGD include:

- Thalassemia
- Phenylketonuria
- Cystic fibrosis
- α-1-antitrypsis deficiency
- Retinitis pigmentosa
- Alport syndrome
- Gaucher disease
- Tay-Sachs disease
- Sickle-cell anemia
- Myotonic dystrophy
- Ampullar epidermolysis
- Long-chain acyl-coenzyme A
- Dehydrogenase deficiency
- Achondroplasia
- Deaminase adenosine deficiency
- Alzheimer disease
- Some types of cancer
- Marfan syndrome
- Spinal muscular atrophy
- Fragile X chromosome syndrome
- Congenital hyperplasia of the suprarenal glands
- Huntington chorea
- Lesch-Nyhan syndrome
- Hemophilia A and B
- HLA typing

Preimplantation genetic diagnosis has also been used as a method of screening for preembryo aneuploidy. It is possible thereby to discard those preembryos that have aneuploidy and to transfer normal preembryos. This non-gene technology, inadequately covered by this survey, should be considered experimental at this point.

ANALYSIS OF SURVEY

Preimplantation genetic diagnosis is practiced in many countries (Table 11). However, even in those countries where it is offered, many times only a limited number of centers can perform it. In France, for example, only three centers offer this technique. There are a number of countries where it is not allowed; or, if allowed, it is not feasible. These would include countries such as Austria, Bangladesh, Bulgaria, Chile, Ecuador, Germany, and Iran.

There are special situations in some countries. For example, in Japan it is allowed; but, according to the Japanese respondent, it has never been practiced because the review body there seems to be reluctant to authorize its use. In addition, in countries like the Netherlands, each case must be reviewed by an official body on a case-by-case basis before it can be applied.

DISCUSSION

The European Society for Human Reproduction and Embryology (ESHRE) formed a consortium in 1997 to undertake a long-term study of the efficacy and clinical outcome of PGD. In January 2002, the consortium published its report for the year 2000 (Hum Reprod 2002;17:233–46) on data collected from 25 centers on referrals, cycles, pregnancies, and babies born after PGD. Data was collected for a total of 1,561 referrals, 370 regular PGD cycles, 334 PGD-aneuploidy screening cycles, and 78 cycles for social sexing. There were 215 pregnancies with 117 babies. About one-half of the referrals were for chromosomal abnormalities. Among the single-gene defects, approximately one-third were X-linked, one-third autosomal recessive, and one-third autosomal dominant.

SUMMARY

Preimplantation genetic diagnosis is widely available geographically and is useful procedure for limiting genetic disease, provided the genetic disease has been previously diagnosed. It prevents an abortion, but requires a moral distinction be made between termination of an affected fetus and the discard of a similarly affected nontransferred preembryo. Its use for aneuploid screening must be considered experimental at the present time. Generally speaking, the procedure is satisfactory, but errors have been reported.

TABLE 11

Is preimplantation genetic diagnosis allowed by statute/guidelines, or used if there is no statutory act or guideline for IVF?

Country	Allowed/ used	Not allowed/ not used	Not mentioned
Argentina			+, used[a]
Australia (West)	+, used		
Australia (South)	+, used		
Australia (Victoria)	+, used		
Australia (Remainder)	+, used[b]		
Austria		+	
Bangladesh		+	
Belgium	+, used		
Brazil	+, used[c]		+, used[c]
Bulgaria		+	
Canada	+, used		
Chile		+	
China	+, used		
Czech Republic	+		
Denmark	+, used[d]		
Ecuador		+	
Egypt	+, used		
El Salvador		+	
Finland	+		
France	+, used[e]		
Germany		+[c]	+, not used[c,f]
Greece	+, used[g]		
Hong Kong	+, used		
Hungary	+, used		
Iran	+, used		
Ireland		+[h]	
Israel	+, used[i]		
Italy			+, used
Japan	+, used[j]		
Jordan	+		
Korea			+, used
Mexico	+, used		
Morocco	+		
Netherlands		+, used[k]	
Norway	+, not used		
Poland			+, not used
Portugal	+, used		
Romania		+	
Saudi Arabia			+, used
Singapore			+
Slovenia	+, used[l]		
South Africa			+, used
Spain	+, used		
Sweden	+, used		
Switzerland		+	
Taiwan	+, used		
Tunisia			+, not used
Turkey			+, used
United Kingdom	+, used[m]		
Uruguay		+	
United States	+, used[n]		
Venezuela	+		

[a] Because of the cost, it is still an exceptional practice.
[b] Routine for genetic disease.
[c] Conflicting reports between correspondents.
[d] In three programs.
[e] Only three centers in France.
[f] Number of embryos is restricted to maximally three per cycle. PGD is therefore not possible.
[g] Indirectly allowed because the law mandates that ART is permitted to avoid the transmission of a severe genetic disease to the child.
[h] Is considered experimental.
[i] Used routinely for many years as standard.
[j] Approval in advance by Japanese Society of Obstetrics and Gynecology is required.
[k] With exceptions. Only allowed when approved by CCMO (Centrale Commissie Menselijk Onderzoek).
[l] Experimentally.
[m] Subject to same provisions as IVF.
[n] Please refer to appropriate guidelines and Ethics Committee statements.

CHAPTER 12: 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 aspects of the procedure are completely covered, as well as the medical aspects.

ANALYSIS OF SURVEY

Approximately one-half of all the surveyed jurisdictions appear to use IVF surrogacy. However, there are often special requirements (Table 12).

Some countries have particular regulations:

- Argentina requires evaluation by a SAEFN 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 allows only a family member to be the surrogate.
- 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.
- 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 to accommodate the surrogacy situation by legislation in some jurisdictions, 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 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 where 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 12

Is IVF surrogacy (the use of gametes of both prospective parents when the female partner does not have a functioning uterus) allowed under statute/guidelines, or used if there is no statutory act or guideline for IVF?

Country	Allowed/used	Not allowed/ not used	Not mentioned
Argentina	+[a]		
Australia (West)	+, used[b]		
Australia (South)		Used[c]	
Australia (Victoria)	+[d]		
Australia (Remainder)	+[e]		
Austria		+	
Bangladesh		+	
Belgium		+	
Brazil	+, used[f]		
Bulgaria		+	
Canada			+
Chile		+	
China		+	
Czech Republic		+	
Denmark		+	
Ecuador	+		
Egypt		+	
El Salvador	+[g]		
Finland	+		
France		+	
Germany		+	
Greece	+, used[h]		
Hong Kong	+, don't know if used[i]		
Hungary		+[j]	
Iran	+, used		
Ireland			+
Israel	+[k]		
Italy		+	
Japan		+	
Jordan		+	
Korea	+		
Mexico			+, used
Morocco		+	
Netherlands	+[l]		
Norway		+	
Poland			+
Portugal		+	
Romania	+		
Saudi Arabia		+	
Singapore		+, don't know if used	
Slovenia		+	
South Africa			+
Spain		+	
Sweden		+	
Switzerland		+	
Taiwan		+	
Tunisia		+	
Turkey		+	
United Kingdom	+, used[m]		
Uruguay		+	
United States	+[n]		
Venezuela	+		

[a] Case by case basis. Evaluation with SAEF Ethics Committee.
[b] In three states; is compassionate surrogacy only.
[c] Very difficult situation. Family Relationship Act bans commercial surrogacy, but altruistic surrogacy allowed by default. Currently under review. Each state is different. Likely to occur in South Australia within 1 to 2 years.
[d] Altruistic surrogacy only; no payment/reward must be exchanged.
[e] Commercial surrogacy not allowed. A.C.T. allows noncommercial surrogacy.
[f] Must be a member of family.
[g] It is allowed because there is not any law that prohibits it.
[h] Court decision, written consent of both parties, no payment, the commissioning woman must be medically incapable to bear the fetus, the surrogate must be medically fit to bear the fetus.
[i] Section 17 of HRTO, pg. A1723.
[j] Allowed, but this specific part of the statute dealing with IVF surrogacy has not come into operation yet.
[k] Couple should be married, surrogate mother should be fertile and single, permission should be given by a special committee established for that reason by the Ministry of Health.
[l] See http://www.ivf.nl
[m] Subject to same provisions as IVF (HFE Act 1990); couple must be married.
[n] State by state variation by state law. Please refer to Ethics Report.

CHAPTER 13: Experimentation on the preembryo

Although research on the preembryo is generally agreed to be essential for the improvement of ART, there is great difference of opinion as to the appropriateness of such research, especially if it involves the destruction of the preembryo. Embryonic stem cell research would be one specific example of this situation. This survey is an attempt to determine the extent of research on the preembryo and the regulations/guidelines involved.

ANALYSIS OF SURVEY

Approximately one-half of the reporting political entities (23 out of 44) allow research, although in essentially all instances there are special regulations or guidelines (Table 13). These are quite variable. At one extreme is the provision that no harm come to the preembryo (Argentina, Fertility Society Guidelines); at the other extreme is that the destruction must be approved by various bodies—for example, in the United Kingdom by license from the Human Fertilization and Embryology Authorities (HFEA), and in the United States by an institutional review board and provided no federal funding is involved.

Curiously enough, 26 of the 44 entities reported that experimentation was prohibited. Different reporters for 5 entities (Argentina, Egypt, Saudi Arabia, Spain, and Switzerland) made discrepant reports as to the yes and no of preembryonic research. These discrepancies are perhaps understandable. Argentina and Egypt have guidelines for research, but cultural pressures have thus far prevented any research. South Africa has no guidelines, but cultural antipathy has prevented any research. In Spain, the laws allow research but only on nonviable embryos, thus essentially negating any result. In Switzerland, a law is pending that will probably allow research.

If research on the preembryo is allowed, it requires an accurate definition: a time limit in development when research is allowed on the preembryo.

The majority of political entities seem to adhere to the 14-day rule, a point in time meant to correspond to the appearance of the primitive streak, the first recognizable event in development that indicates biologic individuation.

However, some entities do not adhere to the 14-day rule. Bangladesh, El Salvador, and South Africa indicate no limits. Finland reports an interval of less than 14 days, but is otherwise not specific. Jordan reports 6 days.

Embryonic stem cell research is a specific type of research on the preembryo requiring its destruction. In general, survey replies to a specific question about embryo stem cell research were consistent with the replies concerning research on the preembryo. However, there were a few discrepancies. Thus, 25 of the 42 respondents indicated that embryonic stem cell research was possible, and 3 indicated that it was possible with severe restrictions. However, it is likely that some regulatory approval is required in almost all jurisdictions.

Fourteen of the 42 political entities indicated that embryonic stem cell research was excluded specifically by law. This was an eclectic group of countries: Austria, Bulgaria, Ecuador, El Salvador, France, Morocco, Norway, Poland, Portugal, Saudi Arabia, Spain, Switzerland, Turkey, and Uruguay.

DISCUSSION

Research on the preembryo is not easy to define. For example, variations in culture media are an effort to improve development of a preembryo, but such variations are not generally considered as experimentation. Thus, in the United States, changes in culture media designed to improve preembryonic development are not normally something that requires institutional review board approval. On the other hand, experimentation that results in the destruction to the preembryo certainly requires third-party approval in jurisdictions where this is required, such as a license by the HFEA in the United Kingdom or approval by an institutional review board in the United States.

The availability of preembryos for research is very controversial and for the most part is related to the evaluation of the moral status of the preembryo, which is discussed in chapter 16.

Many entities confine research to “spare” preembryos, meaning those over and above the number required for the reproductive problem. Relatively little discussion exists in the current literature of the creation of preembryos specifically for research, although this has certainly been done previously in the United Kingdom and more recently in the United States.

No doubt great improvements in development have occurred by experimentation on the preembryo with variations in culture media. Also, much has been learned about chromosomal abnormalities by destruction of preembryos, mostly spare preeembryos. However, pointing to generally accepted therapeutic applications of the latter findings is difficult.

The pros and cons of research on the preembryo would be an attractive topic for discussion in an international forum.

SUMMARY

Although the issue is sensitive, research on the preembryo is certainly done. It generally requires informed consent, and in many countries requires consent of a specific governing

TABLE 13

By statute/guideline/cultural consensus/or recognized prevailing religious decree, is the use of human preembryos for experimental purposes an acceptable procedure?

Country	Yes	No	If yes, is special specific approval of the research proposal required, and if so, by what body?
Argentina	+		Fertility society ethics committee
Australia (West)	+		Yes, ITA (only applies to clinical trials, observation involving embryos, i.e., nondestructive research)
Australia (South)	+[a]		NHMRC subcommittee
Australia (Victoria)		+	
Australia (Remainder)	+[b]		Licensing committee (for proposals after 19 June 2003)
Austria		+	
Bangladesh		+	
Belgium	+		National committee
Brazil		+	
Bulgaria	+		No
Canada	+		Local research ethics board
Chile		+	
Denmark	+		Regional + national ethics committee
Ecuador		+	
Egypt	+[c,d]	+[c]	No special approval
El Salvador		+	
Finland	+		Social and Health Ministry, Ethics Committee
France		+	
Germany		+	
Greece	+[e]		Not mentioned in this law
Hong Kong	+		Approval from institutional research ethics committee
Hungary	+		Committee of Human Reproduction
Iran	+		(Don't know)
Ireland		+	
Israel		+	
Japan	+		Ministry of Education and Science, Ethics Committee Japan Society OB/GYN
Jordan	+		Institutional review board
Morocco		+	
Norway		+	
Poland		+	
Portugal		+[f]	
Saudi Arabia		+	
Singapore	+		Ministry of Health
Slovenia	+[g]		Ethics committee, Committee for Biomedically Assisted Procreation (BMAP)
South Africa	Not mentioned in any guidelines, but frowned upon		Yes, university ethics committee
Spain	+[h]	+[h]	Health authorities and National Committee of Human Assisted Reproduction
Sweden	+		Local ethics committee
Switzerland		+[i]	
Taiwan		+	
Tunisia	+		Ethics committee
Turkey		+	
United Kingdom	+		Yes, HFEA
Uruguay		+	
United States	+[j]		None required, private funds
Venezuela		+	

[a] A license must be obtained from federal government. The purpose must be approved specifically by the couple.
[b] New legislation currently under formulation requires national body to supervise.
[c] Conflicting reports by respondents.
[d] Extra embryos not used when the couple refuse cryopreservation.
[e] Unused (abandoned) gametes and embryos can be used for research.
[f] This does not include already cryopreserved embryos.
[g] Only on surplus embryos if both possible future parents agree.
[h] Yes, with nonviable embryos; no, with viable embryos.
[i] New law prepared at present time; if accepted, will allow use of preembryos for experimentation.
[j] Prohibited if research is with federal funds, OK with private funds.

board. This may be an institutional review committee of a local institution, as in the United States, or approval by a national body, such as HFEA in the United Kingdom. The suitability of research, particularly destructive research, on the preembryo is very much related to an evaluation of the moral status of the preembryo.

CHAPTER 14: Cloning

Cloning as covered by this survey is the type of cloning resulting from the transfer of a nucleus. This results in the production of an individual with the exact nuclear genetic composition of the donor of the nucleus. Nuclear cloning began by the transfer of the nucleus of an embryonic cell of an amphibian, but the embryonic cell transfer has been applied to other species successfully, including the mammal. In 1997, the use of a somatic cell nucleus in the sheep resulted in the birth of the famous Dolly, followed by success in rodents, cats, pigs, cows, sheep, mules, and horses.

Despite great efforts, no primate has been cloned. Somatic nuclear transplant cloning is extremely inefficient and often results in a large percentage of abnormalities in the fetus and even in the newborn. These complications of cloning clearly make it inadvisable to use in the human for reproductive purposes.

The cloning process, sometimes referred to as somatic cell nuclear transfer, also has great research potential. For example, there is the mind-boggling possibility of producing an oocyte from an XX somatic nucleus.

It is clear, therefore, that a sharp distinction needs to be made between nuclear cloning for reproductive purposes and nuclear cloning for investigation. However, in the mind of the public and some legislatures, this distinction is often not made.

ANALYSIS OF SURVEY

Reproductive cloning is not allowed or used in any of the surveyed entities. Indeed, several political groups have specifically enacted laws or decrees prohibiting its use, such as in Argentina, all states in Australia, France, Italy, Japan, and Slovenia; the American Society for Reproductive Medicine Ethics Committee has made a recommendation against using it.

However, some countries allow or even encourage experimental cloning, or "therapeutic cloning" as it is inaccurately called in the survey. China, for instance, is prepared to use somatic nuclear cloning for experimental purposes, and indeed in the United Kingdom it can be done by license (Table 14).

DISCUSSION

Experience in mammals with somatic nuclear cloning indicates its great inefficiency and high degree of abnormality. For this reason, it is extremely unlikely that any responsible clinician would wish to apply this for reproductive purposes. Despite newspaper reports of its application, to date no credible birth has been confirmed, and fear that it would be used has caused some governments to prohibit it. These prohibitions seem not to have been on the practical basis of abnormalities and efficiency, but rather on the cultural notion that cloning of an individual is not consistent with human dignity.

Fortunately, some political jurisdictions have distinguished between reproductive cloning and experimental cloning, because experimental cloning does offer great research potential. Unfortunately, because a distinction between the two types of cloning is often not made, there is danger that important experiments that would be of great benefit to humans might be prohibited out of concern about the application of therapeutic nuclear somatic cloning. Legislation may prohibit experimental procedures that in the long run could develop understanding and technology important in improving the human condition.

It is interesting that cloning has been unsuccessful in primates, leading to the question of whether some inherent biological mechanism prohibits nuclear cloning at the primate level. This matter is under investigation.

SUMMARY

Because somatic nuclear cloning is beset by so many biological problems, clinical application does not seem likely in the near term. Legislation, if not biologically informed, might prohibit experimentation that could be of great value in the long run.

TABLE 14

Is therapeutic cloning allowed under statute/guidelines or used if there is no statutory act or guideline for IVF?

Country	Allowed/used	Not allowed/ not used	Not mentioned/ don't know
Argentina			+
Australia (West)		+	
Australia (South)		+	
Australia (Victoria)		+	
Australia (Remainder)		+	
Austria		+	
Bangladesh		+	
Belgium		+	
Brazil		+[a]	+[a]
Canada		+	
Chile		+	
China	+		
Czech Republic			+[b]
Denmark		+	
Ecuador		+	
Egypt	+[a]	+[a]	
El Salvador		+	
Finland		+	
France		+	
Germany		+[a]	+[a]
Greece			+[c]
Hong Kong			+
Hungary			+
Iran			+
Ireland		+	
Israel		+[d]	
Italy		+	
Japan	+[e]		
Jordan		+	
Korea		+	
Mexico			+
Morocco		+	
Netherlands	+		
Norway		+	
Poland			+
Portugal		+	
Romania		+	
Saudi Arabia		+	
Singapore			+[f]
Slovenia			+[g]
South Africa			+
Spain			+[h]
Sweden	+		
Switzerland		+	
Taiwan		+	
Tunisia		+	
Turkey		+	
United Kingdom	+[i]		
Uruguay		+	
United States	+[j]		
Venezuela		+	

[a] Conflicting reports from correspondents.
[b] A law regarding therapeutic cloning is being prepared.
[c] Because not mentioned, it is considered to be allowed.
[d] Two centers in Israel are involved with stem cells. Any new technique needs the permission of the Ministry of Health.
[e] Animal embryos chimaerized with human cells are the only embryos allowed to procreate at research level for future medical use.
[f] Another statute that deals with it is being debated by government; recommendation is that it will be allowed.
[g] Only spare embryos can be used for research program, and informed consent of participants is needed. The research must be approved by National Ethics and Committee for Biomedically Assisted Procreation (BMAP) Committees.
[h] Spain signed the convention for the Protection of Human Rents and the additional protocol on the Prohibition of Cloning Human Being (Oviedo 1997, Paris 1998).
[i] Only stem cell cloning for specific research projects licensed by HFEA under 2002 law.
[j] Provided no federal funds are used.

CHAPTER 15: GIFT

Gamete intrafallopian transfer (GIFT) emerged in 1983 as an alternative to IVF. In contrast 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 seem to be used under any circumstance in Bulgaria, Denmark, Finland, Ireland, and Slovenia. The same is probably true of other countries for which the GIFT questions were not answered or were indicated as not applicable on the questionnaire.

On the other hand, it is still used in some countries like Saudi Arabia, in areas where IVF facilities are not readily available.

It has been used to sidestep regulatory limits on the number of preembryos to be transferred when IVF is used.

Some countries do have stated limits on the number of oocytes to be used when GIFT is applied.

- Argentina usually transfers four oocytes.
- South Australia has a limit of three oocytes.
- The remainder of Australia allows two and three oocytes under special circumstances.
- Germany allows three oocytes.
- Hong Kong allows three oocytes, but for women over age 34 years a maximum of four are allowed.
- Japan allows three oocytes, but four may be used if the three oocytes are of low quality.
- Morocco allows one oocyte.
- Portugal allows five oocytes.
- Saudi Arabia allows five to six oocytes.
- Singapore allows three oocytes.
- The United Kingdom has no limits.
- Venezuela allows three to four oocytes.

DISCUSSION

Gamete intrafallopian transfer is indicated only in women with 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 remains in the United Kingdom. Under the legislation in force at the time of the survey, the number to transfer with IVF is strictly limited. However, GIFT is not covered by the statute, although there is considerable agitation to include GIFT and particularly to limit the number transferred by GIFT to the same as the number transferred by IVF. There have been examples of the transfer of eggs with GIFT greatly in excess of the number allowed by IVF. There may be a change in the current legislation.

SUMMARY

Gamete intrafallopian transfer is currently used only in niche situations. As noted above, several countries have special legislative limits on the number that can be used with GIFT. A major exception has existed in the United Kingdom, but there is agitation to change the legislation.

CHAPTER 16: Status of the conceptus

The moral and legal status of the preembryo, embryo, and fetus—that is, the moral and legal status of the developing human conceptus—is often key to the acceptability of many procedures made available by the technology of IVF. Examples include preimplantation genetic diagnosis (PGD), selection for transfer and discard of the nontransferred embryos either with or without PGD, cryopreservation, surrogacy, and experimentation on the conceptus.

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 (i.e., protection by society) begins only with viability, but considerable opinion holds that preembryos should not be used for experimentation because they are persons, or at least they require the respect of an individual who is in being (i.e., 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.

ANALYSIS OF SURVEY

The survey brought out the fact that there is great diversity regarding the time during development when a human person is considered to exist. In this context, a human person would be defined as an entity that deserves protection by society. Some replies to the questionnaire interpreted the personhood status to apply to experimentation. The time limit for experimentation may or may not correspond to the time of acquisition of personhood. This uncertainty made the survey difficult to interpret (Table 16).

Three surveyed Latin American countries, Argentina, Chile, and El Salvador, have constitutional provisions that state that personhood begins with fertilization.

One unsurveyed Latin American country, Costa Rica, also has a constitutional provision providing the same statement, that personhood begins with fertilization. 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 and Portugal have laws that state that personhood exists after the pronuclear stage.

The respondent from Greece commented that the Greek Orthodox Church recognizes personhood as beginning with fertilization.

Several jurisdictions, for instance, Western Australia, Canada, Denmark, Egypt, Finland, Hong Kong, Japan, Sweden, the United Kingdom, and the United States have cited the 14-day rule for the limit of embryo research, implying that personhood does not begin up until that time. However, this answer avoids the question of the time of the acquisition of personhood, perhaps later on during development. Several jurisdictions have unique time limits. For example, Iran specifies 3 weeks' gestation, Jordan and Morocco 6 weeks, and Saudi Arabia 120 days.

It is clear that religious tradition has greatly influenced this issue in constitutional provisions, laws, and social practice. According to the Roman and Greek traditions, ensoulment occurs with fertilization, and ensoulment is equated with protection by society. This doctrine has greatly influenced civil practice in many countries, particularly the Latin American countries. Many respondents commented that this issue is a "mess" and expressed the hope that there could be some settlement of this issue on an international basis. This seems unlikely.

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. Although the 14-day rule is most frequently applied with respect to research, this does not address the issue of when, during development, societal protection is extended. It seems clear that religious tradition has had a great influence on this particular question.

TABLE 16

By statute/guideline/cultural practice or recognized and prevailing religious decree, is there a recognized time during human development after which a human person is considered to exist?

Country	Yes			No	If yes, recognized time
	Law	Guideline	Cultural/religious		
Argentina	+				Conception
Australia (West)	+				14 days
Australia (South)	+				Not beyond blastocyst
Australia (Victoria)	+				Synergy
Australia (Remainder)	+				2 PN stage
Austria				+	
Belgium				+	
Brazil	+	+	+		14 days
Bulgaria				+	
Canada	+				14 days
Chile	+				Fertilization
Denmark	+				14 days
Ecuador				+	
Egypt		+[a]	+[a]	+[a]	14 days
El Salvador			+		Union of gametes
Finland	+			+	14 days
France				+	
Germany		+			Zygote
Greece	+				Live birth[b]
Hong Kong	+				14 days
Hungary				+	
Iran			+		3 weeks gestation
Ireland				+	
Israel	+				Delivery
Japan		+			14 days
Jordan			+		6 week
Korea		+			
Morocco			+		6 week
Norway	+				Fertilization
Poland			+		Fertilization
Portugal			+		Fertilization
Saudi Arabia			+		120 days
Singapore				+	
Slovenia				+	
South Africa				+	
Spain	+				Birth
Sweden		+			14 days
Switzerland				+	
Taiwan				+	
Tunisia			+		Implantation
Turkey	+				Birth
United Kingdom	+				14 days for research or live birth for a legal person
Uruguay				+	
United States	+[c]				Viability
Venezuela	+				

[a] Conflicting reports from correspondents.
[b] According to the Greek Orthodox Church, life (person?) starts to exist at the moment of fertilization.
[c] Yes: Law, U.S. Supreme Court decision (Roe *v* Wade).

Overview of summaries

LEGISLATION AND GUIDELINES (SURVEILLANCE)

There continues to be no consensus on the ideal method of surveillance of ART worldwide. Legislation is becoming more frequent worldwide.

Countries with legislative surveillance seem to agree that it works quite well, although there are understandable complaints about the slowness of the legislative process and the difficulty of having regulations changed once they are in place.

INSURANCE COVERAGE

There is no international consensus on the insurance coverage for ART. One-half of surveyed entities had neither public nor private coverage. On the other hand, a few countries such as France and Belgium offer very sophisticated coverage through the public sector.

MARITAL STATUS IN ART

In most countries, ART is supposed to be performed only for heterosexual couples, either married or in a stable relationship. 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 lacking.

ART—THE NUMBER TO TRANSFER

As of 2004, more countries have adopted guidelines or legislation to decrease the number of embryos to transfer. The worldwide trend seems to be to replace two embryos in women under 35 years. The elective transfer of one embryo has been adopted in some countries for the first cycle at least.

The worldwide trend seems to be to replace fewer preembryos. However, the problem is not yet solved, particularly in the United States, where factors on the part of the patient and the ART program seem to require acceptance of an undesirably high multiple pregnancy rate.

CRYOPRESERVATION

There is general agreement that cryopreservation facilities are a necessity for every ART program.

Some agreement has been reached as to the duration of the storage, but there appears to be no scientific basis for selecting a particular length of time with respect to the viability of the preembryos. The duration of storage seems to be more of a social than a scientific decision.

All ART programs and all donors of cryopreserved material must agree in writing on the disposition of any unused cryopreserved material.

DONATION OF GAMETES

In most countries, donation of gametes seems to have worked well, although scientific studies are lacking.

The use of donor sperm generally requires quarantine for 6 months, with a negative HIV test on the donor before and after the interval. In addition, genetic screening by history in sperm or egg donors is widely practiced, and some centers require negative status for hepatitis B and C and other antigens. The risks associated with donor gametes seems to be minimal. Cases of mixed identity have occurred. Opinions differ on whether donors should be anonymous, but there is general agreement that any payment other than of expenses associated with donation is inappropriate. The number of donations has been limited; some countries allow only one, but others allow up to 10 on the basis that the possibility of consanguinity in offspring is minimized.

For the large majority of the donations, the collaboration of the medical profession is needed. This contribution implies the responsibility of the health care provider, as a professional and as private citizen. In addition, it is at all times essential to take into consideration the welfare of the future child.

MICROMANIPULATION

Intracytoplasmic sperm injection has been widely used and can be considered to be a standard technology. Follow-up studies of children born by ICSI mostly seem to show no increase in congenital abnormalities over background, although clear evidence indicates that certain Y chromosome defects (such as microdeletions) can be transmitted. The risk for sex chromosome abnormalities in otherwise normal children may be slightly increased.

Although assisted hatching is widely used, definitive sophisticated data attesting to its usefulness are lacking.

OOCYTE MATURATION

In vitro maturation of unstimulated germinal vesicle eggs is at the present time under serious study in a few centers in various places around the world. The results are not encouraging. The problem must be considered experimental at this time. There seem to be no regulatory uncertainties or problems.

WELFARE OF THE CHILD

In general, consent to treatment legally gives assurance of responsibility for the future children from both parents, whatever their marital status. Although one entity has at least one statute and some comments about the welfare of the child, action under these seems to have never been taken.

As in ART, the best interest of the child must be our priority. Counselors should be morally obligated to provide a realistic picture of the condition to be expected for the offspring and to survey the condition of the children born.

FETAL REDUCTION

Fetal reduction has been established as a means of enhancing the welfare of the mother and the remaining vital fetuses, although there seems to be concern about psychological and emotional trauma experienced by women who undergo the procedure, even in a social situation where abortion is accepted. Although the procedure is widely accepted around the world, there are no data on the frequency with which it is used in any political entity. Furthermore, there have been no long-term follow-up studies of children born after the procedure, although anecdotal evidence suggests no great reason to be concerned.

PREIMPLANTATION GENETIC DIAGNOSIS

Preimplantation genetic diagnosis is a widely available geographically and useful procedure for genetic disease, provided the genetic disease has been previously diagnosed. It prevents an abortion, but requires a moral distinction be made between termination of an affected fetus and the discard of a similarly affected nontransferred preembryo. Its use for aneuploid screening must be considered experimental at the present time. Generally speaking, the procedure is satisfactory, but errors have been reported.

IVF SURROGACY

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

EXPERIMENTATION ON THE EMBRYO

Although the issue is sensitive, research on the preembryo is certainly done. It generally requires informed consent, and in many countries the consent of a specific governing board. This may be approved by an institutional review committee of a local institution, as in the United States, or approval by a national body, as with the HFEA in the United Kingdom. The suitability of research, particularly destructive research, on the preembryo is very much related to an evaluation of the moral status of the preembryo.

CLONING

Because somatic nuclear cloning is beset by so many biological problems, clinical application does not seem likely in the near term. Legislation, if not biologically informed, might prohibit experimentation that would of great value in the long run.

GIFT

Gamete intrafallopian transfer (GIFT) is currently used only in niche situations. Several countries have special legislative limits on the number that can be used with GIFT. A major exception has existed in the United Kingdom, but there is agitation to change this legislative situation.

STATUS OF THE CONCEPTUS

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 was so related that the replies must be evaluated in that connection. The 14-day rule is the most frequently applied with respect to research, but it does not address the issue of when, during development, societal protection is extended.

Appendix: Surveillance 2004 I.F.F.S. questionnaire for countries with statutory, voluntary, or no guidelines for assisted reproductive technology (ART)

(Please answer this questionnaire as to the status on April 30, 2003)

Respondent:
For the sovereign country of:
Number of centers in your country:
Date of response:

Note: Each respondent is requested to fill out *either* Section I, or II, or III, and Sections IV, V, and VI. If your country has statutory provisions, laws, or official regulations for ART, use Section I. If your country operates under guidelines by a voluntary, religious, or other organization, use Section II. If your country has neither statutory regulations nor guidelines, use Section III. You may find that in your country some ART items are covered by statute and other items are covered by guidelines or not covered at all, i.e., there may be regulations that cover the embryology or endocrinology laboratories, but not other aspects of the program. Thus, you have a mixed situation. In this case, please make a mixed response, i.e., use Section I for statutory items, Section II for guideline items, and Section III for no coverage items.

You must answer according to the situation at the time of the answer. If there is in your country a project of law or of modification of the regulations being currently discussed, fill a last page with explanations.

If there is no change from the situation of 2000 (Surveillance 2001), answer as idem 00.

Please return this questionnaire by May 30, 2003, to: Dr Henk J Out, Organon International, KA4006, PO Box 20, 5340 BH Oss, The Netherlands, E-mail: henkjan.out@organon.com.

SECTION I–STATUTORY IVF ONLY

1. Are there statutes, i.e., law? (national or other political sub-division) governing the use of ART? *(Yes/No)* If yes, please supply a copy of the statute or indicate where one may be obtained. If yes, is there a licensing body? *(Yes/No)* If yes, what is the composition? If yes, what are the criteria for a license? If there is a law, how is clinical surveillance carried out? *(Circle correct answer or answers.)* [a] Periodic report, [b] On-site inspection, [c] Other. If other, please describe. Are penalties designated for violation of statutes with regard to clinical practice? *(Yes/No)* If yes, what are they? If there is a law, how is embryological laboratory surveillance carried out? *(Circle correct answer or answers.)* [a] Periodic report, [b] On-site inspection, [c] Other. If other, please describe. Are penalties designated for violation of statutes with regard to laboratory procedures? *(Yes/No)* If yes, what are they? If no, please proceed to Section II or III as appropriate. If yes, complete the additional questions in Section I to which the statute applies.
2. Are the techniques of ART covered or reimbursed by *(circle a, b, or c)*? [a] A national health plan, [b] Private insurance, [c] No coverage. If *a* or *b* is the coverage: Complete? Partial? *(Comment.)*
3. The law specifies that the couple for IVF must have *(circle correct answer)*: [a] A marriage, [b] A stable relationship, [c] No requirement, [d] ART in single women is permitted, [e] ART in lesbian couples is permitted. *(Comment.)*
4. The law specifies the number of preembryos which can be transferred (replaced). *(Yes/No)* If yes, how many and are there any exceptions? What is penalty for violation?
5. Is selective reduction allowed by the statute? *(Allowed/Not allowed/Not mentioned)* If not prohibited, is selective reduction practiced by programs in your country? *(Yes/No/Don't know)*
6. Does the IVF law allow donor sperm to be used in IVF? *(Allowed/Not allowed/Not mentioned)* If allowed, are there any specific requirements?
7. Does any law (other than the IVF law) allow the use of donor sperm in non-IVF infertility? *(Allowed/Not allowed/Not mentioned)* If allowed, are there any requirements? If not prohibited, are donor sperm used for non-IVF infertility used by programs in your country? *(Yes/No/Don't know) (Comment.)*
8. Is posthumous insemination allowed? *(Allowed/Not allowed/Not mentioned)* If not prohibited, is posthumous insemination used? *(Used/Not used/Don't know) (Comment.)*
9. Does the law allow donor eggs to be used in IVF? *(Allowed/Not allowed/Not mentioned)* If yes, are there special requirements?
10. Does the statute allow the offspring to be provided on request with non-identifying information about the donor? *(Allowed/Not allowed/Not mentioned) (Comment.)*
11. Does the statute allow the offspring to be provided on request with identifying information about the donor? *(Allowed/Not allowed/Not mentioned) (Comment.)*

12. Does the statute impose on the IVF program any admonition about the welfare of any resulting offspring? *(Yes/Not mentioned) (Comment.)*
13. Under the statute, is cryopreservation of fertilized eggs (prezygotes to blastocysts) allowed? *(Allowed/Not allowed/Not mentioned)* Are there any special requirements?
14. If cryopreservation of fertilized eggs (prezygotes to blastocysts) is permitted, is there a limit to the duration of storage? *(Yes/No)*If yes, how long? *(Comment.)*
15. Under the statute, is cryopreservation of oocytes allowed? *(Allowed/Not allowed/Not mentioned)* If not mentioned, is oocyte cryopreservation practiced by programs in your country? *(Yes/No/Don't know) (Comment.)*
16. Is oocyte maturation allowed under the statute? *(Allowed/Not allowed/Not mentioned) (Comment.)*
17. Under the statute is cryopreservation of ovarian or testicular tissue (as in patients to be treated for malignancy) allowed? *(Allowed/Not allowed/Not mentioned)* If not mentioned, is cryopreservation of ovarian or testicular tissue practiced by programs in your country? *(Yes/No/Don't know)* Is ovarian or testicular tissue donation possible? *(Comment.)*
18. Is microinsemination (e.g., ICSI) allowed under the statute? *(Allowed/Not allowed/Not mentioned) (Comment.)*
19. Are other types of micromanipulation (for cloning see 20), e.g., cytoplasmic transfer, allowed under the statute? *(Allowed/Not allowed/Not mentioned) (Comment.)*
20. Is reproductive cloning allowed under the statute? *(Allowed/Not allowed/Not mentioned) (Comment.)* Is therapeutic cloning allowed under the statute? *(Allowed/Not allowed/Not mentioned) (Comment.)*
21. Is assisted hatching allowed under the statute? *(Allowed/Not allowed/Not mentioned)* If not prohibited in your country, is assisted hatching used in some programs in your country? *(Yes/No/Don't know) (Comment.)*
22. Is preimplantation genetic diagnosis (PGD) allowed under your statute? *(Allowed/Not allowed/Not mentioned)* If not prohibited in your country, is preimplantation diagnosis used by some programs in your country? *(Yes/No/Don't know) (Comment.)*
23. Is preimplantation genetic diagnosis (PGD) allowed for embryo screening? *(Allowed/Not allowed/Not mentioned)* If not prohibited, is PGD for embryo screening used in your country? *(Used/Not used/Don't know) (Comment.)*
24. Is IVF surrogacy, i.e., the use of gametes of both prospective parents when the female partner does not have a functioning uterus, allowed under the statute? *(Allowed/Not allowed/Not mentioned)* If allowed, are there special stipulations, and if so, what are they? If not prohibited, is IVF surrogacy used by some programs in your country? *(Yes/No/Don't know)*
25. Please point out any regulations that seem to be medically naive or even contradictory, or not in the medical best interest of the infertile couple.
26. How could the current regulations be improved?

SECTION II—GUIDELINE IVF ONLY

1. Are there guidelines by a medical society, religious body, or other such entity for the use of ART? *(Yes/No)*If yes, please supply a copy of the guidelines or indicate where one may be obtained. If yes, is any clinical surveillance carried out? *(Yes/No)*If yes, how is this done? *(Circle correct answer.)* [a] Periodic report, [b] On-site inspection, [c] Other. If other, please describe. If yes, what body carries out the clinical surveillance? If yes, is any embryological surveillance carried out? *(Yes/No)*If yes, how is this done? *(Circle correct answer.)* [a] Periodic report, [b] On-site inspection, [c] Other. If other, please describe. If yes, what body carries out the embryological surveillance? If you are reporting for a guideline country, complete the additional questions in Section II to which the guidelines apply.
2. Are the techniques of ART covered or reimbursed by *(circle either a, b or c)*? [a] A national health plan, [b] Private insurance, [c] No coverage.
3. The guidelines specify that the couple for IVF must have *(circle correct answer)*: [a] A marriage, [b] A stable relationship, [c] No requirement, [d] ART in single women is permitted, [e] ART in lesbian couples is permitted. *(Comment.)*
4. The guidelines specify the number of preembryos that can be transferred (replaced). *(Yes/No)*If yes, how many and are there any exceptions?
5. Is selective reduction approved by the guidelines? *(Yes/No/Not mentioned)* If not prohibited (or if it is), is selective reduction practiced by programs in your country? *(Yes/No/Don't know)*
6. Do the IVF guidelines allow donor sperm to be used in IVF? *(Yes/No/Not mentioned)* If yes, are there any specific requirements?
7. Does any law or guideline (other than the IVF guidelines) speak to the use of donor sperm in non-IVF infertility? *(Yes/No)*If yes, are there any requirements? If no, are donor sperm used for non-IVF infertility? *(Yes/No/Don't know) (Comment.)*
8. Is posthumous insemination allowed? *(Allowed/Not allowed/Not mentioned)* If not prohibited, is posthumous insemination used? *(Used/Not used/Don't know) (Comment.)*
9. Do the guidelines allow donor eggs to be used in IVF? *(Yes/No/Not mentioned)* If yes, are there any special requirements?
10. Do the guidelines allow the offspring to be provided on request with non-identifying information about the donor? *(Allow/Not allowed/Not mentioned) (Comment.)*
11. Do the guidelines allow the offspring to be provided on request with identifying information about the donor? *(Allow/Not allowed/Not mentioned) (Comment.)*
12. Do the guidelines impose on the IVF program any admonition about the welfare of any resulting offspring? *(Yes/Not mentioned) (Comment.)*

13. Under the guidelines, is cryopreservation of fertilized eggs (prezygotes to blastocysts) permitted? *(Yes/No/Not mentioned)* Are there any special requirements?
14. If cryopreservation of fertilized eggs (prezygotes to blastocysts) is permitted, is there a limit to the duration of storage? *(Yes/No)*If yes, how long? *(Comment.)*
15. Under the guidelines is cryopreservation of oocytes allowed? *(Yes/No/Not mentioned)* If not mentioned is oocyte cryopreservation practiced by programs in your country? *(Yes/No/Don't know) (Comment.)*
16. Is oocyte maturation allowed under the guidelines? *(Yes/No/Not mentioned)* If not mentioned, is oocyte maturation practiced by programs in your country? *(Yes/No/Don't know) (Comment.)*
17. Under the guidelines is cryopreservation of ovarian or testicular tissues (as in patients to be treated for malignancy) allowed? *(Allowed/Not allowed/Not mentioned)* If not mentioned, is cryopreservation of ovarian or testicular tissue practiced by programs in your country? *(Yes/No/Don't know) (Comment.)*
18. Is microinsemination (e.g., ICSI) allowed under the guidelines? *(Allowed/Not allowed/Not mentioned) (Comment.)*
19. Are other types of micromanipulation (for cloning see 20), e.g., cytoplasmic transfer, allowed under the guidelines? *(Allowed/Not allowed/Not mentioned) (Comment.)*
20. Is reproductive cloning allowed under the guidelines? *(Allowed/Not allowed/Not mentioned) (Comment.)* Is therapeutic cloning allowed under the guidelines ? *(Allowed/Not allowed/Not mentioned) (Comment.)*
21. Is assisted hatching allowed under the guidelines? *(Allowed/Not allowed/Not mentioned)* If not prohibited under the guidelines, is assisted hatching used in at least some programs in your country? *(Yes/No/Don't know) (Comment.)*
22. Is preimplantation genetic diagnosis allowed under your guidelines? *(Allowed/Not allowed/Not mentioned)* If not prohibited under the guidelines, is preimplantation diagnosis used in at least some programs? *(Yes/No/Don't know) (Comment.)*
23. Is preimplantation genetic diagnosis (PGD) allowed for embryo screening? *(Allowed/Not allowed/Not mentioned)* If not prohibited is PGD for embryo screening used in your country? *(Used/Not used/Don't know) (Comment.)*
24. Is IVF surrogacy, i.e., the use of gametes of both perspective parents where the female partner does not have a functioning uterus, allowed under the guidelines? *(Allowed/Not allowed/Not mentioned)* If allowed, are there special stipulations, and if so, what are they?
25. Please point out any guidelines which seem to be medically naive, or even contradictory, or not in the medical best interest of the infertile couple.
26. How could the current guidelines be improved?

SECTION III—NO STATUTORY ACT OR GUIDELINES FOR IVF

1. Are there statutes, i.e., law? (national or other political subdivision) or voluntary guidelines governing the use of IVF? *(Yes/No)*If no, complete the additional questions in Section III.
2. Are the techniques of ART covered or reimbursed by *(circle a, b, or c)*? [a] A national health plan, [b] Private insurance, [c] No coverage. If *a* or *b* is the coverage: Complete? Partial? *(Comment.)*
3. Does prevailing custom cause the couple for IVF to have *(circle correct answer)*: [a] A marriage, [b] A stable relationship, [c] Not an issue, [d] ART in single women is permitted, [e] ART in lesbian couples is permitted. *(Comment.)*
4. Does prevailing custom limit the number of preembryos which are transferred (replaced)? *(Yes/No)*If yes, how many and are there any exceptions? If no, please estimate the maximum number of preembryos which might be transferred.
5. Is selective reduction generally practiced? *(Yes/No/Don't know)*
6. Are donor sperm used in IVF? *(Yes/No)*If yes, are there any specific circumstances?
7. Does any law speak to the use of donor sperm in non-IVF infertility? *(Yes/No)*If yes, are there any requirements? If no, are donor sperm used for non-IVF infertility? *(Yes/No) (Comment.)*
8. Is posthumous insemination used? *(Used/Not used/Don't know)*
9. Are donor eggs used in IVF? *(Yes/No)*If yes, are there any special circumstances?
10. If donor gametes are used is it customary for the offspring to be provided with non-identifying information about the donor? *(Customary/Not customary/Varies/Don't know) (Comment.)*
11. If donor gametes are used is it customary for the offspring to be provided with identifying information about the donor? *(Customary/Not customary/Varies/Don't know) (Comment.)*
12. Does custom impose on the IVF program any consideration for the welfare of any resulting offspring? *(Yes/No) (Comment.)*
13. Is cryopreservation of fertilized eggs (prezygotes to blastocysts) used? *(Yes/No)*Are there any special requirements?
14. If cryopreservation of fertilized eggs (prezygotes to blastocysts) is used, is there a consensus as to the duration of storage observed? *(Yes/No)*If yes, how long? *(Comment.)*
15. Is cryopreservation of oocytes used? *(Yes/No/Don't know) (Comment.)*
16. Is oocyte maturation used? *(Used/Never used/Don't know) (Comment.)*
17. Is cryopreservation of ovarian tissue (as in patients to be treated for malignancy) used? *(Yes/No/Don't know) (Comment.)*
18. Is microinsemination (e.g., ICSI) used? *(Yes/No) (Comment.)*
19. Are other types of micromanipulation (for cloning see 20), e.g., cytoplasmic transfer, used? *(Used/Not used/Don't know) (Comment.)*
20. Is reproductive cloning used? *(Used/Not used/Don't know) (Comment.)* Is therapeutic cloning used ? *(Used/Not used/Don't know) (Comment.)*

21. Is assisted hatching used? *(Yes/No) (Comment.)*
22. Is preimplantation genetic diagnosis used? *(Yes/No) (Comment.)*
23. Is preimplantation genetic diagnosis used for embryo screening? *(Used/Not used/Don't know)*
24. Is IVF surrogacy, i.e., the use of gametes of both prospective parents where the female partner does not have a functioning uterus, used? *(Yes/No) (Comment.)*
25. Which of the following best describes your opinion about statutory or voluntary guidelines for your country? Prefer as is; prefer statutory regulations; or prefer voluntary guidelines. *(Comment.)*

SECTION IV—GIFT

In some countries, GIFT is not included under the umbrella of regulations/guidelines covering IVF. It has been excluded on the theory that with GIFT, fertilization is not extracorporal and, therefore, should be carried out under different regulations/guidelines. The purpose of Section IV is to document the extent of this concept.

1. For your country, do the statues/guidelines/or practice customs recognize a difference between IVF and GIFT? *(Yes/No) (Comment.)*
2. Where differences exist, GIFT is generally not included under the IVF umbrella of statues/guidelines/or practice customs. Is that true for your country? *(True/False/Not applicable) (Comment.)*
3. Is there a limit by statute/guidelines/or practice customs as to the number of oocytes that are to be transferred in a GIFT procedure? *(Yes/No)*If yes, how many? Any exceptions?

SECTION V—THE MORAL STATUS OF THE CONCEPTUS AFTER FERTILIZATION

1. For your country, by statute/guideline/cultural practice/or recognized and prevailing religious decree, is there a recognized time during human development after which a human person is considered to exist? *(Yes/No)*What is this recognized time? If yes, is this time determined by: Law? Guideline? Cultural practice? Recognized and prevailing religious decree? *(Comment.)*
2. For your country, by statute/guideline/cultural consensus/or recognized and prevailing religious decree, is there a recognized time during human development *before* which a human person is considered *not* to exist? *(Yes/No)*If yes, when is it? If yes, is this time determined by: Law? Guideline? Cultural practice? Recognized and prevailing religious decree? *(Comment.)*

SECTION VI—EXPERIMENTATION ON THE PREEMBRYO

The preembryo can be defined as the interval of development after fertilization until the appearance of a single primitive streak, i.e., at approximately 14 days. Experimentation can be defined as any procedure that results in the destruction of the preembryo, as for example, in stem cell research.

1. For your country, by statute/guideline/cultural consensus/or recognized prevailing religious decree, is the use of human preembryos for experimental purposes an acceptable procedure? *(Yes/No)*
2. Is the yes or no by virtue of: Law? Guidelines? Cultural practice? Recognized and prevailing religious decree? Please list specifics, if any.
3. If yes, is special specific approval of the research proposal required, and, if so, by what body?
4. If your country defines for experiments on the developing conceptus, a developmental age other than the 14 days specified above after which experiments cannot be done, please indicate the number of days used in your country. *X* number of developmental days used in my country.
5. In your country is cloning possible? Reproductive cloning: Yes/No/With restrictions. Therapeutic cloning: Yes/No/With restrictions.
6. In your country is research on stem cells possible? Embryonic stem cell: Yes/No/With restrictions. Fetal stem cell: Yes/No/With restrictions. Adult stem cell: Yes/No/With restrictions.
7. In your country is gene therapy research possible? *(Yes/No)*