for Panacea Biotec by UNICEF [Internet]. New Delhi: Panacea Biotec; 2009 Aug 19 [cited 2011 Mar 13]. Available from : http://www.panacea-biotec.com/press_releases/PR19082009.pdf
16. Universal Hepatitis B vaccination. In: National Coordination Committee, Jan Swasthya Abhiyan. *New technologies in public health - who pays and who benefits?* JSA; 2007 Jan; 41- 57.
17. [No authors listed]. Hepatitis B vaccines. *Wkly Epidemiol Rec.* 2009 Oct 1 84(40): 405-19.
18. Ghendon Y. WHO strategy for the global elimination of new cases of hepatitis B. *Vaccine*, 1990 Mar; 8 Suppl: S 129-33.
19. Puliyel JM, Rastogi P, Mathew JL. Hepatitis B in India: systematic review & report of the 'IMA sub-committee on immunization'. *Indian J Med Res.* 2008 May; 127: 494-7.
20. Batham A, Narula D, Toteja T, Sreenivas V, Puliyel JM. Systematic review and meta-analysis of prevalence of hepatitis B in India. *Indian Pediatr.* 2007 Sep; 44(9): 663-75.
21. Thyagarajan SP,.Jayaram S, Mohanvalli B. Prevalence of HBV in the general population of India. In: Sarin SK, Singhal AK, editors. *Hepatitis B in India*. New Delhi: CBS Publishers & Distributors; 1996. p. 9.
22. Muraskin W. The Global Alliance for Vaccines and Immunization: is it a new model for effective public-private cooperation in international public health? *Am J Public Health*. 2004 Nov; 94 (11): 1922-5.
23. Minz S, Balraj V, Lalitha MK, Murali N, Cherian T, Manoharan G, Kadirvan S, Joseph A, Steinhoff MC. Incidence of *Haemophilus influenzae* type b meningitis in India. *Indian J Med Res*. 2008 Jul; 128: 57-64.
24. Gupta Neeraj, Puliyel Jacob. WHO study suggests low incidence of Hib in india is due to natural immunity. *Indian J Med Res*. 2009 Feb; 129(2): 205.
25. Invasive Bacterial Infections Surveillance (IBIS) Group of the International Clinical Epidemiology Network. Are *Haemophilus influenzae* infections a significant problem in India? A prospective study and review. *Clin Infect Dis.* 2002; 34 : 949-57.
26. Puliyel JM, Agarwal KS, Abass FA. Natural immunity to Haemophilus influenzae in infancy in Indian children. *Vaccine*. 2001 Sep 14; 19: 4592-4.
27. Ramamurty N, Murugan S, Raja D, Elango V, Mohana, Dhanagaran D. Serosurvey of rubella in five blocks of Tamil Nadu. *Indian J Med Res*. 2006 Jan; 123: 51-54.
28. [No authors listed]. Rubella vaccines: WHO position paper. *Wkly Epidemiol Rec.*. 2000; 75(20): 161-72
29. Yadav S, Wadhwa V, Chakravarti A. Prevalence of rubella antibody in school going girls. *Indian Pediatr.* 2001 Mar; 38(3): 280-3.
30. Yadav S, Thukral R, Chakravarti A. Comparative evaluation of measles, mumps & rubella vaccine at 9 & 15 months of age. *Indian J Med Res.* 2003 Nov; 118: 183-6.
31. [No authors listed]. Pneumococcal conjugate vaccine for childhood immunization - WHO position paper. Wkly Epidemiol Rec. 2007 Mar 23; 82(12): 93-104.
32. Chowdhary S, Puliyel J. Incidence of pneumonia is not reduced by pneumococcal conjugate vaccine. *Bull World Health Organ*. 2008 Oct; 86(10): A.
33. Dabade G, Khan AB, Pawar SL (Drug Action Forum-Karnataka). Profit making vaccine companies and WHO - open letter.. All India Drug Action Network [Internet]. 2008 Sep 2 [cited 2011 Mar 13]. Available from: http://aidanindia.wordpress.com/2008/09/15/vaccine-companies-and-who/

Living unrelated kidney donors: ethical aspects of living kidney donation in Brazil

GUSTAVO FERNANDES FERREIRA [1], CLARISSA DINIZ GUEDES [2]

[1] Transplant Renal Unit, Medical School University of Sao Paulo BRAZIL e-mail: gustavofferreira@gmail.com [2] School of Law University of Sao Paulo BRAZIL Rua Doutor Jose Bastista de Oliveira 321 Ap 801, CEP:36021-680 Juiz de Fora - MG- BRAZIL e-mail: clarissadinizguedes@gmail.com

Abstract

Brazil has established the largest public kidney transplantation system in the world.46.2% of transplants in 2008 came from living donors. The vast majority of these involved relatives of the recipient; less than 8% came from unrelated donors. In 2008, Brazil's health minister proposed banning unrelated donors in kidney transplantation. A large number of the over 35,000 Brazilians on the waiting list for a kidney would be denied a transplant without the use of unrelated donors. Brazilian culture has a unique feature, the "informal family", that is not legally recognised as a "family entity and is bound by affection rather than genetic or legal ties. It is vital that Brazil establishes a regulated, standardised, and ethical system of organ procurement; creates awareness about transplantation in physicians and the public; upgrades facilities and standardises medical care, and enforces legislation for transplantation. However, outlawing the use of unrelated donors would result in injustice for many patients who seek kidneys.

Introduction

Brazil, which occupies nearly half the land area of South America, is the fifth most populous country in the world. The last census in 2007 revealed a population of 189,987,291. Brazil's current constitution defines it as a federal republic. The country also boasts the world's tenth largest economy at market exchange rates. Economic reforms have given the country new international influence. Brazil is a founding member of the United Nations and the Union of South American Nations. It is a predominantly Roman Catholic, Portuguese-speaking, and multiethnic society.

Of course, Brazil has had some struggles as well. The country is grappling with substantial problems characteristic of the developing world, including enduring poverty, urban violence and widespread social inequity. Brazil has among the highest income inequality discrepancies and poverty rates in the world, although these values are declining. In March 2002, 18.5 million Brazilians were living in poverty. In June 2009, this number had dropped to 14.4 million. The Gini Index, which

measures the degree of inequality in the distribution of family income in a country, placed Brazil in the tenth worst position in the world in 2005.

The history of kidney transplantation in Brazil began in 1965, when the first related living donor transplant took place in Sao Paulo (1); one year later, the first deceased donor kidney transplant took place in Ribeirao Preto. Since then, Brazil has established a public programme and now has the largest public kidney transplantation system in the world (2).

Brazilian kidney transplantation in numbers

In 2008, the number of kidney transplants reached a historically high number of 3,780, the second highest in the world. However, when we divide this number by the nation's population (20.5 per million), the value is frustratingly low compared to those in the developed countries. An estimated 35,000 Brazilians are on the waiting list for a kidney transplant (3).

The world's largest kidney transplantation centre is located in Brazil (3). In 2008, 136 renal transplant centres were active in Brazil, although 229 were registered with the Ministry of Health. The majority of these centres are located in the south and south-eastern parts of the country.

Living kidney donors in Brazil were responsible for 46.2% of kidney donations in 2008 (4). The vast majority of living kidney transplants involved relatives of the recipients, less than 8% came from unrelated donors. In 2008, the number of deceased donors per million population - 7.2 per million - was very low (3).

Further, there is no active programme, in Brazil, on live kidney donation from what are currently termed non-directed donors or altruistic donors. These include live-donor paired exchange programmes (exchanges involving two donors who are incompatible with their intended recipients so that each donates to a compatible recipient) and live-donor/deceased-donor exchange programmes. In the latter, one donor who is incompatible with his intended recipient donates his organ to the highest ranking appropriate individual on the centre list, while the incompatible recipient for whom the donor kidney was originally intended receives the right of first refusal for the next ABO identical or O-type deceased-donor kidney available. These programmes have resulted in an increase in the number of living donors in the United States (5).

The Brazilian legislation

1997's Rule 9.434, Article Nine of the Federal Legislation states, "Individuals are legally able to dispose of free tissues, organs and body parts, for therapeutic purposes or for transplantation to a spouse or blood relatives within the fourth degree, inclusive, pursuant to § 4 of this article, or any other person, by judicial authorization..." Based on the words "or any other person, by judicial authorization", some centres perform living kidney transplants from unrelated donors.

In 2008, Brazil's health minister placed before the legislature an ordinance under public consultation from the Technical Regulation of the National Transplantation System, approved by Ordinance 3.407/GM of 1998, regarding the need to upgrade, improve and standardise the operation of the National Transplant System in Brazil. The text included the following statement: "We will only accept living unrelated donors for recipients whose time on the waiting list has been more than 1,350 days..."

Why outlaw unrelated donors in Brazil?

It is abundantly clear that the Brazilian government is opposed to any type of transplant commercialism. In a country with high income inequality, this could raise significant ethical issues. Transplant commercialisation would only introduce larger disparities into the population. This is very different from a country like Sweden, where there is very little income disparity and the literacy rate is above 99%.

On the other hand, outlawing unrelated donation could be devastating for the over 35,000 patients who are on the waiting list for a kidney, and others who were never on the list because they already have identified unrelated donors. Keeping patients on dialysis for approximately four years while on the waiting list and then assigning an unrelated donor for transplantation could also result in poor prognoses for recipients. The medical literature shows that increased time on dialysis is associated with lower quality in resulting grafts and diminished patient survival (6-8).

The adjusted 5-yr allograft survival for an unrelated kidney transplant is no different from the survival achieved with the transplantation of a kidney from a parent or child of the recipient or from a 50% identical sibling (9). Moreover, a kidney transplant from haploidentical parents or siblings has outcomes similar to those from a human leukocyte antigen (HLA)-mismatched spouse or friend (10).

The life spans of kidney donors are similar to those of persons who have not donated a kidney (11). The risk of end-stage renal disease does not appear to be increased among donors, and their current health seems to be similar to that of the general population. In addition, the donors' quality of life appears to be excellent (12).

The poorly served population

A large number of Brazilians would be poorly served without the use of unrelated donors. In the past few decades, Brazilian culture has developed a unique feature, the "informal family". Informal families are not legally recognised "constitutionalised family entities". The patriarchal family, upon which much of Brazil's civil legislation was modeled in the 20th century, is in crisis. Affection, rather than genetic bonds, has come to characterise many families in the country (13).

Gay people would be poorly served because, in Brazil, federal law and the constitution do not recognise same-sex couples as spouses, due to the definition of marriage as being between a man and a woman.

Foster children with no ties to natural or adoptive family in Brazil are often from the lower social strata and may be raised by neighbours or others without legal recognition.

Unrelated individuals who live together permanently but are not wedded have generally decided to live with one another based on affection and mutual help, rather than for sexual or economic purposes.

A concubine union, in which there are impediments to an individual marrying one or more partners, is another example of an informal family that would be poorly served without the use of unrelated donors.

Conclusion

It is vital that Brazil establishes a regulated, standardised, and ethical system of organ procurement, creates awareness of transplantation in physicians and the public, upgrades facilities and standardises medical care, and enforces legislation for transplantation. On the other hand, outlawing the use of unrelated donors would introduce greater inequity for many patients who seek kidneys.

The aphorism *"primum non nocere"* (first do no harm) was introduced to guide physicians in making difficult and potentially hazardous decisions; it should always be kept in mind when dealing with live kidney donors. Offering information to potential donors is a key point in the decision-making process, along with giving individuals the liberty to decide, on the basis of this information, what is best for them. Whether the individual is related or unrelated to the recipient makes no difference to the level of potential harm to the donor. If the medical literature establishes greater risks associated with being a live kidney donor, living kidney donation should be discontinued.

The first article of the Universal Declaration of Human Rights says, "All human beings are born free and equal in dignity and rights. They are endowed with reason and conscience and should act towards one another in a spirit of brotherhood." Adopted by the United Nations General Assembly in Paris in 1948, the statement captures the spirit of what should be acceptable in organ donation. We should never alter this principle or discriminate between donors based on their family relationships. A physician has the duty to avoid harm. We should always think of the donor as a person who could benefit someone, and, as such, should offer pertinent information and the autonomy to make a decision about one's body.

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References

1. Freire JG, Sabbaga E, Cabral AD, Verginelli G, de Góes GM, Ianhez LE. Renal homotransplantation. Analysis of the first 15 cases in the University of São Paulo. *AMB Rev Assoc Med Bras.* 1968; 14: 133-8. Portuguese.
2. Zatz R, Romao JE Jr, Noronha IL. Nephrology in Latin America, with special emphasis on Brazil. *Kidney Int Suppl.* 2003 Feb;83: S131-4
3. Medina-Pestana JO. Organization of a high-volume kidney transplant program--the "assembly line" approach. *Transplantation* 2006 Jun 15; 81(11):1510-20.
4. Brazilian Organ Transplant Registry 2008. http://www.abto.com.br
5. Delmonico FL. Exchanging kidneys--advances in living-donor transplantation. *N Engl J Med* 2004 Apr 29; 350(18): 1812-4.
6. Kasiske BL, Snyder JJ, Matas AJ, Ellison MD, Gill JS, Kausz AT. Preemptive kidney transplantation: the advantage and the advantaged. *J Am Soc Nephrol*. 2002; 13: 1358-64.
7. Davis CL, Delmonico FL. Living-donor kidney transplantation: a review of the current practices for the live donor. *J Am Soc Nephrol*. 2005 Jul;16(7): 2098-110.
8. Mange KC, Joffe MM, Feldman HI. Effect of the use or nonuse of long-term dialysis on the subsequent survival of renal transplants from living donors. *N Engl J Med.* 2001 Mar 8; 344(10): 726-31.
9. Ahmad N, Ahmed K, Khan MS, Calder F, Mamode N, Taylor J, Koffman G. Living-unrelated donor renal transplantation: an alternative to living-related donor transplantation? *Ann R Coll Surg Engl* 2008; 90: 247-50.
10. Terasaki PI, Cecka JM, Gjertson DW, Takemoto S. High survival rates of kidney transplants from spousal and living unrelated donors. *N Engl J Med* 1995 Aug 10; 333(6): 333-6.
11. Segev DL, Muzaale AD, Caffo BS, Mehta SH, Singer AL, Taranto SE, McBride MA, Montgomery RA. Perioperative mortality and long-term survival following live kidney donation. *JAMA* 2010 Mar 10; 303(10): 959-66.
12. Ibrahim HN, Foley R, Tan L, Rogers T, Bailey RF, Guo H, Gross CR, Matas AJ. Long-term consequences of kidney donation. *N Engl J Med*. 2009 Jan 29;360(5): 459-69.
13. Lôbo PLN. A repersonalização das relações de família [Repersonalisation from family relationships][Internet]. [cited 2011 Mar 16]. Available from: http://jus.uol.com.br/revista/texto/5201/a-repersonalizacao-das-relacoes-de-familia. Portuguese