

OPINION

Regulatory approaches to reproductive genetic testing

Bartha M.Knoppers^{1,2} and Rosario M.Isasi¹

¹Centre de Recherche en Droit Public (CRDP), Faculté de Droit, Université de Montréal, CP 6128 succ., Centre-ville, Montreal, Quebec, Canada H3C3J7

²To whom correspondence should be addressed. E-mail: knoppers@DROIT.UMontreal.CA

This report analyses the ethical and legal aspects of reproductive genetic testing in 11 countries (Australia, Austria, Canada, France, Germany, India, Israel, Japan, The Netherlands, Switzerland and the UK). The legal status of reproductive genetic testing in the countries under analysis is difficult to generalize due to the different regulatory systems adopted. These approaches are a reflection of the legal traditions and cultural and socio-religious beliefs which inform and shape public policy on assisted reproductive technologies and genetic testing. We divide approaches into two groups: public ordering (legislative, top-down approach) and private ordering (non-legislative, bottom-up approach). Even limiting our analysis to a number of countries that span the range from restrictive to pragmatic approaches, there is remarkable symmetry in both the (i) substantive requirements (i.e. gravity, health indications generally) and (ii) procedural safeguards (i.e. informed consent, counselling, confidentiality, civil status, oversight and accreditation) surrounding reproductive genetic testing. Indeed, irrespective of whether a country adopts a prohibitive or a permissive approach through legislation or self-regulation or a mix of both, the ultimate decision is—and should continue to be—a medical one. Nowhere is this more evident than in the substantive requirements.

Key words: genetic testing/legal and ethical aspects/policy/preimplantation genetic diagnosis/prenatal testing

Introduction

At a time when the initiative to adopt an international convention banning human cloning has stalled and after a decade of attempts, Canada has finally adopted a law on reproductive technologies; reprogenetic testing is inexorably integrating mainstream medicine.

Indeed, even if circumscribed to include only genetic testing for reproductive purposes whether before pregnancy (e.g. carrier or preimplantation testing) or prenatally, it constitutes standard practice in most industrialized countries.

The potential applications of prenatal diagnosis (PND) and especially preimplantation genetic diagnosis (PGD) for non-medical purposes are growing (i.e. sex selection of embryos or fetuses solely for social or cultural reasons). This shows a departure from an exclusive medical use that limited testing of embryos or fetuses for X-linked disorders.

A public ordering approach involves a State-led initiative to frame emerging biotechnologies. Legislative approaches can range from permissive, to administrative oversight, to restrictive, through prohibitive laws. Austria, France, India, Germany, Israel, The Netherlands, Switzerland and the UK, for example, have enacted laws setting conditions on accessibility to PND. Regarding PGD—with great variations in the degree of permissiveness and oversight—France, Canada, South Australia and Victoria (Australia), India,

The Netherlands and the UK allow it; while Austria, Switzerland, Germany and the State of Western Australia prohibit PGD. Even among countries that have adopted statutory requirements with relation to oversight and enforcement mechanisms for PND and PGD, thereby adhering to a public ordering approach, we will see that there are significant differences.

Other countries have opted for a private ordering approach through self-regulation, thus permitting these technologies under strict professional guidelines. The regulation of PND in Australia and Japan are examples of a private ordering approach since these countries have professional guidelines. Professional guidelines have also been adopted by Israel, Japan and the UK, but the latter mix private–public ordering approaches in the case of PGD.

The legal status of reproductive genetic testing in the countries under analysis¹ is difficult to generalize due to the different regulatory systems adopted. These approaches are a reflection of the legal traditions and cultural and socio-religious beliefs which inform and shape public policy on assisted reproductive technologies and genetic testing. We divide approaches into two groups: public ordering (legislative, top-down approach) and private ordering

¹Australia, Austria, Canada, France, Germany, India, Israel, Japan, The Netherlands, Switzerland and the UK.

(non-legislative, bottom-up approach) (Knoppers and Le Bris, 1994)². Limiting our analysis then to a number of countries that span the range from restrictive to pragmatic approaches, there is remarkable symmetry in both the substantive requirements and procedural safeguards surrounding reproductive genetic testing. Indeed, irrespective of whether a country adopts a prohibitive or a permissive approach through legislation or self-regulation or a mix of both, the ultimate decision is—and should continue to be—a medical one. Nowhere is this more evident than in the substantive requirements.

Substantive requirements for PND and PGD

Two broad categories serve to regroup the substantive criteria as medically determined, the first being that of gravity and the second that of health indications generally.

Gravity

The ultimate aim of PND and PGD is to give prospective parents the ‘opportunity’ of giving birth to a healthy child. Nevertheless, there is a fundamental difference between the two procedures.

PND is a diagnostic or pre-symptomatic test carried out on a developing fetus. After PND is carried out, if the fetus is found to be affected by a genetic condition, both parents (or the mother) have the alternative to either (in jurisdictions where abortion is permitted) terminate the pregnancy (for medical reasons) or continue with the pregnancy and prepare for the future knowing that the child will be born with a genetic condition. In turn, PGD offers the alternative of screening early embryos *in vitro* after IVF but before implantation so that an unaffected embryo can be selected and implanted. In short, PGD avoids the need to terminate a pregnancy when a genetic condition is found in the fetus since it involves an *in vitro* embryo.

The requirement that the nature of the genetic condition to be tested or screened be ‘grave’, i.e. ‘serious’ or ‘severe’, is found at all levels, from carrier testing to PND and PGD. There are, however, a variety of qualifiers that serve to distinguish the approaches taken by different countries with regard to ‘gravity’ when regulating these technologies. Those qualifiers require that the ‘risk’ of the embryo or fetus being affected by a genetic condition be either: (i) substantial; (ii) serious or severe/grave; or (iii) untreatable and/or incurable.

Substantial risk

This first qualifier of ‘substantial risk’ has to do not with the gravity or seriousness of the genetic condition, but rather with the probability of its realization. The language used in countries that have adopted this requirement is illustrative. While the UK requires ‘a *substantial risk* that the foetus would suffer from such abnormality (...)’ (United Kingdom, 1990), Australia (National Health and Medical Research Council, 2000) and Canada (Canadian Fertility and Andrology Society and Society of Obstetricians and Gynaecologists

of Canada, 1999) maintain that in the case of PND, the ‘foetus (be) at *increased risk* of having a particular disorder’. Switzerland adopts a *well-founded fear* criterion (Swiss Academy of Medical Sciences, 1993).

Countries permitting PGD such as France (France, 1994), State of South Australia (South Australia, 1988), Victoria (Australia, 2002), India (India, 2003), The Netherlands (The Netherlands, 2001), the UK (United Kingdom, 1990), Israel³, Canada (Canada, 2004) and Japan (Japan Society for Human Genetics, 2001) have adopted this additional level of scrutiny as well by using expressions such as ‘*greatly increased risk*’ (France, 1994) or ‘*increased probability*’ (Canada, 2004) or just require ‘*a risk*’ (The Netherlands, 2001; Australia, 2002) with no further justification. The degree or probability of risk has not been defined further in any jurisdiction under study. Nevertheless, it constitutes the first socio-political (if not moral) filter affecting admissibility, the most obvious one being the gravity of the condition under question.

Serious or severe/grave

This is the most commonly adopted criterion. In the case of carrier testing, it is attached to ‘chromosomal conditions’ (Human Fertilisation and Embryology Authority, 2001; Japan Society for Human Genetics, 2001; India, 2003) and ‘single-gene disorders’ (Human Fertilisation and Embryology Authority, 2001; Japan Society for Human Genetics, 2001; Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists and Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada, 2001)^{4,5}.

For PND, this indication requires that the embryo or fetus must be ‘affected by an affection of *particular gravity*’ (France, 1994), or ‘the danger of transmission of a *serious disease* that cannot be averted in any other way’ (Swiss Academy of Medical Sciences, 1993), or ‘the fetus is predicted to contract a *severe disease*’ (Japan Society for Human Genetics, 2001), or suffer from ‘Duchenne-type muscular dystrophy or *similarly severe* sex-linked genetic disease’ (Germany, 2001) or, finally, that the fetus be ‘*seriously handicapped*’⁶. Japanese guidelines provide an additional example of the use of this qualifier when they state: ‘invasive prenatal diagnosis should be considered when (...) the fetus is predicted to contract a *severe disease*’ (Japan Society for Human Genetics, 2001).

³See, Israel, ‘Genetic Information Law No. 5761’ (2000), ‘Surrogacy Agreements Law No. 5756’ (1996), ‘National Health Regulations on IVF’ (1987), ‘Rules as to the Administration of a Sperm Bank’ (1992) and Guidelines for Performing Artificial Insemination (1992).

⁴Indian Council for Medical Research (ICMR), ‘Statement of Specific Principles on Human Genetics Research’ (2000) and India, the Pre-natal Diagnostic Techniques, Regulation and Prevention of Misuse, of 1998 (amended 2003).

⁵Australian Medical Association, ‘Human Genetics Issues’ (2000): ‘Genetic Testing of pre-implantation embryos or of a foetus should be restricted to fatal or seriously and permanently disabling disease’.

⁶See, United Kingdom, Human Fertilisation and Embryology Authority and Advisory Committee on Genetic Testing, ‘Consultation Document on PGD’ (2000) and South Australia Reproductive Act, ‘An Act to regulate the use of reproductive technology and research involving experimentation with human reproductive material’ (1988).

²See in general, <http://www.humgen.umontreal.ca/> for a comprehensive international database on legal, social and ethical policy statements related to human genetics.

In almost all jurisdictions that allow PGD, the practice is still considered experimental, due to ongoing scientific uncertainty. There is also hesitation to adopt this technique because of its eugenic potential. PGD is thereby subject to restrictions that limit its application to serious disorders or conditions (France, 1994; Canadian Fertility and Andrology Society and Society of Obstetricians and Gynaecologists of Canada, 1999; Japan Society for Human Genetics 2001; The Netherlands, 2001). This much abused term evokes an intent to improve or eliminate the influence of certain presumed genetic characteristics. While often used for political expediency in the public debate, it properly remains limited to state programmes (e.g. Nazism) and has no value or place in the complex choices facing couples and their physicians.

The aforesaid restriction of ‘severity’ (Australian Medical Association, 2000)⁵ with some subtle differences, is virtually universally accepted by the scientific community. French legislation represents a clear example, where PGD is restricted ‘to couples found to be at greatly increased risk of having a child with a *severe* genetic disease’ (France, 1994). While the French legislation does not contain a list of indications, it clearly limits its permissibility to cases where ‘relevant hereditary predispositions have previously been demonstrated to exist in the parents (or in one parent) and only with the purpose of avoiding a severe genetic pathology’ (*authors’ translation*).

The Netherlands endorses the same principle, by restricting PGD to the diagnosis of ‘*severe* and untreatable genetic conditions’ (The Netherlands, 2001). In this way, The Netherlands as well as France (France, 1994), Japan (Japan Society for Human Genetics 2001)⁷, the UK (Human Genetics Commission, 2001) and Australia (Australian Medical Association, 2000)⁵ aim that PGD be used to achieve the birth of a healthy child.

It should be mentioned that at the regional level, article 14 of the 1997 European Convention on Human Rights and Biomedicine endorses the same principle by prescribing that ‘the use of techniques of medically assisted procreation shall not be allowed for the purpose of choosing a future child’s sex, except where a *serious* hereditary sex-related disease is to be avoided.’

Untreatable/incurable

Standards set in The Netherlands’ regulations, as mentioned above, as well as in Australia are examples of the use of this further qualifier. The Australian Medical Association (2000)⁵ in their recommendations on genetic testing for PGD and

⁷In Japan, professional guidelines recommend PGD in cases where both parents are carriers of ‘severe’ autosomal dominant or recessive, X-linked disease. Japan Society of Human Genetics, Guidelines for Genetic Testing (2001).

⁸France, Law No. 94-654, governing the donation and use of elements and products of the human body, medically assisted reproduction, and prenatal diagnosis (29 July 1994): ‘A physician practicing in a pluridisciplinary Antenatal Diagnosis Centre (...) must certify that, because of the couples family circumstances, there is a strong probability that the unborn child will be affected by a particular severe disorder, known to be incurable at the time of diagnosis’; article L2131-4 (*author’s translation*).

PND require that the disease affecting the embryo or fetus be ‘*permanent*’.

In Switzerland (Switzerland, 1998a,b), PND and PGD for sex selection of embryos and fetuses is allowed only to prevent the risk of transmission of serious and *incurable* disease to the descendants. The same terminology has been adopted by France (France, 1994)⁸ for cases of late abortion following PND⁹ (‘*incurable* at the time of diagnosis’) and for PGD^{1,2}. This is also the standard in Australia (Australian Medical Association, 2000)⁵. This last substantive criterion, if strictly applied, could totally close down access. Modern technology and improved social security and care for the disabled make untreatable or incurable extremely elastic terms that go well beyond personal or medical judgement to questions of socio-economic infrastructure in a given society.

Health purposes

This criterion refers to the purpose of a genetic test and includes countries that adopt a list of indications or general health conditions under which genetic testing can be performed for PND and PGD. This category can in turn be subdivided according to the following procedures: (i) predictive/susceptibility testing; (ii) carrier testing; (iii) genetic screening of pregnant women; (iv) fetal health; (v) embryo health; and (vi) general health conditions.

Predictive/susceptibility testing

Austria (Austria, 1994), Switzerland (Swiss Academy of Medical Sciences, 1993)¹⁰ and India (Government of India, Department of Biotechnology, 2001)¹¹ specify that genetic testing generally may be carried out where it is at the request of a medical geneticist and for the ‘verification of a *predisposition* to a late onset disorder or for carrier status’ without further justification. No country mentions ‘susceptibility’. The other countries under study do not specifically address or limit predictive genetic testing. This is the one category where there is a pressing need for public debate and information considering that the detection of genetic risk factors in common diseases is expanding exponentially.

⁹France’s Code of Public Health allows late abortion when there is a ‘high probability for the child to be affected by a particularly serious disease considered incurable at the time of the diagnosis’, art. L 2213-1.

¹⁰Swiss Academy of Medical Sciences, Medical–Ethical Guidelines for Genetic Investigations in Humans (1993): ‘Medical indications for genetic investigations (genetic tests) are ethically justified if they serve the following purposes (...) determination of a predisposition for an hereditary disease or handicap, with a view to appropriate planning for the life of the individual, and family planning’, Section 2.

¹¹Government of India, Department of Biotechnology, ‘Ethical Policies on the Human Genome, Genetic Research and Services’ (2001): ‘When genetic testing of an individual reveals that he/she has a predisposition to suffer disease or disability in the future, then the tested individual shall have the right exercised by freedom of choice whether to be informed of the result of the testing’, Section 2.

Carrier testing

For genetic testing for carrier status generally, the UK (Human Fertilisation and Embryology Authority, 2001) HFEA's Code of Practice requires—as a minimum standard—that centres performing genetic testing limit their determination of *carrier status* to inherited recessive disorders. Regulations in Japan (Japan Society for Human Genetics, 1996, 2001)¹² and Israel¹³ are also examples of the use of this criterion (i.e. Tay–Sachs carrier testing offered prior to reproduction in Israel). Regarding carrier testing during PND, Canadian (Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists and Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada, 2001) guidelines recommend it 'for individuals belonging to population groups known to have an increased risk for carrying certain genetic disorders'. Little is known of the legal status or use of carrier screening in the other countries under study. Realistically, even if limited to known conditions prevalent in a society or subpopulation (i.e. ethnic grounds), such screening would have to occur in minors in order to afford reproductive choice. This fact clashes with notions of parental authority, personal autonomy and the legal capacity of minors, to say nothing of their understanding the 'odds' involved.

Genetic screening of pregnant women

On the subject of genetic screening of pregnant women, Australia's guidelines (Royal Australian and New Zealand College of Obstetricians and Gynaecologists, 2001) treats PND as a population screening test, i.e. maternal serum screening is offered to all pregnant woman to determine if their fetus is at increase risk of suffering from certain chromosomal conditions (i.e. Down's syndrome) or genetic disorders (i.e. spina bifida). It is also present in the countries under study through generally available ultrasound screening for advanced maternal age and fetal malformations.

Germany (Germany, 2001) considers PND as part of standard antenatal care for the identification of a variety of risks in all pregnant woman. In turn, Japanese guidelines suggest recommending PND¹⁴ or PGD (Japan Society for Human

Genetics, 2001)¹² 'if either one of the parents is a carrier of a chromosomal abnormality, severe autosomal dominant disease or recessive disease, or the mother is a carrier of a severe X-linked disease'. Ironically, because of its close relationship to hard-won abortion rights for women, 'offering' PND for an increasing number of conditions as part of standard prenatal care has generally escaped public scrutiny.

Fetal health

German (Germany, 1990) law determines that doctors carrying out PND should take into account the life interest of both the fetus and the expectant mother. The same principle is present in Indian⁴ policy which mandates that PND 'should be performed only for reasons relevant to the health of the fetus or of the mother'. Furthermore, Australian (National Health and Medical Research Council, 1992) guidelines consider it 'ethical to carry out research on the fetus *in utero*' when 'consistent with the promotion of life or health of the fetus'. It is interesting to note that the 1989 United Nations' International Convention on the Rights of the Child indirectly protects the future health of the child (albeit, the latter being undefined), when it mandates 'ensuring appropriate pre-natal and post-natal health care for mothers' under article 24 (d).

It should be noted that Israel's Genetic Information Law³ prescribes that communication of genetic information could be transmitted to third parties if it is 'required for the maintenance of the health of a relative or to improve such person's health, and for the prevention of death, illness or serious disability of such relative, including an *unborn* relative.' This duty to warn even unborn family members is unique.

Embryo health

An illustrative example of this 'health' criterion is found in Germany (Germany, 1990) which mandates the preservation of the life of the embryo (broadly defined). Western Australia (Western Australia, 1996) mandates that diagnostic genetic tests would be granted approval 'if they are intended to be therapeutic and current scientific and medical knowledge demonstrate to be unlikely to harm the embryo.' Moreover, Australian (Royal Australian and New Zealand College of Obstetricians and Gynaecologists, 2001) guidelines recommend that 'embryo experimentation should normally be limited to therapeutic procedures which leave the embryo (...) with an expectation of implantation and development'.

In turn, the fundamental principle of French law, as explained by the National Ethics Advisory Committee (2002) 'is that) any action or medical process affecting an embryo, which is to be reimplanted, must have as its primary aim the welfare of the embryo itself and be of direct benefit to the future child' (*authors' translation*). The 1989 Convention on the Rights of the Child did not address the issue of research involving either the embryo or the fetus.

¹²Japan Society of Human Genetics, 'Guidelines for genetic testing', (2001): 'Pre-implantation testing/diagnosis is one of the genetic tests. When (a) either parent is a carrier of chromosomal abnormality, or (b) a carrier of severe autosomal dominant disease, or (c) both parents are carriers of severe autosomal recessive disease, or (d) the mother is a carrier of a severe X-linked disease, and, in addition, (e) does not wish for a genetic abortion.'

¹³For example in Israel under the 'Genetic Information Law' No. 5761 (2000), genetic testing of a minor, ward or incompetent persons can be carried out only to 'clarify the existence of a carrier gene of a disease or handicap which, according to reasonable medical assessment, can be prevented, or the spread of which can be delayed, or the state of the minor, ward or incompetent persons can be improved or advanced', art. 24 (2).

¹⁴See, Japan Society for Human Genetics. Guidelines for Genetic Counselling and Prenatal Diagnosis (1996): 'Invasive prenatal test/diagnosis procedures, such as chorionic villus sampling and amniocentesis, should be considered when the mother wishes to have a test/diagnosis in the following situations: (a) if either one of the parents is a carrier of chromosomal abnormality, (d) if the pregnant woman is heterozygous for a serious X-linked disease, (e) if both of the parents are heterozygous for a serious autosomal recessive disease, (f) if either of the parents is heterozygous for a serious autosomal dominant disease.'

General health conditions

Specific health indications for the permissibility of PND and PGD are not found in most jurisdictions. For example, the general criterion of advanced maternal age is a requirement in India (India, 2003), Japan (Japan Society for Human Genetics, 2001), Canada (Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists and Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada 2001) and Australia's (Royal Australian and New Zealand College of Obstetricians and Gynaecologists, 2001) regulations. Yet, specific indications such as repeat spontaneous abortions are found in India (India, 2003), and a history of birth of children affected with chromosomal abnormalities or previously affected by pregnancies is mentioned in Japan (Japan Society for Human Genetics, 2001) and Australia (Royal Australian and New Zealand College of Obstetricians and Gynaecologists, 2001).

Australia's Medical Research Council policy also highlights the potential of genetic testing to provide 'significant health benefits' (National Health and Medical Research Council, 2000)¹⁵. Swiss (Swiss Academy of Medical Sciences, 1993) guidelines would not permit sex selection of embryos or fetus (prenatally or preimplantation) for factors that do not constitute a threat to 'health.'

The 1997 European Convention on Human Rights and Biomedicine (to which France, The Netherlands and Switzerland are signatories) applies the 'health' limitation to all applications of genetic testing (whether predictive, carrier or susceptibility testing) by maintaining that it be used only for 'health purposes'¹⁶. While ostensibly limiting access to genetic information in health records, or the requiring of genetic tests by insurers and employers, indirectly, this sets a very broad criterion for the acceptability of genetic testing in countries that have ratified the Convention.

In short, whether countries centre their substantive criteria for admissibility and accessibility on carrier, preimplantation or prenatal testing or screening, or on the gravity of the genetic condition, or within general health conditions, none are left unregulated in the countries under study. Irrespective of the approach (gravity or general health) and their translation into either permissive or prohibitive legislation or professional guidelines, the locus of decision making remains within the confines of the physician–patient relationship. For decisions that are as intensely personal as reproduction, this is laudable and necessary for ensuring respect for patient autonomy and privacy. Definitions of what is significant or

serious are best left to those confines, although some general guidance can be provided (Wertz and Knoppers, 2002).

The sum total of individual decisions, however, not only constitutes the effective translation of policy positions but can also subtly and over time affect policy change. The speed or direction of that change depends on the procedural frameworks in which such decisions reside.

Procedural safeguards

Procedural safeguards provide another layer of protection and control of reproductive genetic testing. In reality, such safeguards may have a greater systemic impact than the substantial requirements. They can be subdivided into two broad categories: (i) safeguards related to patients' rights (since genetic testing is also a medical intervention), which include provisions for informed consent, counselling and confidentiality; and (ii) safeguards related to civil status, oversight and licensing mechanisms.

Informed consent, counselling and confidentiality

Patients' rights apply to persons undergoing a genetic test. Following international legal and ethical norms, informed consent is a process required in all jurisdictions under study, as well as safeguards for the protection confidentiality and privacy. Provisions regarding counselling, however, vary greatly from country to country. Nations vary in that some have mandatory pre- and post-counselling requirements, such as Australia (Royal Australian and New Zealand College of Obstetricians and Gynaecologists, 2001; Australia, 2002), Austria (Austria, 1994), France (France, 2004), the UK (Human Fertilisation and Embryology Authority, 2001)¹⁷ and India (Government of India, Department of Biotechnology, 2001)¹⁸, and other

¹⁷The UK's Human Genetics Commission (HGC) in its 'Response to the Human Fertilisation and Embryology Authority on the Consultation on preimplantation genetic diagnosis' (2001), attempts to define the notion of 'seriousness of inherited conditions' as follows: 'Decisions about the seriousness of a condition should be made by the parents in collaboration with clinicians. In this process: disabled people and parents of disabled children should be involved in putting together information for prospective parents about the reality of living with a disability. Information should be clear and accessible. Relevant patient organisations, many coming under the Genetic Interest Group (GIG) umbrella, provide a source of written information and practical support for couples making reproductive decisions. Decisions on the use of PGD should depend on many things, including:

- the clinical burden which is a composite of:
- the parents' view of the condition,
- the likely degree of suffering associated with the condition, the availability of effective therapy or treatment,
- the speed of degeneration in progressive disorders,
- the extent of any intellectual impairment;
- the sensitivity and specificity of the tests in general and in the hands of the local team;
- the individual circumstances of the family or woman, including other siblings.'

¹⁸Government of India, Department of Biotechnology, 'Ethical Policies on the Human Genome, Genetic Research and Services' (2001): 'When genetic testing of an individual reveals that he/she has a predisposition to suffer disease or disability in the future, then the tested individual shall have the right exercised by freedom of choice whether to be informed of the result of the testing', Section 2.

¹⁵Australia, National Health and Medical Research Council (NHMRC), 'Ethical Aspects of Human Genetic Testing: An Information Paper' (2000): Article 2.8 on Equity of access to genetic testing states that 'access to genetic services which have been shown to have potential to provide significant health benefits should not be dependent on where a person lives or on their socio-economic status.'

¹⁶The European Convention on Human Rights and Biomedicine (1997) states that 'tests which are predictive of genetic disease or which serve either to identify the subject as a carrier of a gene responsible for a disease or to detect a genetic predisposition or susceptibility to a disease may be performed only for health purposes or for scientific research linked to health purposes, and subject to appropriate genetic counseling', article 12.

countries require 'offering' the service [i.e. Japan (Japan Society for Human Genetics, 2001), Switzerland (Switzerland, 1998a,b), Israel³ and Canada¹⁹].

Civil status, oversight and accreditation

An additional layer of protection (or limit on access) is achieved through requirements of civil status. Most jurisdictions allow access to heterosexual couples (whether married or in a stable relationship)²⁰. Other countries, such as Canada (Canadian Fertility and Andrology Society and Society of Obstetricians and Gynaecologists of Canada, 1999)^{2,7}, Israel³, The Netherlands (The Netherlands, 2001), Switzerland (Switzerland, 1998a,b) and the UK (United Kingdom, 1990; Human Fertilisation and Embryology Authority, 2001) allow access to single women.

Only a few countries have established sanctions for the violation of regulatory requirements regarding reproductive technologies in general, and genetic testing in particular²¹. Sanctions range from imprisonment to the imposition of fines.

A necessary safeguard is the establishment of oversight agencies and enforcement mechanisms. Probably the best model of effective oversight and licensing is the UK's (United Kingdom, 1990) HFEA. The HFEA is the national regulatory authority in charge of licensing and monitoring clinics that carry out IVF procedures as well as reproductive genetic testing (PGD). Other countries also have statutory licensing and oversight mechanisms, such as Australia (Reproductive Technology Accreditation Committee), France (National Committee for Reproduction and Prenatal Diagnosis Medicine and Biology), The Netherlands (Central Committee for Research) and Israel (under the Ministry of Health). The bill on assisted reproductive technologies recently adopted in Canada foresees the creation of a national oversight and licensing body. This adds another 'barrier' since, in the absence of accreditation, certain technologies will not be offered. There is no doubt that such quality assurance is essential to the potential well being of the couple, the woman and their future children. Delay in implementation or efficiency, however, may constitute a systemic impediment.

Indeed, it goes without saying that even more than civil status or mandatory counselling, the imposition of accreditation through licensing as a condition of operation is the one procedural mechanism with the greatest impact on reproductive genetic testing. Such an oversight mechanism with its traditional requirements of certification, quality assurance, standard operating procedures, reporting procedures and ethics approval of the introduction of technologies or

for research can effectively curtail the availability of reproductive genetic testing. Furthermore, like the physician–patient relationship, the 'culture' of interpretation of a law or of professional guidelines can limit or expand the ambit of individual choices.

While this study has not examined the public–private mix (if any) of facilities available to exercise reproductive options (Gunning and Szoke, 2003), if a law is only applicable to the public sector, the societal impact and, indeed, the societal goals underlying the law can easily be thwarted by untrammelled choice in the private sector (Parens and Knowles, 2003). Similarly, lack of harmonization of consent and privacy standards can foster forum shopping among applicants for testing.

Conclusion

In relation to human reproductive technologies and human genetics, generally, four models of policy development have been adopted in the last two decades. The market model, the human rights approach, self-regulatory mechanisms and, finally, legislation²².

In this analysis of reprogenetic testing, no country under study has adopted the market or laissez-faire approach. The human rights approach with its dependence on the interpretation of basic rights by the courts as a delimitation of these technologies is also not favoured in this particular setting. This latter route is lengthy, expensive and cumbersome (though the written judgements whatever their outcome are usually rich in policy discussion).

All countries studied have a mix of the self-regulatory and legislative-specific approaches. Unitary countries such as, for example, Austria, France, The Netherlands and Israel, rely heavily on legislation as opposed to federal countries (e.g. Canada, Switzerland and Australia). This is more a reflection of internal constitutional possibilities than of greater internal domestic consensus on controversial issues.

Countries that adopted prohibitive legislative approaches in the 1990s such as Austria and Germany require revisiting their statutes in order to accommodate PGD. While forestalling such techniques may have been the original intent, this illustrates both the strength (i.e. certainty) and yet the weakness of the 'genetic-specific' approach (i.e. inability to adapt). Finally, professional guidelines, while flexible, can be fraught with inconsistent interpretations and so create social inequities. Indeed, in the absence of efficient accreditation mechanisms and oversight bodies, they can be quite arbitrary in their interpretation and application.

Even limiting ourselves to the interaction of these models in the countries under study, it is self-evident that the adoption of a restrictive law tends to pre-empt the parallel promotion of professional guidelines. Even if only serving as interpretative tools, the latter are essential to an equitable application of a law. Paradoxically, reliance on professional

¹⁹See, Canadian College of Medical Geneticists, the Canadian Association of Genetic Counsellors, the Canadian Nurses Association, the College of Family Physicians of Canada and the Genetic Committee of the Society of Obstetricians and Gynaecologists of Canada, 'Practice Guidelines for Health Care Providers involved in Prenatal Screening and Diagnosis' (1998) and Canadian Fertility and Andrology Society and Society of Obstetricians and Gynaecologists of Canada. 'Joint Policy Statement, Ethical Issues in Assisted Reproduction.' (1999).

²⁰Australia, Austria, Canada, France, Germany (only married couples), India, Israel, The Netherlands, Switzerland and the UK.

²¹Legislation in Australia, Canada, Germany, India, The Netherlands and UK.

²²See Knoppers BM (2000) Reflections: The Challenge of Biotechnology and Public Policy. 45 McGill L. 559, and Knoppers BM and Le Bris S (1994) Genetic choices: a paradigm for prospective international ethics? Pol Life Sci 13, 228–230.

guidelines alone without accreditation and oversight mechanisms can have the same effect.

While not the subject of this study, it bears noting in closing that the adoption in Italy on December 12, 2003 of the Assisted Reproduction Bill illustrates the *a contrario* argument—a quarter of a century of a permissive, laissez-faire approach can backfire and lead to overly restrictive legislation. Hoping to end its ‘Wild West’ reputation, this law requires that the limit of three IVF-created embryos be implanted immediately without any genetic testing or selection! (Italy, 2004).

What is needed then is a clear understanding of the various roles of these mechanisms. Legislated criminal offences could focus and be limited to morally reprehensible behaviour in a given society but should be used sparingly. Health legislation can provide administrative and oversight approaches that responsibly and systematically integrate technologies into the health care system. Professional guidelines can be an adjunct to the latter or they can stand alone as standards generally accepted in and elaborated by the professionals themselves as science evolves. They do, however, require disciplinary oversight or the public will see them as self-interested and not effective. The latter, by creating a normative standard of professional care, can also create the possibility of legal action (negligence) for failure to respect such an accepted standard.

It is, however, the failure to be public and transparent about the system in place (whatever it be) that constitutes the greatest threat to the exercise of reproductive choice and access to accompanying genetic tests. This is extremely important considering the vulnerability and hopes of those suffering from infertility or genetic conditions.

Acknowledgements

We are grateful to Marie-Hélène Régnier for her research assistance. This paper was commissioned by the Genetics & Public Policy Center at Johns Hopkins University, which is supported by The Pew Charitable Trusts. The opinions expressed are solely those of the authors.

References

- Australia (2002) Victoria Infertility Treatment Act No. 63/1995 (amended 2002).
- Australian Medical Association (2000) Human Genetic Issues.
- Austria (1994) The Gene Technology Law.
- Canada (2004) Act respecting assisted human reproductive technologies and related research.
- Canadian Fertility and Andrology Society and Society of Obstetricians and Gynaecologists of Canada (1999) Joint Policy Statement, Ethical Issues in Assisted Reproduction.
- France (1994) Law No. 94-654 governing the donation and use of elements and products of the human body, medically assisted reproduction, and prenatal diagnosis. Article R2131-7.
- France (2004) Code of Public Health, Art. L 2213-1.
- Germany (2001) Act for the Protection of Embryos (Embryo Protection Act).
- Government of India, Department of Biotechnology (2001) Ethical Policies on the Human Genome, Genetic Research and Services.
- Gunning J and Szoke H (eds) (2003) The Regulation of Assisted Reproductive Technology. Ashgate Publishing Limited, Hampshire, UK.
- Human Fertilisation and Embryology Authority (2001) HFEA Code of Practice, 5th edn.
- Human Genetics Commission (2001) Response to the Human Fertilisation and Embryology Authority on the Consultation on preimplantation genetic diagnosis. UK.
- India (2003) The Pre-natal Diagnostic Techniques, Regulation and Prevention of Misuse, of 1998 (amended 2003).
- Italy (2004) Medical Assisted Procreation Law, No. 40.
- Japan Society for Human Genetics (1996) Guidelines for Genetic Counseling and Prenatal Diagnosis.
- Japan Society for Human Genetics (2001) Guidelines for Genetic Testing.
- Knoppers BM and Le Bris S (1994) Genetic choices: a paradigm for prospective international ethics? *Pol Life Sci* 13,228–230.
- National Ethics Advisory Committee (2002) Reflections Concerning the Extension of Preimplantation Genetic Diagnosis.
- National Health and Medical Research Council (1992) Statement on Human Experimentation Supplementary Notes. Australia.
- National Health and Medical Research Council (2000) Ethical Aspects of Human Genetic Testing: An Informative Paper. Australia.
- Parens, E., Knowles, L (2003) *ReproGenetics and Public Policy: Reflections and Recommendations*. Special Supplement to the Hastings Center Report.
- Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists and Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada (2001) Canadian Guidelines for Prenatal Diagnosis: Genetic Indications for Prenatal Diagnosis.
- Royal Australian and New Zealand College of Obstetricians and Gynaecologists (2001) Prenatal Diagnosis Interim Policy.
- South Australia (1988) South Australia Reproductive Act, an act to regulate the use of reproductive technology and research involving experimentation with human reproductive material.
- Swiss Academy of Medical Sciences (1993) Medical–Ethical Guidelines for Genetic Investigation in Humans.
- Switzerland (1998a) Federal Constitution of the Swiss Confederation (Federal Order of December 1998 on the revision of the Federal Constitution).
- Switzerland (1998b) Federal Law on Medically Assisted Reproduction.
- The Netherlands (2001) Act containing Rules relating to the Use of Gametes and Embryos (The Embryos Act) of 2001.
- United Kingdom (1990) The Human Fertilisation and Embryology Act.
- Wertz D and Knoppers BM (2002) Serious genetic disorders: can or should they be defined? *Am J Med Genet* 108,29–35.
- Western Australia (1996) Human Reproductive Technology Act of 1991 (amended by the Human Reproductive Technology Act of 1996).