BACKGROUND: A new law in Italy imposes strict conditions on assisted reproduction at a time when many other countries have become more accepting of these techniques. The law has been criticized both in and outside of the country because of its excessive concern with the status of embryos and disregard for the interests of women and infertile couples. METHODS: Bioethical, legal and policy analysis based on published materials. RESULTS and CONCLUSIONS: This article shows that ethical concerns about respect for human life and protection of the family and offspring need not burden women and infertile couples to the extent that the new Italian law does. Defining embryos as existing only at syngamy, allowing unpaid sperm and oocyte donation, and permitting the screening of embryos for genetic disease would greatly improve the situation of infertile women in Italy without greatly compromising the values and goals of the Italian law.

Key words: embryonic stem cells/Italy/oocyte donation/preimplantation genetic diagnosis/syngamy

Reducing risks to women while protecting embryos

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a policy imposes on women and children through increased multiples, more failed and repeat cycles, and possible resort to highly experimental and unreliable options such as oocyte freezing. Clarity about the trade-offs, however, may not sway decision-makers committed to upholding a view of the inherent moral status of early embryos. After all, if the embryo is a person or moral subject (the Vatican position), causing its death to save some costs and burdens on women would not be justified.

Despite this apparent impasse, it would be possible to improve the situation of women undergoing IVF in Italy while maintaining respect for embryos by explicitly recognizing that embryos exist only when the two haploid pronuclei merge at syngamy into the new unique genome of the zygote. Occurring ~20h after fertilization, syngamy and gene activation is an important developmental milestone. Syngamy should also be key for persons who believe that the moral duty to protect embryos rests on their possessing a unique genome with the potential to become an adult. Only at syngamy does that new unique genome exist.

Recognition of syngamy and gene activation as the point at which the protection of embryos begins would reduce the need for women to go through repeated stimulation and retrieval cycles and lessen the need to transfer three embryos in every cycle, with its attendant risks of multiple gestation. Such a line would give physicians freedom to create and freeze pre-zygotic fertilized embryos at the pronuclear stage. Multiple oocytes could be retrieved and fertilized, and all but the few to be transferred frozen at the pronuclear stage for later use. If the first cycle failed, remaining pronuclear fertilized embryos could be thawed and after further cleavage transferred to the uterus. If the first transfers had produced a child, then the cryopreserved pronuclear embryos could be used to have another child. (Indeed, the highest success rate for subsequent pregnancy and live-births after cryopreservation occurs with pre-zygotic fertilized embryos.)

The idea of defining an embryo as existing only at syngamy has been adopted in other countries that are highly protective of human embryos. Germany, for example, passed one of Europe’s strictest embryo protection laws in 1990 but made clear at the time that embryos exist only at syngamy. As a result, German doctors are able to hyperstimulate IVF patients, retrieve multiple oocytes, fertilize all that seem viable, and freeze at the pronuclear stage all but the two or three embryos that will be transferred in the fresh cycle. As a result, Germany has reasonably high success rates for IVF (ESHRE, 2001). If the first transfer fails, the frozen pronuclei embryos can be used without requiring the woman to undergo another stimulation and retrieval cycle. It also avoids the contradiction of allowing a multiple gestation to be selectively reduced, say from triplets to twins or singletons, but not allowing pronuclear freezing, which would avoid the need for transfer of the three embryos that increases the risk of the need for selective reduction.

Because defining embryos as existing only at syngamy still provides a robust protection of embryos, such an approach should be as acceptable in Italy as it is in Germany. The Italian law, however, has not defined ‘embryo’, thus suggesting the popular understanding that an embryo exists from fertilization. The Italian law needs to be clarified or amended to identify syngamy and gene activation as the key event so that pre-zygotic fertilized (pronuclear) embryos are not included in its protection of embryos. Italian legislative and regulatory authorities, in consultation with the national medical association and national bioethics committee, will have to decide how best to accomplish this goal. Such a clarification would go a long way to improving the lot of infertile women while still maintaining strong protection of embryos.

Permitting unpaid oocyte donation

The Italian law also bans the use of donor gametes at a time when many other countries have accepted the use of sperm or even oocyte donation to overcome a couple’s infertility. A ban on the use of donor gametes hurts women (as well as their partners) in several ways. An infertile couple with male factor infertility will not be able to have a child through donor sperm, even though the woman is fertile and the husband consents. Where infertility is due to absent or insufficient ovarian function, barring the use of donor oocytes prevents a woman from gestating an embryo created with her partner’s sperm.

Why the resistance in Italy to sperm and oocyte donation to married/stable heterosexual couples when many other countries permit at least the use of donor sperm? One explanation no doubt is the strong opposition of the Vatican to gamete donation because of the fear that third party provision of oocyte or sperm will weaken family bonds and confuse the heritage of children. There is no evidence, however, that the use of donor gametes has led to dysfunctional families or confused offspring in the thousands of cases in Europe and the United States in which gamete donation has been used.

A second explanation is the fear that acceptance of gamete donation will lead to large-scale commercialization of the donor process. Although commercialization could arise with both sperm and oocyte donors, the greatest concern is that it will lead to women undergoing hyperstimulation and oocyte retrieval solely for money. The American approach of paying oocyte donors, however, assumes that few unrelated women will have an incentive to undergo an IVF cycle solely to donate oocytes unless they are compensated for the burdens and risks that they incur (Ethics Committee, American Society of Reproductive Medicine, 2000). Indeed, some persons argue that it is exploitative and unfair not to compensate donors for their services. Critics, on the other hand, point to the commodification of human oocytes that has increasingly crept into American oocyte donation practices. In any event, resort to oocyte donation is a rapidly growing practice in the United States. With over 6600 transfer cycles in 2000 and over 2900 children born, it has helped women with premature ovarian failure and those over 40 to gestate and rear children conceived with their partner’s sperm (Society for Assisted Reproduction, 2004).

But if other countries that now ban oocyte donation do so because of fear of a commercial market, they could still ban payments while allowing those women who have a family
member or friend willing to donate to do so. Both unpaid sperm and oocyte donation should be permitted to assist infertile couples. Indeed, the United Kingdom, which is quite permissive on many aspects of assisted reproduction, allows both oocyte and sperm donation but no payments beyond expenses necessary to the donation. If Italy and Germany, which also bans oocyte but not sperm donation) had due regard for the interests of infertile couples, including older women who have pursued careers or have new mates, they should allow oocyte and sperm donation as long as it remains unpaid.

In countries where unpaid oocyte donation is permitted, additional ways to facilitate oocyte donation while avoiding commercialization exist. One alternative would be to permit oocyte sharing between a woman in need of IVF who lacks the funds to pay for it and a woman in need of donor oocytes who can pay the cost of an IVF cycle. There is now considerable experience with oocyte sharing practices in the United States, and policies have been devised in the United Kingdom to make sure that oocyte sharing does not cloak a commercial transaction (Human Fertilisation and Embryology Authority, 2004). A country interested in meeting the needs of women but also avoiding the excesses of commercialization might fruitfully consider oocyte sharing programs as they exist in Britain.

Preimplantation genetic diagnosis

The Italian law is also burdensome to fertile couples who are at risk for transmitting severe autosomal or X-linked genetic diseases to their offspring. Although they may engage in prenatal diagnosis and terminate fetuses that test positive for those diseases, such couples are not permitted to use preimplantation genetic diagnosis (PGD) to screen out embryos for this purpose. Embryo biopsy itself is not illegal, but all biopsied embryos, including those that are positive for the disease, must be transferred to the uterus. In addition, fertile couples who are at risk for genetic disease do not meet the law’s requirement that the assisted reproduction necessary for PGD be provided only to infertile couples.

As a result, couples at risk for having offspring with severe genetic disease must either forego having children or take the 25% or 50% risk that the child will be born with the disease. Alternatively, they may coitally conceive, undergo prenatal diagnosis, and terminate those pregnancies that are positive for the disease. The new law thus protects embryos from discard prior to transfer, while allowing them to be aborted at a later stage of fetal development.

The ban on IVF for fertile couples and the requirement that all embryos be transferred to the uterus also means that families with children with Fanconi anemia or other blood disorders—and Italy has a high rate of thalassemias—will be barred from using PGD to try to have a child without inherited disease who could serve as an umbilical cord blood donor of hematopoietic stem cells for an existing child. In the United States, United Kingdom, and Norway it is now acceptable for couples with children with those diseases to undergo IVF and PGD to make sure that the embryos transferred to the uterus are free of the disease and a good HLA match for a successful umbilical cord blood donation from that new child. For families with a sick child, PGD for HLA matching provides a needed alternative to watching their child deteriorate and die because a suitably matched HLA donor is not available. PGD could be permitted for this purpose without also allowing PGD for sex selection or the other non-medical uses that have made it so controversial (Robertson, 2003).

Embryonic stem cell research and therapy

A similar dilemma would arise if cell replacement therapies derived from embryonic stem (ES) cells prove to be safe and effective. The ability to culture human ES cells in the laboratory has opened the door to promising research to treat a range of chronic diseases. An ES cell treatment for spinal cord injuries is close to clinical trials in humans, and trials for diabetes and heart disease are expected in the next 3–5 years.

Because Italy requires that all embryos be transferred to the uterus and prohibits embryo freezing and embryo research, couples going through IVF may not donate embryos to ES cell researchers, as now occurs in the United Kingdom, Israel, Singapore, Belgium, India and the United States. As a result, Italian scientists are not permitted to derive ES cells from preimplantation human embryos for research or therapy.

Still unresolved is whether it would be lawful to conduct ES cell research or therapy in Italy with ES cells derived outside of Italy. Because ES cells are not themselves embryos, the new law should not be a direct barrier, but official recognition that ES cells derived outside of Italy may be used in Italy may be needed to encourage Italian scientists to undertake such work.

If Italy takes the position that research or therapy in Italy with ES cells derived outside of Italy is not permissible, this will hurt Italian stem cell science and have a devastating impact on the thousands of Italian citizens who could benefit from ES cell therapies developed in the future. Italy could still protect embryos by banning derivation of ES cells in Italy, while permitting Italian researchers and sick patients to have access in Italy to ES cell lines and therapies created outside of Italy, as has occurred in Germany (Robertson, 2004).

Reproductive tourism is a poor solution

The new Italian law applies to actions done on Italian soil but does not penalize Italians who obtain banned assisted reproductive procedures outside of Italy. Indeed, although the law penalizes individuals who publicize locations abroad where gamete donation is available, it recognizes that if gamete donation is obtained outside of Italy resulting children born in Italy are the children of the infertile couple and not that of the gamete donor.

Legal acceptance of reproductive tourism will enable some Italians to soften the harsh impact of the law by obtaining those services abroad. A thriving industry catering to the needs of Italian patients no doubt will develop, with Italian
fertility doctors setting up clinics just across the border in Croatia and internet sites informing patients of assisted reproductive opportunities in neighboring countries (Arie, 2004).

Reproductive tourism as a solution, however, is grossly unfair because it enables only those with funds to escape the law’s strictures. Those who are able to travel to obtain services must also bear the additional burdens of being away from home for substantial periods, making the already psychologically fraught and stressful situation of infertility all the more difficult.

**Conclusion**

Countries, like individuals, differ in their perception of the worth of embryos, the nature of family, burdens on infertile couples, and the other values at stake in assisted reproduction. While each country is free to take the position that best reflects its cultural traditions and social needs, there may be better or worse ways to protect its values and achieve the goals that it seeks.

The Italian law shows that a country might choose to be highly protective of embryos while minimizing the burdens on women by making clear, as Germany has done, that prezygotic fertilized embryos are not protected by the law. It could also allow unpaid gamete donation, including oocyte donations from family members and women with extra oocytes, without encouraging a commercial system of gamete donation. Given that Italy already allows abortion for any reason, including serious genetic disease, it should allow fertile couples to have access to IVF so that they may screen embryos and not transfer those that are positive for genetic disease. Finally, Italy should make clear that Italian scientists may use ES cells derived in other countries and that Italian physicians may treat patients in Italy with ES cell therapies derived and developed in other countries.

**References**


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